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Roxadustat for the Treatment of Anemia in CKD Patients Not on Dialysis (NDD): A Phase 3, Randomized, Open-Label, Active-Controlled Study

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Background: Roxadustat is an orally administered hypoxia-inducible factor prolyl hydroxylase inhibitor to treat anemia in adult CKD patients (pts). Efficacy and safety of roxadustat versus darbepoetin alfa (DA) were assessed in NDD CKD pts in a randomized, open-label, controlled phase 3 study.

Methods: NDD CKD pts with anemia were randomized to roxadustat or DA for up to 2 years. Dose adjustments were permitted to correct and maintain hemoglobin (Hb) within 10–12 g/dL. The primary endpoint was Hb response, defined as Hb ≥11.0 g/dL and an increase of ≥2.0 g/dL with BL Hb >8.0 g/dL, during the first 24 weeks of treatment without rescue therapy. Noninferiority of roxadustat to DA was declared if the lower bound of the two-sided 95% confidence interval (CI) for the difference (roxadustat – DA) in proportion of responders was >0.15. Key secondary endpoints included change in low-density lipoprotein (LDL) cholesterol, time to first IV iron use, change in mean arterial pressure (MAP), and occurrence of hypertension. Treatment-emergent adverse events (TEAEs) were assessed.

Results: Of 616 randomized pts (roxadustat, 323; DA, 293), 424 completed 2 years of treatment (roxadustat, 215; DA, 209). Mean BL Hb was 9.55 g/dL in both groups. In the per protocol set, the proportion of pts who achieved Hb response during the first 24 weeks was 89.5% (roxadustat; n=256/286) and 78.0% (DA; n=213/273), with a difference of 11.5% (95% CI: 5.6%, 17.3%). Noninferiority of roxadustat to DA was demonstrated for MAP and time to occurrence of hypertension. Superiority of roxadustat to DA was demonstrated for decreasing LDL cholesterol (p<0.001) and increasing time to first IV iron use (p=0.004). The incidence of TEAEs was comparable between roxadustat (91.6%) and DA (92.5%). Common TEAEs in both groups were end-stage renal disease, hypertension, depression, eGFR, and peripheral edema.

Conclusions: Roxadustat was noninferior to DA for Hb response during the first 24 weeks of treatment in NDD CKD pts. Safety profiles were comparable between groups.

Commercial Support - Akebia Therapeutics, Inc.
**Results:** In the NDD population, 4270 patients were randomized (roxadustat=2386, placebo=1884), corresponding to 3870.7 and 2323.2 patient-exposure years (PEY), respectively. Neoplasm-related AE rates were 2.5/100 PEY in both the roxadustat and placebo groups. Neoplasm-related SAE rates were 1.1/100 PEY and 1.3/100 PEY in the roxadustat and placebo groups. In the DD population, 3880 patients were randomized (roxadustat=1940, epoetin alfa=1940), corresponding to 3315.3 and 3743.6 PEY, respectively. Neoplasm-related AE rates were 2.7/100 PEY and 2.3/100 PEY in the roxadustat and epoetin alfa groups. Neoplasm-related SAE rates were 1.1/100 PEY and 1.2/100 PEY. In both the NDD- and DD-CKD populations, there were no between-treatment-group differences in neoplasm-related AE and SAE rates in the roxadustat phase 3 clinical trials.

**Conclusions:** There were no clinically meaningful between-treatment-group differences in neoplasm-related AE and SAE rates in the roxadustat clinical trials.

**Funding:** Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

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**TH-OR05**

Roxadustat Treatment Results in Consistent Improvements in Hemoglobin (Hb) vs. Placebo: An Analysis of Three Multinational Randomized Clinical Trials in Patients with Non-Dialysis-Dependent CKD (NDD-CKD)

**Background:** Roxadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor that increases endogenous erythropoietin and enhances iron utilization. To evaluate the consistency of Hb increases across studies and global geographic regions, we analyzed data from three pivotal Phase 3 trials of roxadustat in patients with anemia and NDD-CKD.

**Methods:** While based on the same trial design, the studies were performed by different investigators and companies in differing global regions. Patients with baseline Hb <10 g/dL and eGFR <60 mL/min/1.73 m² not on dialysis were randomized to roxadustat or placebo (pbo) in the OLYMPUS (North and South America, Asia-Pacific, and Europe; N=2781, 1:1 ratio to pbo), ALPS (South America, Europe, and South Africa; N=597, 2:1 ratio to pbo), and ANDUS (North and South America, Asia-Pacific, and Australasia; N=922, 2:1 ratio to pbo) double-blind randomized controlled trials (RCTs). Oral iron was administered unrestricted; intravenous (IV) iron was limited to rescue therapy with roxadustat. Mean changes from baseline in Hb, hepcidin, and iron parameters were evaluated. Pooled results are reported.

**Results:** Significant (P<0.001) and consistent improvements in Hb were observed with roxadustat vs pbo across all studies (Figure) and were maintained over time. IV iron rescue therapy use was lower with roxadustat vs pbo (Figure). Overall safety of roxadustat with roxadustat vs pbo across all studies (Figure) and were maintained over time. IV iron rescue therapy use was lower with roxadustat vs pbo (Figure). Overall safety of roxadustat with roxadustat vs pbo across all studies (Figure) and were maintained over time.

**Conclusions:** Roxadustat consistently improved anemia in patients with NDD-CKD across the global roxadustat clinical program, in studies performed by different investigators and companies in varying global locations.

**Funding:** Commercial Support - AstraZeneca

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**TH-OR06**

Hemoglobin (Hb) Correction with Roxadustat Is Associated with Improved Iron Homeostasis in Patients with Dialysis-Dependent CKD (DD-CKD)

**Background:** In the setting of chronic kidney disease (CKD), both decreasing enteral phosphate absorption and improving iron status could lower pathologically elevated FGF23 levels and indirectly improve kidney function. In a murine model of CKD, we assessed how FC (and iron status in general) affects FGF23 levels and kidney function.

**Methods:** Five-week-old Col6a2 knockout mice were placed on five-week diets containing low iron (4 ppm), standard iron (48 ppm), or standard iron supplemented with FC (48 ppm + 1% FC) (n = 15-20 mice per group). Mice were euthanized at ten weeks of age.

**Results:** Compared to the standard iron diet group, the mice on low iron diets developed iron deficiency anemia (lower liver iron, lower hemoglobin, lower mean corpuscular volume, and higher red cell distribution width); markedly worsened kidney function (higher serum urea nitrogen, creatinine, and phosphate); and markedly higher FGF23 levels (increased bone and marrow Fgf23 mRNA expression, and approximately ten-fold higher plasma intact FGF23 concentrations) (Figure). Conversely, compared to the standard iron diet group, the mice treated with FC had similar hemoglobin (with increases in liver and serum iron not reaching statistical significance), but decreased serum phosphate; decreased marrow Fgf23 mRNA expression; approximately ten-fold lower plasma intact FGF23 concentrations; decreased systemic inflammation; and markedly improved kidney function (decreased serum urea nitrogen, serum creatinine, urine albumin-to-creatinine ratio, and expression of renal fibrosis markers, along with increased kidney Klotho mRNA expression (Figure)).

**Conclusions:** In the setting of CKD, iron deficiency anemia is associated with markedly increased FGF23 levels and worsened kidney function. In this CKD model, compared to either iron-deficient or standard iron conditions, FC decreased serum phosphate, markedly decreased intact FGF23, and dramatically improved kidney function. These data support further human studies of how FC affects CKD progression.

**Funding:** Commercial Support - Akemia Therapeutics, Inc.
TH-OR08
Regional Variation of Erythropoietin-Stimulating Agent Hyporesponsiveness in the Global Dopadistol Dialysis Study (ASCEND-D)
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Background: Hyporesponsiveness to erythropoiesis-stimulating agents (ESA) is present in 10%–15% of the prevalent dialysis population. We explored baseline characteristics and predictors of ESA hyporesponsiveness in a global randomized cardiovascular outcomes study comparing an investigational hypoixa-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), dopadistol, with conventional ESA treatment.

Methods: ASCEND-D (NCT02879305) recruited 2964 prevalent dialysis patients receiving ESA treatment randomized to weekly intravenous (IV) epoetin or who were iron replete at baseline. Primary ESA hyporesponsiveness definition: ESA Resistance Index (ERI, ESA Units/kg/week/hemoglobin g/L) ≥ 2 or IV ESA equivalent dose ≤ 450 Units/kg/week. Predictors of ESA hyporesponsiveness were determined using a multivariable regression model. Alternate hyporesponder definitions were explored.

Results: Using the primary defined population, 342 (12%) patients were ESA hyporesponsive. Selected baseline characteristics in the overall population and by ESA responsiveness, along with the results from the multivariable analysis, are shown below. Additional predictors of ESA hyporesponsiveness include a history of heart failure (0.013), dialysis vintage (0.033), smoking status (0.046), aspirin use (0.039), and ACEI/ARB use (0.061).

Conclusions: This is the first global HIF-PHI study to report pre-defined predictions and predictors of ESA hyporesponsiveness. While most of the strong predictors identified in our study have been previously reported, geographic region stands out as an unexpected finding that requires further investigation.

Funding: Commercial Support - GlaxoSmithKline

TH-OR09
Adverse Event Rates Are Higher Post-Transfusion vs. Overall Follow-Up and Independent of Background Anemia Treatment in Patients with CKD
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Background: The use of transfusion can treat anemia in the short term but may increase the risk of adverse events. Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) that stimulates erythropoiesis and improves iron metabolism. Roxadustat has been shown to decrease the need for transfusions in patients with chronic kidney disease (CKD).

Methods: Data were pooled from three pivotal, phase 3 studies of roxadustat vs. placebo in patients with non-dialysis-dependent (NDD-CKD) and three pivotal phase 3 studies of roxadustat vs. epoetin alfa in patients with dialysis-dependent (DD) CKD. We evaluated rates of intravascular volume-related adverse events (AEs; reported from a predefined list [heart failure, pulmonary edema, respiratory failure]) as a direct cause of excess intravascular volume or as a potential symptom) and treatment-emergent adverse events (TEAEs) during the 14-day post-transfusion period and the overall follow-up period (last dose + 28 days) in patients who had a transfusion.

Results: Intravascular volume-related AE and TEAE rates were at least 9-fold higher during the 14-day post-transfusion period vs. the overall follow-up period across all subgroups (Table). Trends in overall TEAE rates were similar across treatment groups.

Conclusions: Intravascular volume-related AEs occurred at higher rates post-transfusion across all populations. The reduction in transfusions for patients taking roxadustat could lower patient risk and healthcare resource use in managing CKD-related anemia.

Funding: Commercial Support - Fibrogen, Inc; AstraZeneca plc; Astellas Pharma Inc.

TH-OR10
A Real-World Longitudinal Analysis of Anemia Treatment Prescriptions in Non-Dialysis-Dependent CKD Patients, a CKDopps Study
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Background: Previously lacking in the literature, this analysis aims to comprehensively describe longitudinal patterns of anemia management, including prescriptions of ESA and iron replacement, for non-dialysis dependent chronic kidney disease (NDD-CKD) stage 3 to 5 patients under nephrologist care.

Methods: We analyzed data from a prospective cohort of 2455 NDD-CKD patients from Brazil, Germany and the US, who were not using anemia medications (oral iron, intravenous [IV] iron, or erythropoiesis stimulating agent [ESA]) at enrollment in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps). We reported the cumulative incidence function (CIF) [HK1] of anemia treatment initiation, stratified by patient characteristics. For patients that started therapy, we report the frequency of medication type at the moment of initiation, as well as switches and discontinuation over 12 months.

Results: The CIF of any anemia treatment initiation at 12 months was 54% for patients with Hb <10 g/dL. For oral iron therapy, the CIF at 12 months was 26% (19%, 32%) for TSAT=20%, and 22% (17%, 28%) for ferritin <100. For IV iron use, CIF at 12 months was 6% (3%, 11%) for patients with TSAT<20% and 4% (2%, 7%) for patients with ferritin<100mg/mL. For ESA use, the CIF at 12 months was 38% (29%, 47%) for patients with Hb <10 g/dL, and 11% (8%, 14%) for Hb 10 to <12 g/dL. Medication types at initiation and longitudinal treatment patterns (switches and discontinuation) are shown in the figure.

Conclusions: In a period of 12 months, anemia medication is initiated in a limited number of NDD-CKD patients with clinical signs that would indicate to do so. This longitudinal analysis using data from the real-world setting, call attention to a sub-optimally management of anemia in the NDD CKD setting.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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Results: Deletion of Hif1α delayed progression of CKD, as CPD mice showed reduced rate of bone loss of BUN-corrected age-matched Col4a3KO mice (p<0.05). CPD mice also showed lower Fgf23 levels (80% vs. Col4a3KO) and we obtained similar results in Col4a5KO mice administered with a HIF inhibitor (-30% FGF23, -30% BUN, vs. Ctrl. Col4a5KO). CPD mice also improved trabecular and cortical bone parameters (-50% trabecular bone volume, -20% cortical porosity vs. Col4a3KO). Finally, deletion of Hif1α increased alkaline phosphatase (ALP) positive colonies and mineral deposits in Hif1αKO cultures compared to Ctrl cells, and led to a 30% reduction in Fgf23 expression.

Conclusions: Our data suggest that osseous Hif1α stimulates Fgf23 production in CKD and is a negative regulator of osteoblast differentiation and function. Thus, inhibition of Hif1α in bone might represent a novel therapeutic strategy to improve bone and mineral outcomes in CKD.

Funding: NIDDK Support

TH-OR13
Deletion of the Sodium-Hydrogen Exchanger Isoform 6 in Mice Is Associated with an Age-Dependent Loss of Bone Volume
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Background: The sodium/hydrogen exchanger isoform 6 (NHE6) localizes to recycling endosomes, where it mediates endosomal alkalization through K+/H+ exchange. NHE6 function in the endosome is essential for clathrin-mediated endocytosis, recycling of ligand and endosomal signaling. Mutations in the SLC9A6 gene encoding the NHE6 isoform cause severe X-linked mental retardation, epilepsy, autism and corticobasal degeneration in humans. Patients with SLC9A6 mutations exhibit skeletal malformations, and a previous study suggested a role of NHE6 in osteoblast-mediated mineralization. The goal of this study was to explore the role of NHE6 in bone homeostasis.

Methods: NHE6 expression, osteoclast differentiation and cell-mediated resorption were assessed in osteoclast precursor cells isolated from wild-type and NHE6 knock-out mice. In a next series of experiments, we used primary osteoblasts, extracted from calvariae of new-born mice, to study NHE6 expression, proliferation, and cell-mediated mineralization in vitro. To determine the impact of the in vivo findings on structural bone parameters, we performed high-resolution microcomputed tomography (µCT) studies on lumbar vertebrae of wild-type and NHE6 knock-out mice.

Results: NHE6 protein and transcript are expressed in both primary osteoclasts and osteoblasts. In two studies with osteosarcoma and osteoblasts derived from NHE6 knock-out mice demonstrated normal osteoclast differentiation and osteoblast proliferation. However, NHE6-deficient osteoblasts exhibited a repressive deficit, and the mineralization capacity was increased in osteoblasts lacking NHE6. Microcomputed tomography studies revealed a reduced bone volume at a single lumbar vertebral site (L4) but otherwise unaltered structural bone parameters in NHE6 knock-out mice compared to wild-type mice at 3 months of age. At 6 months of age, however, NHE6 knock-out mice displayed a significantly reduced bone volume and trabecular number as well as an increased trabecular space at all lumbar vertebral studied (L3-L5) compared to wild-type mice.

Conclusions: Thus, loss of NHE6 results in an age-dependent loss of bone volume in mice. The results of our in vitro studies argue against a direct bone cell-autonomous cause of the bone phenotype observed in NHE6 knock-out mice and suggest extraneous factors as likely mediators.

Funding: Government Support - Non-U.S.

TH-OR14
Circadian PTH Secretion Is Entrained by Feeding, While the Internal Circadian Parathyroid Clock Is Independent but Affected by CKD
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Background: We have previously shown that an internal molecular circadian clock operates in the parathyroid gland. We now demonstrate that the circadian clock is entrained by a 24h rhythm of PTH secretion and whether it is impacted by feeding or CKD is unknown.

Methods: Rats were kept in 12h:12h light:dark cycle and fed ad libitum. Blood samples and parathyroid glands were harvested at 4h interval (N=38). Then feeding was restricted to the inactive period inverted to the parathyroid gland clock. Mice were then fed ad libitum. Blood samples and parathyroid glands were harvested at 4h interval (N=38)

Results: Circadian rhythm was found for PTH (p<0.0002), P, FGF23 (p<0.02), and urea (p<0.0001). Restricted feeding to the habitual inactive period inverted the acrophase timing of PTH (ZT9 = ZT23, P = ZT7 = ZT21), FGF23 (ZT7 to ZT4), and urea were measured. Parathyroid expression of core circadian clock genes was examined by qPCR.

Conclusions: There are several factors that can affect PTH secretion and whether it is impacted by feeding or CKD is unknown.

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significant rhythm of Per1 (p=0.02) was abolished. In CKD the best fitting period of rhythmicity was reduced to 20h as opposed to the normal 24h for Per1, Per2, Per3 and Cry2. Significant shifts in acrophase were found for Npas2, Per3 and Cry1, while amplitude of Rev-erba increased.

Conclusions: Feeding restricted to the inactive period inverted the acrophase of plasma Ca levels. We confirmed a clear dissociation between the phase of PTH secretion rhythm and the phase of the circadian clock in the parathyroid glands. In CKD the circadian rhythm of core clock genes were significantly interfered, affecting MESOR, phase, period, amplitude as well as rhythmicity.

TH-OR15


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Background: Secondary hyperparathyroidism (SHPT) is one of the common complications in patients with chronic kidney disease. The development of SHPT is accompanied by the change of cell composition, while the exact cell type changes and mechanism are yet to be defined. Therefore, single cell sequencing was conducted to analysis the cell composition of parathyroid gland.

Methods: In current study, parathyroids from 3 SHPT patients were digested to obtain single cell suspension. A total of 21519 cells were obtained and the mRNA expression profiles were analyzed by single cell sequencing and bioinformatics. Furthermore, the development separation track of cell subpopulations was constructed by pseudotime analysis (Figure 1A).

Results: There may be 21 cell subpopulations in parathyroid, among which 6 subpopulations (clusters 0, 1, 2, 5, 11, 17) are high function subpopulations of parathyroid, which were indicated by high expression of gene (such as insulin-like growth factor 2, PTH (parathyroid hormone), Calr (calcium receptor) and KL (Klotho) genes) (Figure 1B-D). The results of pseudotime analysis in the 6 high function subpopulations show that cluster 0 is at the beginning of the main group separation track, cluster 1, 2, 5 are in the middle, while cluster 11 and 17 are at the end (Figure 1E). Multiple genes may play major role in the differentiation of cluster 0, including tspan1, park4, atp6v0c, rpl11, rps8 and hem (Figure 1F).

Conclusions: There are 6 subpopulations out of total 21 cell subpopulations of parathyroid cells with higher parathyroid hormone secretion and regulation function in SHPT patients. Among which, cluster 0 may be the initiation differentiation cell of high functional cells, because it may be a subpopulation with high proliferation and differentiation potential.

Funding: Government Support - Non-U.S.

Identification and analysis of subpopulations of uremic hyperparathyroidism glands.

TH-OR16

Calcium Isotopes: A Novel Biomarker of Bone Mineralization in CKD

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Background: Serum Ca, bone biomarkers and radiographic imaging do not allow accurate evaluation of bone mineral balance (BMB), a key determinant of bone mineral density (BMD) and fracture risk. Naturally occurring stable (non-radioactive) Ca isotopes, 44Ca and 43Ca, are absorbed from our diet and sequestered into different body compartments following kinetic principles of isotope fractionation. Isotopically light 44Ca is preferentially incorporated into bone, and heavier 43Ca excreted in urine and feces. Their ratio (δ44/43Ca) in serum and urine gives a direct measure of BMB; δ44/43Ca is higher during bone formation than bone resorption.

Methods: Ca isotopes were measured by plasma-ionization mass-spectrometry in blood, urine, feces and dialysate. The relationship between bone Ca gain and loss was calculated using a compartment model, and expressed as δ44/43Ca. In 124 children 1009 years old (10 years of age) were measured, bone biomarkers, DXA and tibial peripheral quantitative CT (pQCT), an accurate measure of cortical BMD.

Results: In healthy children the δ44/43CaBone and δ44/43CaSerum were higher in adults (p=0.001), reflecting avid Ca uptake during bone formation. Since urinary Ca excretion is impaired in CKD, δ44/43CaBone was higher and δ44/43CaSerum lower in CKD4-5D compared to controls (p=0.001 for both). In CKD2-5D δ44/43CaBone was positively correlated with cholecalciferol (p=0.01) and alfacalcidol (p=0.02) doses, implying increased bone Ca uptake when Ca bioavailability is increased. δ44/43CaSerum was inversely correlated with biomarkers of bone formation (ALK, p=0.05) and inversely with resorption markers (PTH, p=0.013; TRAP5b, p=0.01 and CTX, p=0.006). δ44/43CaBone correlated positively with cortical BMD-Z-score (p=0.006, R2=0.39), and DXA hip BMD-Z-score (p=0.02). Significant and independent predictors of cortical BMD-Z-score were δ44/43CaBone (p=0.068, p=0.006) and PTH (p=0.039, p=0.04), together predicting 67% of the variability in BMD.

Conclusions: Ca isotope ratios provide a novel, non-invasive method of assessing bone mineralization. Defining an accurate biomarker of BMB forms the basis of future studies investigating Ca dynamics in disease states and the impact of treatments that affect bone homeostasis.

Funding: Government Support - Non-U.S.

Secondary Hyperparathyroidism Is Associated with Weight Loss and Longer-Term Mortality Among Patients Undergoing Hemodialysis: Results from the Dialysis Outcomes and Practice Patterns Study

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Background: Wasting is a common complication of kidney failure that leads to weight loss and poor outcomes. Recent experimental data identified parathyroid hormone (PTH) as a driver of adipose tissue browning and wasting, but little is known about the relations among secondary hyperparathyroidism (SHPT), weight loss, and risk of mortality in patients undergoing hemodialysis.

Methods: We included 42,319 participants receiving hemodialysis for at least one year in the DOPPS phases 2-6 (2002-2018). Linear mixed models were used to estimate the association between baseline PTH and percent weight change over 12 months, adjusting for country, demographics, comorbidities, and labs. Accelerated failure time models were used to assess 12-month weight loss as a mediator between baseline high PTH and mortality after 12 months.

Results: At baseline, mean (SD) body weight was 74 (22) kg and the median PTH level was 251 pg/mL (interquartile range [IQR], 131-444 pg/mL). Baseline PTH was inversely associated with 12-month weight change: 12-month weight loss >5% was observed in 21%, 18%, 18%, 17%, and 16%, and 14% of patients for PTH ≥600 pg/mL, 450-600, 300-450, 150-300, 50-150, and <50 pg/mL, respectively. In adjusted analysis, 12-month weight change compared to PTH 150-299 pg/mL was -0.60%, -0.12%, 0.10%, +0.15%, and +0.35% for PTH ≥600, 450-600, 300-450, 150-50, and <50 pg/mL, respectively (P<0.01). Interacting baseline PTH*appetite, high PTH was associated with weight loss only in persons with preserved appetite (P<0.01). During follow-up after the 12-month weight measure (median, 1.0 [IQR, 0.6-1.7] years; 6,127 deaths), patients with baseline PTH ≥600 pg/mL had 11% (95% CI, 9-13%) shorter lifespan, and 18% (95% CI,14-23%) of this effect was mediated through weight loss a 2.5%.

Conclusions: Our findings indicate that SHPT may be a novel mechanism of wasting in dialysis patients, corroborating experimental data, and that this pathway may be a mediator when elevated PTH levels and mortality. Future research should examine whether PTH-lowering therapy can limit or prevent weight loss and improve longer-term dialysis outcomes.

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TH-OR18

SNF472 Consistently Slows Progression of Coronary Artery Calcification Across Subgroups of Patients on Hemodialysis

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Background: In the CalLPSO study, SNF472 significantly attenuated progression of coronary artery calcium (CAC) volume score compared with placebo. This pre-specified analysis examined CAC progression in key subgroups.

Methods: Patients were randomized to SNF472 300 mg (n=92), SNF472 600 mg (n=91) or placebo (n=91) infused 3x/week during hemodialysis (HD) for 52 weeks on standard care therapy determined by each investigator. We examined change in log CAC volume score from baseline to week 52 in the combined SNF472 dose groups vs placebo for subgroups of age, sex, diabetes, dialysis vintage, arteriosclerotic cardiovascular disease (ASCVD), use of non-Ca phosphate binders, Ca-based phosphate binders, calcimimetics, activated vitamin D, warfarin, or statins in the modified ITT population (mITT, defined as subjects who received at least one dose of study drug and had an evaluable post-baseline CT scan).

Results: Baseline characteristics were similar across treatment groups: mean age was 64 y, 39% were female, 62% had diabetes, and 41% had prior ASCVD. Median HD vintage was 42 mo; 33% received HD for ≥5 years. Concomitant medications at baseline were: 62% non-Ca phosphate binders, 28% Ca-based phosphate binders, 31% calcimimetics, 51% activated vitamin D, 8% warfarin, and 64% statins. In the overall mITT, CAC progression volume was 11% in the combined SNF472 groups vs 20% in placebo (p=0.016). Treatment differences for CAC volume progression were similar across subgroups (Figure). All interaction p-values were non-significant and comparisons favored SNF472 vs placebo in each subgroup.

Conclusions: SNF472 treatment for 52 weeks attenuated CAC progression compared with placebo in all subgroups.

Funding: Commercial Support - Sanifit

TH-OR19

Pharmacodynamic (PD) Profiling of Reloxaliase in Patients with Severe Hyperoxaluria

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Background: Hyperoxaluria is a major risk factor for kidney stones and can lead to chronic kidney disease (CKD). With decreasing kidney function, plasma oxalate (POx) rises and oxalate may deposit in the kidneys and other tissues (systemic oxalosis) leading to ESRD. Reloxaliase (REL), a non-absorbed, oxalate specific oral enzyme therapy designed to degrade oxalate along the GI tract, may potentially reduce the systemic and renal oxalate burden in patients with enteric and primary hyperoxaluria (EH and PH). This study tested the PD of REL, and addressed questions regarding potential systemic accumulation (by-product of oxalate degradation) and systemic absorption of oxalate decarboxylase (OxDc, the active component of REL).

Methods: This 12-week, open label study enrolled subjects with EH, CKD and hyperoxalemia (UOx ≥40 μg/dL, eGFR <55 mL/min and POx>5μmol/L, n=10) and PH (UOx ≥40 μg/dL, n=5) who received 7,500u of REL 5x/day with meals/snacks. Parameters assessed at baseline, and weeks 4, 8 and 12 included POx and UOx (only if eGFR >15 mL/min), plasma formic acid (pre- and post-prandial/post-dose; Q' Solutions) and OxDc (specific ELISA, Absorption Systems).

Results: Reported adverse events (AEs) were mostly GI related; there were no related serious AEs. In EH, both POx and UOx decreased substantially; in PH, UOx did not change, and POx stayed normal at baseline and during treatment (Table). There was no systemic accumulation, as all samples were below or within normal range (1-9 mg/L). Similarly, there was no detectable absorption of REL, as all samples were below the limit of detection of the assay for OxDc (<0.0001% of the administered dose of 37,500 u/day).

Conclusions: Reloxaliase was well tolerated; the absence of formate accumulation further supports its safety. The lack of REL absorption, in addition to supporting low potential for systemic toxicity, confirms its site of action within the GI tract. This best aligns with the pathophysiology of EH as evidenced by the substantial reduction in both POx and UOx in EH subjects with CKD/ESRD.

Funding: Commercial Support - Allena Pharmaceuticals

TH-OR20

Efficacy and Safety of Upacicalcet in Hemodialysis Patients with Secondary Hyperparathyroidism: A Phase 3 Study

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Background: Secondary hyperparathyroidism (SHPT) is a major complication of hemodialysis (HD) patients. Calcimimetics suppress the hyperfunction of parathyroid and reduce serum calcium and phosphorus levels, and are currently used for the treatment of SHPT. Upacicalcet (UPA) is a novel intravenous small molecule calcimimetic in late stage development in Japan to treat SHPT of HD patients. We report the efficacy and safety of UPA in HD patients.

Methods: This study was a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. UPA or placebo (PBO) was administered i.w. at the end of HD at an initial dose of 50 mcg or 25 mcg. The doses were subsequently adjusted to maintain serum intact PTH (iPTH) levels between 60-240 pg/ml (recommended level of Japanese guideline) every 3 weeks between 25 and 300 mcg during 24 weeks of treatment. The primary endpoint was the proportion of patients who achieved a mean iPTH level of 60-240 pg/ml in weeks 22 to 24.

Results: A total of 154 SHPT patients were enrolled, and randomly allocated to UPA group (n: 103) or PBO group (n: 51). The primary endpoint, percentage of patients achieving the target iPTH range was greater for UPA (67.0%) than for PBO (8.0%) (P<0.001). UPA significantly reduced iPTH and cCa levels compared with PBO (Fig.). Concerning phosphorus, no statistically significant difference between the groups was observed while it tended to decrease in the UPA group. In the safety assessment, treatment emergent adverse events (AE) occurred in 88 patients (85.4%) and 36 patients (72.0%) in the UPA and the PBO groups. The incidences of upper-gastrointestinal-related AE were 20.4% in the UPA and 18.0% in the PBO groups (P=0.8298). As an AE, hypocalcemia did not occur in either group.

Conclusions: This study demonstrates that UPA significantly decreases iPTH without increasing the incidence of upper-gastrointestinal symptoms as compared to PBO. It is suggested that UPA will be a promising calcimimetic agent capable of safe and appropriate management of SHPT.

Funding: Commercial Support - Sanwa Kagaku Kenkyusho Co., Ltd.
Background: The primary cilium is an organelle found on essentially all epithelial cells. Similarly, the glyocalyx is a matrix-like layer of proteoglycans, glycosaminoglycans (GAGs) and proteins covering the surface of all cells. In vascular endothelial cells, primary cilia and GAGs such as heparan sulfate and chondroitin sulfate mediate responses to the mechanical forces exerted by blood flow. In thick ascending limbs, increases in luminal flow enhance nitric oxide (NO) production, an important regulator of the kidney function including sodium reabsorption; however, the role of primary cilia and the glyocalyx in NO production by thick ascending limbs is unknown. We hypothesized that primary cilia and the glyocalyx act as flow sensors and thus mediate flow-induced NO production by thick ascending limbs.

Methods: We measured flow-induced NO in isolated rat thick ascending limbs using DAF-FM. Intracellular NO was first measured during the control period without and with luminal flow. NO was measured again during the experimental period after treating tubules for 15 min to deciliate cells or to degrade major glyocalyx GAGs. Dibucaine (0.1 mM) was used to remove cilia from cells. Heparinase III (0.2 or 0.4 U/ml) and chondroitinase ABC (0.2 U/ml) were used to degrade heparan sulfate and chondroitin sulfate, respectively.

Results: In untreated control tubules, flow-induced NO did not differ between the two periods, 4.3 ± 1.03 vs 4.68 ± 0.84 arbitrary units (AU)/min. Dibucaine decreased flow-induced NO from 4.25 ± 0.62 to 1.19 ± 0.65 AU/min (p < 0.002). Heparinase (0.2 U/ml) attenuated flow-induced NO from 4.02 ± 0.84 to 1.70 ± 0.74 AU/min (p < 0.04), a higher concentration (1.0 U/ml) caused a greater effect (0.96 ± 1.36 vs 0.41 ± 0.14 AU/min; p < 0.006). Heat inactivation of heparinase (0.2 U/ml) abolished its effect (3.01 ± 0.34 vs 2.83 ± 0.22 AU/min). Chondroitinase (0.2 U/ml) decreased flow-induced NO from 4.17 ± 0.96 to 2.45 ± 0.49 AU/min (p < 0.038).

Conclusions: We conclude that both primary cilia and the glyocalyx act as flow sensors in thick ascending limbs and transduce mechanical stimuli into chemical signals that ultimately result in NO production by this segment.

Funding: Other NIH Support - NHLBI

TH-OR22

Cell-Autonomous Expression of Membrane Transport Proteins in Mammalian Distal Nephron


Background: Reabsorption of NaCl in kidney thick ascending limb (TAL) via NKCC2 involves the action of luminal (ROMK) and basolateral (Kır4.1/Kir5.1) multionis, potassium channels, a basolateral calcium sensing receptor (CaSR), and the claudin (Cldn) family of proteins. Morphological heterogeneity of TAL cells has been reported, as well as mosaic expression of ROMK and Kir.4.1. We hypothesized that this variability between TAL cells extends to other aspects of their function.

Methods: We studied TAL EM morphology, zonal and cell-autonomous heterogeneity of the transport proteins at steady state in mice, rats and humans, and under stimulation by vasopressin (AVP; V2R agonist dDAVP for 72 h) using AVP-deficient Brattleboro rats. NKCC2, phosphorylated (p) NKCC2, ROMK, Kir4.1, CaSR, Cldn-10 and Cldn-16 signals were induced by immunofluorescence, in situ hybridisation (ISH), EM and Western blot (WB).

Results: Between cortex and medullary kidney zones, TAL morphological cell heterogeneity was observed, but not at a cell-to-cell level within each zone. NKCC2 was continuously expressed in all TAL cells, while pNKCC2 signals were heterogeneous, increasing from inner stripe of outer medulla to cortex and varying between cells of each zone. ROMK and Kir.4.1 protein expression showed conspicuous heterogeneity in a mutually exclusive pattern, with stronger pNKCC2 expression in the ROMK-negative or Kir.1-positive cell type. CaSR and Cldn-16 signals were moderate to absent in ROMK-positive cells, but intensified in ROMK-negative cells, while Cldn-10 was strongly expressed only in ROMK-positive cells. ISH revealed no cell heterogeneity of ROMK mRNA. In Brattleboro rats, 72h dDAVP increased the number of ROMK- and Kir.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 ROMK mRNA. In Brattleboro rats, 72h dDAVP increased the number of ROMK- and Kir.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 ROMK mRNA.

Cldn-10 expression was induced in the outer stripe of outer medulla. Kir4.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 ROMK mRNA. In Brattleboro rats, 72h dDAVP increased the number of ROMK- and Kir.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 ROMK mRNA. In Brattleboro rats, 72h dDAVP increased the number of ROMK- and Kir.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 ROMK mRNA.

In Brattleboro rats, 72h dDAVP induced NO from 4.02 ± 0.84 to 1.54 ± 0.49 AU/min (p < 0.002). Heparinase (0.2 U/ml) attenuated flow-induced NO from 4.25 ± 0.62 to 1.19 ± 0.65 AU/min (p < 0.002). Heparinase (0.2 U/ml) attenuated flow-induced NO from 4.02 ± 0.84 to 1.70 ± 0.74 AU/min (p < 0.04), a higher concentration (1.0 U/ml) caused a greater effect (0.96 ± 1.36 vs 0.41 ± 0.14 AU/min; p < 0.006). Heat inactivation of heparinase (0.2 U/ml) abolished its effect (3.01 ± 0.34 vs 2.83 ± 0.22 AU/min). Cldn-10 (0.2 U/ml) decreased flow-induced NO from 4.17 ± 0.96 to 2.45 ± 0.49 AU/min (p < 0.038).

Conclusions: We conclude that both primary cilia and the glyocalyx act as flow sensors in thick ascending limbs and transduce mechanical stimuli into chemical signals that ultimately result in NO production by this segment.

Funding: Other NIH Support - NHLBI

TH-OR24

Positive Allosteric Modulation of the Calcium-Sensing Receptor (CaSR) by Glucose or Fructose Induces Activation of the Sodium-Chloride Cotransporter (NCC)

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Background: The abundance of the distal convoluted tubule (DCT) thiazide-sensitive sodium chloride cotransporter (NCC) is greater in females than males. Because structural remodeling of the DCT is dependent on NCC activity, it has been generally assumed that there is a corresponding sexual dimorphism in DCT morphology. Until now, this has never been directly examined. Here, combining new optical clearing techniques with structural analyses of DCT segments, volumetric imaging we quantitatively assess DCT morphology in male and female mice and study DCT remodeling response to furosemide.

Methods: Male and Female (3-month-old) mice were treated with vehicle or Furosemide administered in the food (100 mg/kg per day) for seven days. Total NCC and phospho-active NCC abundance (pNCC) was evaluated by Western Blot in one kidney, the other kidney was perfused and fixed for imaging. Kidneys were cleared using the Clear, Unobstructed Brain/Body Imaging Cocktails and Computational Analysis (CUBIC) pipeline, co-stained with antibodies that label the early DCT (DCT1, paravalbumin) and the entire DCT (DCT2 & NCC), imaged using a high-speed spinning disc confocal microscope, and processed with 3D rendering and analysis software (IMARIS).

Results: We confirmed previous studies that females have greater NCC abundance in the basal state. Surprisingly, the length of the DCT was longer in males (~620 μm) than female mice (~560 μm). Furosemide treatment significantly increased the abundance of NCC and pNCC in both sexes. Furosemide delivery to the DCT was paralleled by an increase in DCT length and volume. The remodeling response to furosemide was more profound in females (~20% increase in DCT length and 50% in DCT1 volume) than males (~8% and 30%, respectively). The DCT extension of furosemide treatment in females stemmed largely from an increase in DCT1 length. Furosemide expanded the DCT2 significantly in males but not females.

Conclusions: Our study reveals a surprising sexual dimorphism of the DCT. The greater NCC density in a shorter structure may provide a means for females to protect sodium balance. Further work to unravel the DCT remodeling response to furosemide, but have larger reserve and remodeling capacity to adapt to unique physiological stresses.

Funding: NIDDK Support, Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
first evidence of NCC activation via CaSR with cinacalcet in humans. Our results suggest that the presence of glucose or fructose in DCT could increase the activity of NCC via CaSR-WNK4-SPAK pathway.

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TH-OR25

**Cross-Talk Between Epithelial Sodium Channel and Basolateral Kir4.1/Kir5.1 Channels in the Cortical Collecting Duct**

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**Background:** The growing body of evidence suggest that inwardly rectifying K⁺ (Kir) channels located on the basolateral membrane of epithelial cells in the distal nephron play a crucial role in K⁺ handling and blood pressure control, making these channels attractive targets for the treatment of hypertension. The purpose of the present study was to determine how the inhibition of basolateral Kir4.1 homomeric or Kir4.1/Kir5.1 heteromeric K⁺ channels affects ENaC-mediated Na⁺ transport in the cortical collecting duct (CCD) principal cells.

**Methods:** Electrophysiological approaches were used to test the effect of fluoxetine, amitriptyline, and, recently developed Kir4.1 inhibitor, VU0134992, on the activity of Kir4.1, Kir4.1/Kir5.1, and ENaC. Channel activity was recorded in CHO cells transfected with respective channel subunits, cultured polarized epithelial mCCD cells, and native freshly isolated rat and human CCD tubules. To test the effect of pharmacological Kir4.1/Kir5.1 inhibition on electrolyte homeostasis in vivo, Dahl salt-sensitive rats were injected with amitriptyline (15 mg/kg/day).

**Results:** We found that inhibition of Kir 4.1/4.5, but not K⁺ 4.1 channel, substantially suppresses both amiloride-sensitive Iₘ₈ in mCCD cells and single-channel ENaC activity in principal cells of rat and human CCD tubules. Furthermore, we demonstrated that i.p. injection of Kir4.1/Kir5.1 antagonist for three days leads to a significant drop in plasma K⁺ level, triggering sodium excretion, and diuresis.

**Conclusions:** These data uncover a putative mechanism underlying a renal control of blood electrolytes mediated by Kir4.1/5.1 and introduce a new molecular target for the treatment of salt-sensitive hypertension.

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TH-OR26

**CIC-K2 Chloride Channel Determines Acid-Base Transport and Chloride Reabsorption in Intercalated Cells of the Collecting Duct**

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**Background:** Intercalated cells (ICs) of the collecting duct (CD) play a critical role in regulation of systemic acid-base homeostasis. In addition, ICs are capable of performing trans-cellular Cl⁻ reabsorption particularly during volume depletion. While the major apical membrane transport systems are well characterized, little is known about mechanisms and contribution of the basolateral membrane in both processes. Kidney specific CIC-K2 is expressed in the basolateral membrane of the distal nephron segments, including the CD.

**Methods:** We generated CIC-K2 deficient mice using Cre-loxP strategy to investigate the role of the channel in acid-base and Cl⁻ transport. We combined BCECF-sensitive intracellular pH (pH) measurements with fluorescent AQPB2-based identification of principal cells (PCs) and ICs to assess CIC-K2-dependent pH changes in different cell types.

**Results:** CIC-K2 inhibition with NPPB (100 µM) had no effect in PCs of WT mice, whereas it induced rapid intracellular acidification in B-type and alkalinization in A-type of ICs. NPPB failed to significantly affect pH in CD from CIC-K2 deficient mice. Extracellular Cl⁻ removal to drive basolateral Cl⁻ exit via CIC-K2 had no effect on pH in PCs, but caused alkalinization in B-type and acidification in A-type of ICs. Importantly, Cl⁻ removal did not induce pH changes in both A- and B-type of ICs from CIC-K2 deficient mice. This suggests that CIC-K2 mediates trans-cellular Cl⁻ reabsorption and determines apical acid-base transport by controlling intracellular Cl⁻ concentration. Moreover, application of Angiotensin II (Ang II, 500 nM) increased ClC-K2 single channel activity whereas it induced rapid intracellular acidification in B-type and alkalization in A-type of ICs. Importantly, Cl⁻ removal to drive basolateral Cl⁻ exit via ClC-K2 had no effect on pHi in different cell types.

**Conclusions:** Together, our results show that CIC-K2 is central for acid-base transport in the CD. CIC-K2 activity can be independently regulated in A- and B-type of ICs during different physiological conditions to allow fine tuning of renal acid-base handling.

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TH-OR27

**Evolutionary Conserved TLDc Domain Defines a New Class of V-ATPase Interacting Proteins**

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**Background:** Kidney-specific V-ATPase regulates acid-base homeostasis, and its dysfunction causes distal renal tubular acidosis (dRTA). We recently found that nuclear receptor coactivator 7 (Ncoa7) interacts with kidney V-ATPase, and its deletion in mice resulted in dRTA. Ncoa7 belongs to a group of proteins playing a role in the oxidative stress response, that contain the evolutionarily conserved TLDc domain. We found that another of these proteins, Oxr1, also interacts with the V-ATPase. Here we asked if other proteins from this family, i.e. Tbc1d24, Tdcl and Tdcl2 interact with V-ATPase in kidney and if their TLDc domains mediate this interaction.

**Methods:** Interaction between endogenous Tbc1d24, Tdcl and Tdcl2 and V-ATPase was assessed by co-immunoprecipitation (co-IP) and western blotting of mouse kidney lysates. Interaction with the V-ATPase was also studied by GST pull-downs from kidney lysates using purified GST-tagged wild-type TLDc domains of Ncoa7, Oxr1, Tbc1d24, Tdcl and Tdcl2, or mutant TLDc domains of Ncoa7 (G802A, G815A, S817A, G845A, G889A, L926A, E938A) followed by western blotting for B1.

**Results:** In Co-IP studies of mouse kidney lysates we found that endogenous Tbc1d24 interacted with the B1 subunit isoform of V-ATPase, but not with the more ubiquitous B2 subunit isoform. However, we did not detect any interaction between V-ATPase and endogenous Tdcl or Tdcl2 in Co-IPs, possibly due to low sensitivity of the anti-Tdcl1 and anti-Tdcl2 antibodies. Additionally, we found that the purified TLDc domains of Ncoa7, Oxr1 and Tdcl2, but not Tbc1d24 or Tdcl1, interacted with V-ATPase in GST pull-downs. Finally, the G815A, G845A and G896A mutants in evolutionarily conserved regions of the Ncoa7 TLDc domain did not interact with V-ATPase, L926A and E938A mutations resulted in a decreased interaction, while S817A or the non-conserved G802A mutation (used as a positive control), did not decrease interaction at all.

**Conclusions:** In the kidney, Tbc1d24 and possibly Tdcl2, as well as Ncoa7 and Oxr1, interacted with V-ATPase and may play a role in the V-ATPase-dependent regulation of renal acid-base homeostasis. We conclude, that the Tdcl motif is a protein-protein interaction domain that defines a new class of V-ATPase interacting regulatory proteins. The evolutionary conserved amino acids within the TLDc domain of Ncoa7 are critical for its interaction with the V-ATPase.

**Funding:** NIDDK Support

TH-OR28

**Lysine Acetylation of Aquaporin 3 Affects Water Permeability of the Collecting Duct**

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**Background:** We recently reported that there are > 400 proteins in the inner medullary collecting duct (IMCD) that are post-translationally lysine acetylated (ac), including the basolateral water channel, aquaporin-3 (AQ3). The purpose of this study was to determine if lysine acetylated AQP3 (acAQP3) affects water permeability.

**Methods:** We developed an antibody to detect acAQP3 and found acAQP3 localized to the basolateral membrane of the cortical and outer medullary CD in mice and human kidney biopsies. In mice, following 24 h of water deprivation, acAQP3 was also found in the IMCD. Next, we developed acQP3 K point mutation plasmids; an acetylated mimetic K282Q (AQP3α), and a deacetylated mimetic K282R (AQP3β). These were stably expressed in vasopressin-responsive mouse cortical CD cells and loaded with a volume sensitive dye. Finally, using CRISPR/CAS we engineered whole body point mutation mice. The AQP3α, AQP3β and lattternate controls AQP3W1/W1 were placed on standard chow and: 1) ad lib water, 2) 5% sucrose water for hydration, or 3) 24 h water deprivation and urine flow measured.

**Results:** Following osmotic stimulus, we found AQP3α cells had the highest water permeability followed by the AQP3W1/W1 cells and the AQP3β cells. From our mutant mice, as adults, control and AQP3β mice had similar urine flow on all protocols. However, the AQP3α mice produced double the urine on protocols 1 and 2. Thus, maintenance of deacetylated AQP3 enhances fluid excretion under normal and hydrated conditions. To further determine whether the increased urine flow was due to impaired water permeability, we immunolocalized AQP2 and AQP3 under ad lib conditions. AQP3α mice had enhanced expression of AQP3 in the basolateral membrane, and reduced AQP2 expression in the apical membrane. In contrast, the AQP3β mice had diffuse AQP3 localization in the CD, with no obvious change in AQP2.

**Conclusions:** Together, these preliminary data suggest that acAQP3 promotes localization to the basolateral membrane of the CD and supports the hypothesis that acAQP3 could serve as an important regulator of CD function in fluid homeostasis.

**Funding:** NIDDK Support
Role of TRPC3 in the Control of Osmosensitivity and Renal Water Handling in the Mouse Collecting Duct

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Background: Kidney is central in the control of systemic water balance of the organism. A VP facilitates aquaporin 2 (AQP2) translocation to the apical membrane and regulates AVP-dependent water excretion.

Methods: The employed techniques include simultaneous measurement of [Ca2+]i, with Fura 2 and the rate of cell swelling as a readout of the AQP2-dependent water reabsorption in freshly isolated split-opened CD of wild type and TRPC3−/− mice; immunofluorescent detection of AQP2-induced AQP2 trafficking to the apical membrane and metabolic cage balance studies.

Results: TRPC3 is a Ca2+-permeable mechano-activated channel abundantly expressed in the CD. We found that TRPC3 deletion or pharmacological inhibition precluded [Ca2+]i elevations induced hypotonicity and severely slowed the rate of cell swelling indicative of diminished water transport in the CD. TRPC3−/− and WT mice had comparable serum and urine osmolality in control conditions, but exhibited a significantly greater bodyweight loss, and urine volume excretion after 24 h of water deprivation (WD) despite higher AQP levels when compared to WT. Furthermore, osmosensitive [Ca2+]i elevations were greatly increased in CD from WT but not TRPC3−/− animals after 24 h WD. Greatly accelerated rate of cell swelling was observed in WT, while it was only modestly increased in TRPC3−/− mice under the same condition. Using immunofluorescent microscopy, we found that AQP2 translocated to the apical plasma membrane in WT, while maintaining mostly cytosolic localization in TRPC3−/− after 24 h WD, which favors a significant role of TRPC3 in osmosensitivity and regulation of AVP-dependent AQP2 trafficking in the CD. TRPC3 deletion compromises systemic water balance producing an ND-like phenotype.

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Distinct Cellular Osmoregulatory Response in the Skin of Patients with Disturbed Glycosaminoglycan Biosynthesis

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Background: Several studies have shown that during high Na+ diet (HSD) sodium content of the skin increases. Nuclear factor of activated T cells 5 (NFAT5) is a hypotonicity-induced transcription factor that is upregulated by the hypertonic conditions present in the skin. Sulfated glycosaminoglycans (GAGs) have been suggested to neutralize Na+-induced hypertonicity driven transcription factor responsive to environmental osmotic changes. Extracellular hypotonicity increases [Ca2+]i and causes cell swelling due to AQP2-driven water influx. The role of the osmosensitive [Ca2+]i signaling in renal water transport and urine concentration remains unknown.

Methods: The techniques used in this study included simultaneous measurement of [Ca2+]i dynamics with Fura 2 and the rate of cell swelling as a readout of the AQP2-dependent water reabsorption in freshly isolated split-opened CD of wild type and TRPC3−/− mice; immunofluorescent detection of AQP2-induced AQP2 trafficking to the apical membrane and metabolic cage balance studies.

Results: TRPC3 is a Ca2+-permeable mechano-activated channel abundantly expressed in the CD. We found that TRPC3 deletion or pharmacological inhibition precluded [Ca2+]i elevations induced hypotonicity and severely slowed the rate of cell swelling indicative of diminished water transport in the CD. TRPC3−/− and WT mice had comparable serum and urine osmolality in control conditions, but exhibited a significantly greater bodyweight loss, and urine volume excretion after 24 h of water deprivation (WD) despite higher AQP levels when compared to WT. Furthermore, osmosensitive [Ca2+]i elevations were greatly increased in CD from WT but not TRPC3−/− animals after 24 h WD. Greatly accelerated rate of cell swelling was observed in WT, while it was only modestly increased in TRPC3−/− mice under the same condition. Using immunofluorescent microscopy, we found that AQP2 translocated to the apical plasma membrane in WT, while maintaining mostly cytosolic localization in TRPC3−/− after 24 h WD, which favors a significant role of TRPC3 in osmosensitivity and regulation of AVP-dependent AQP2 trafficking in the CD. TRPC3 deletion compromises systemic water balance producing an ND-like phenotype.

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Risk Factors for AKI During Autologous Stem Cell Transplantation in AL Amyloidosis

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Background: Acute kidney injury (AKI) is a common complication after high dose melphalan and autologous stem cell transplantation (HDM/SCT) in AL amyloidosis patients. However, its incidence, outcome, and risk factors are not well known.

Methods: This observational study included 173 AL amyloidosis patients who underwent HDM/SCT in the Amyloidosis Center at Boston University School of Medicine. Demographic, laboratory and clinical data were prospectively collected and analyzed retrospectively. AKI was defined as an increase in serum creatinine ≥1.5 times the baseline value and occurring within the first 30 days after HDM/SCT.

Results: The median age was 57 years (range 32-77). Fifty-nine percent of patients were male. Renal and cardiac involvement were present in 65.3% and 19.7% of patients, respectively. Median eGFR was 83 mL/min/1.73m2 (range 9-213) and median proteinuria was 2.503 mg/dL (range 0-19.996). The median time from diagnosis to SCT was 4 months (range 1-100). AKI occurred in 28.3% of patients. The causes of AKI were: ATN (27.9%), pre-renal injury (26.4%), melphalan-induced AKI (12.0%), cardio renal physiology (5.8%), ATN (2.9%), contrast-induced AKI (1.5%), obstructive nephropathy (1.5%), and no clear etiology (22.0%). AKI was associated with increased overall mortality with a hazard ratio of 4.78 (95% CI, 1.9-11.9, p=0.001). The 10-year overall survival was 87.5% for patients who did not have AKI versus 56.2% who had AKI. Baseline characteristics significantly associated with AKI development were: amyloid renal involvement, renal function, proteinuria, hypoalbuminemia, IVSD, atrial fibrillation, use of midodrine or diuretics. Sepsis in the post-transplant period, IV vancomycin use, and C. difficile infection were significantly associated with AKI. In terms of hematologic factors, anemia severity, and the need for red blood cell transfusion were significantly associated with AKI. Prolonged thrombocytopenia was associated with AKI; however, delayed WBC engraftment was not associated with AKI.

Conclusions: AKI occurs frequently after HDM/SCT in AL amyloidosis patients and is associated with several risk factors and an increased overall mortality. Prophylactic measures addressing some of these risk factors may reduce this risk.

Associations Between the Immunoglobulin Germline Gene Usage and the Tropism of Organ Involvement and Renal Amyloid Deposition Patterns in Immunoglobulin Light-Chain Amyloidosis by Mass Spectrometry

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Background: The goal of this study was to characterize the associations between the immunoglobulin light chain variable region (IGVL) germline gene usage and organ tropism, renal amyloid deposition patterns in Chinese patients with AL amyloidosis. Methods: 105 patients were selected randomly from an overall database of 310 patients with AL amyloidosis diagnosed by renal biopsies during 2000 to 2018. The clinical manifestation and organ involvement were assessed. The renal amyloid deposits on different compartments were evaluated and classified into three patterns: (1) glomerular dominant amyloid deposition pattern (G-AL, n=27); (2) vascular dominant deposition pattern (V-AL, n=32); (3) diffuse amyloid deposition pattern (D-AL, n=46). IGVL germline gene usage was identified based on proteomic analysis of renal amyloidotic tissue by mass spectrometry using a reference database supplemented with sequences of IGVL genes. AL amyloidosis. The association of IGVL genes with organ involvement, renal amyloid deposition patterns and survival were assessed.

Results: IGVL genes were successfully identified in 84.8% patients (89/105). LV 9-67 (31.2%) was the most common α IGVL gene identified among patients with AL amyloidosis, and KV 1-33 (50.0%) was predominant in x IGVL patients. When compared with patients with renal involvement, the frequency of LV 1-44 (12.1% vs 4.3%) was P=0.639
Great Neck, NY

Kenar

Naoka

Roberta

Treatment of AL Amyloidosis with Daratumumab Monotherapy

TH-OR33

Whereas, the results were preliminary and exploratory, and should be proved in a large cohort of AL amyloidosis patients.

Funding: Government Support - Non-U.S.

TH-OR33

Treatment of AL Amyloidosis with Daratumumab Monotherapy

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Background: Immunoglobulin light chain amyloidosis (AL) is characterized by poor outcome. Daratumumab (D) is a first in class anti CD38 human antibody (IgG1κ) which proved to be effective in combination with bortezomib in MM refractory to conventional bortezomib-based regimens. Its effectiveness and safety in the treatment of AL amyloidosis is under study. This study reports the experience of D monotherapy in a series of severe patients (pts) with AL amyloidosis and multorgan and biopsy-proven renal involvement.

Methods: Five pts, mean age 64 years were treated with D following antibody testing and extended RBC antigen phenotyping. Treatment protocol was as follows: 16 mg/kg D i.v. administered weekly for 8 weeks, then every 2 weeks (8 doses), and then monthly for 1 year.

Results: In pt #1, in dialysis, who was refractory to conventional therapies D administration resulted in normalization of the FLC ratio with disappearance of serum M-component and Bence-Jones (BJ) proteinuria. In pt #2 who had a relapsing disease, D treatment resulted in a rapid decrease of proteinuria and N-terminal propeptide (NT-proBNP) levels with disappearance of serum M-component and BJ proteinuria and normalization of the FLC ratio. Pt #3 was treated front-line. He had an impressive decrease of proteinuria and NT-proBNP levels with normalization of FLC ratio and disappearance of serum M-component. In pt #4, who was intolerant to conventional regimens, D therapy resulted in decrease in proteinuria, disappearance of serum M-component and improvement in the FLC ratio, which were paralleled by a reduction of NT-proBNP levels. Pt #5 had a relapsing disease. D achieved a decrease of proteinuria, a decrease of serum M-component with increase of FLC ratio. This was the only patient who experienced an infusion reaction during the first dose. The 4 pt with still preserved renal function also showed renal response with sCr improvement or stabilization and a decrease of serum M-component with increase of FLC ratio. Pt #5 had a relapsing disease. D achieved a decrease of proteinuria, and extended RBC antigen phenotyping. Treatment protocol was as follows: 16 mg/kg D i.v. administered weekly for 8 weeks, then every 2 weeks (8 doses), and then monthly for 1 year.

Conclusions: Daratumumab monotherapy resulted in the disappearance of M-proteinemia in every pt of D-Clin group normalized in 4 out of 5 subjects and impressive decrease of proteinuria and pro-BNP values proving to be an effective therapeutic option for pretreated/ naïve patients with severe AL with renal involvement.

TH-OR34

Immune Checkpoint Inhibitor Use in Kidney Transplant Recipients: A Multicenter Study

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Background: Immune checkpoint inhibitors (ICIs) significantly improved the survival in many cancers, but the data on survival benefit in KTxs recipients are lacking. ICIs are reported to be associated with higher acute rejection rate in KTxs recipients, but the risk factors of ICI-associated rejection are not fully understood.

Methods: We conducted a multicenter observational study to investigate the clinical characteristics of ICI-associated rejection and the survival outcomes of KTxs recipients treated with ICI. 66 KTxs patients with a functioning allograft at the time of ICI initiation were collected from 18 institutions. In addition, historical control groups of KTxs recipients with advanced stage melanoma (AACC stage III-IV, n=17) and cutaneous squamous cell carcinoma (cSCC, AACC stage III (unresectable)-IV, n=23), who could be considered as potential ICI candidates, were collected to compare the overall survival (OS).

Results: In ICI cohort, median age was 64, male dominant (83%) and transplant to ICI initiation was median 11 years. cSCC was the most frequent malignancy (n=22), followed by melanoma (n=28) patients (42.4%) experienced rejection, of which 19 (64.2%) lost allograft and returned to dialysis. Median time from ICI initiation to rejection was 26 days. In biopsy-proven rejection (n=13), both mixed acute cell and antibody-mediated rejection (n=7, 53%) and acute cell-mediated rejection (n=6, 47%) were seen. By Chi square test, mTOR inhibitor use (P=0.012) and the use of higher number of immunosuppressive drugs (P=0.06) were associated with higher risk of rejection. For both melanoma and cSCC cohort, ICI groups experienced higher rejection rate (57% and 40%, for melanoma and cSCC, respectively, compared to non-ICI control groups (12% and 4.3%), suggesting the higher rejection rate in ICI groups was not solely explained by reduction in immunosuppression. OS didn’t show statistical difference in melanoma cohort (log rank test P=0.22), but OS was significantly longer in cSCC cohort (log rank test P=0.015), when compared ICIS vs non-ICI control groups.

Conclusions: Our multi-center study provides a novel data on the survival benefit and the risk factors of rejection in KTxs recipients with ICI use compared to non-ICI control groups.

Funding: NIDDK Support, Private Foundation Support

TH-OR36

Daily Caffeine Consumption and Risk of AKI Related to Platinum-Salt Chemotherapy: A Prospective Cohort Study

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Background: Although their efficacy has been well-established in Oncology, the use of platinum salts remains limited due to the occurrence of acute kidney injury (AKI). Caffeine has been suggested as a potential pathophysiological actor of platinum salt-induced AKI, through its hemodynamic effects. This work aims to study the association between caffeine consumption and the risk of platinum salt-induced AKI.

Methods: We conducted a single-center prospective cohort study that has included 108 consecutive thoracic cancer patients receiving a first-line platinum-salt chemotherapy between January 2017 and December 2018. Before the first course of chemotherapy, they were all invited to fill in a previously validated auto-questionnaire, designed for a detailed evaluation of their daily caffeine consumption (mg/day). The association of daily caffeine consumption with the risk of platinum-salt induced AKI was estimated by cause-specific Cox proportional hazard model adjusted for several known confounders (baseline renal function and serum albumin level, nature and dose of platinum-salt, tobacco exposure, and Performans status).

Results: Overall, 34 patients (31.5%) (mean age 61.7 years, 65% men, 80% tobacco users) experienced a platinum salt-induced AKI (67% grade 1) and 47 (43.5%) died during follow-up (6.2 months [3.4; 8.4]). The group of high-caffeine consumption (a 386mg/day) had a twice higher risk of AKI (HR=2.12 [1.01; 4.45]) in the fully adjusted model. The cumulative incidence of AKI (considering the competing risk of death) was also significantly increased in the high-caffeine consumption group (p=0.03, see figure 1).

Conclusions: In a population of thoracic cancer patients, the group of high-caffeine consumption was exposed to a significantly higher risk of platinum salt-induced AKI.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Results: We identified 183 patients (98 gem-cis, 32 split and 53 gem/gem-cis). Median follow-up was 57 months (IQR: 64-73). Multivariate analysis showed a significant increase in risk of progressing to proteinuria of greater than 1.0 g/g, Age and hypertension were not associated with increased risk. Due to lack of randomization and incomplete data, further analysis is needed.

Conclusions: A presence of baseline P/Cr greater than 0.25 g/g, type 2 diabetes, and CKD III, all showed a significant increase in risk of progressing to proteinuria of greater than 1.0 g/g. Age and hypertension were not associated with increased risk. Despite the lack of long-term follow-up, the study provides important insights into the risk factors associated with proteinuria in patients receiving Bevacizumab.

TH-OR39

CKD Prevalence, Patterns of Treatment, and Outcomes in Patients with Cancer: A Population-Based Cohort Study

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Background: Chronic kidney disease (CKD) may impede optimal cancer treatment and result in worse outcomes. There are limited data to assess receipt of systemic therapy, radiation, and palliative care in patients with cancer and CKD.

Methods: We conducted a population-based cohort study of all patients (≥18 years old) with a new cancer diagnosis in Ontario, Canada (2007-2015). We categorized patients according to CKD status at cancer diagnosis [estimated glomerular filtration rate (eGFR) ≥60 (referent group), 45-59, 30-44, 15-29, <15 mL/min/1.73m², dialysis and transplant recipients]. We used multivariable Fine and Gray proportional hazards models to assess overall survival, receipt of systemic therapy, radiation and palliative care (6-months prior to death) in the 5 most common solid cancers (bladder, breast, colon, prostate, lung) and kidney cancer.

Results: We identified 128,489 patients with a new cancer diagnosis, of whom 16% had pre-existing CKD (eGFR ≤60 mL/min/1.73m²). Patients with the 6 cancers of interest accounted for 73% (93,751). Kidney function at cancer diagnosis was associated with (progressively) worse overall survival in CKD stages 3a-5, dialysis, and transplant recipients (Figure a). Increasing CKD stage was associated with significantly reduced receipt of all treatment modalities [systemic therapy, radiation and palliative care (Figure b-d)]. Patients receiving dialysis had 2-fold increased mortality in bladder, breast and ovarian cancers, and 3-fold mortality in kidney cancer.

Conclusions: In patients with cancer, CKD is associated with reduced exposure to systemic, radiation and palliative treatments and worse overall survival. Strategies to improve cancer care in the CKD population are needed.

TH-OR38

Characterizing the Risk of Development of Proteinuria with Bevacizumab Therapy

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Background: Bevacizumab is a well-known cause of proteinuria. There are multiple hypotheses regarding mechanism that involve the VEGF receptor, nitric oxide metabolism and increased arterial glomerular pressure. The most accepted explanation is that Bevacizumab induces thrombomicroangiopathy. However, there is no current model or description of potential risk factors to identify at-risk patients who may need closer follow-up. Although CKD has been described as a risk factor, there exists no proven therapy for mitigating or reversing the proteinuria. Current guidelines advise that therapy be either discontinued or completely stopped depending on the level or proteinuria that develops. Some authors have proposed RAAS inhibition, but no data is available to support that therapy.

Methods: 1224 patients on Bevacizumab were sampled, with 714 having at least one P/Cr value needed for analysis. The time frame in which data was collected was 600 days. Data sampled included, age, baseline P/Cr, status of type 2 diabetes, chronic kidney disease stage 3, hypertension, use of Angiotensin Converting Enzyme inhibition, and sequential P/Cr values. Cox proportional hazard models were used to assess differences in the instantaneous risk of the event by categories, no violations of proportional hazard models were observed. The primary endpoint was defined as a P/Cr of 1.0 g/g, indicative of progression of proteinuria.

Results: A baseline P/Cr above 0.25 (HR 5.83, p < 0.001), Type 2 Diabetes (HR 1.69, p = 0.074), and CKD III (HR 3.25, p = 0.007) were associated with an increased risk of developing proteinuria, while age, hypertension (HR 1.11, p = 0.86), a baseline P/Cr < 0.25 (HR 1.04, CI 0.53,2.04, p = 0.001) were not. ACE inhibitors had the following association: (Losinopril; 10 mg, 20 mg, > 20mg), HR (1.47, 1.76, 1.67), p=0.67. Treatment duration was also shown to increase risk of the primary endpoint. The cumulative incidence was 23% after 600 days of treatment.

Conclusions: The risk factors for nephropathy with high-dose methotrexate (HDMTX) in haematological malignancies, and the role of age, hypertension and urinary alkalisation are emphasized in this study, but despite these measures, nephrotoxicity remains 2-12%. Determination of risk factors is key in order to further stratiﬁcation and ameliorate the risk of acute kidney injury.

Methods: A retrospective review of the electronic medical record was conducted to identify patients with leukaemia or lymphoma who received HDMTX from 1/1/2002 to 12/31/2015. We characterised the incidence of AKI using the acute kidney injury network criteria, and the time to AKI. We assessed key baseline demographics, underlying malignancy, delivered MTX dose, and previous nephrotoxicity. Significant factors on univariate analysis were further assessed on Multivariate analysis. Analysis was performed on Minitab.

Results: We identified 3091 cycles of HDMTX with lymphoma accounting for 90.7% of cases. The incidence of AKI was 19.1% in the lymphoma cohort and 13.6% in the leukaemia cohort (p=0.023). The median time to AKI grade shortened with higher severity of AKI (p<0.001). In those with AKI N3, creatinine increased to this level in a median time of 1 day. All patients requiring dialysis (n=7) developed an AKI at day 1 post HDMTX. Univariate analysis revealed age (p=0.022), Gender (p=0.001), higher BSA (p=0.001), type of malignancy (p=0.023), nephrotoxicity on previous dose (p=0.001), cycle number (p=0.001), GFR by Cockcroft-Gault (p=0.016) and 48-hour MTX level (p=0.001). There was no association between AKI and MTX dose (p=0.225), or GFR by MDRD (p=0.497). Multivariate analysis revealed increased age (p=0.001), male Gender (p=0.001), Lymphoma (p=0.002), previous AKI (p=0.001), cycle number (p=0.032), and 48-hour MTX level (p=0.001) to be significant risk factors for nephrotoxicity.

Conclusions: Nephrotoxicity remains a significant complication with HDMTX despite current measure standards. High grade AKI occurs early post HDMTX and therefore, risk stratiﬁcation is vital. Our study identiﬁed key risk factors as older, male, AKI on previous dose, diagnosis of lymphoma, elevated 48-hour MTX level and earlier cycle.
is less influenced by muscle mass or nutritional status, and eGFR using both markers (eGFRcr-cys) is more accurate than either eGFRcr or eGFRcys, but not as widely assessed in cancer patients. Our aim is to compare the performance of eGFR equations (Table) in cancer patients compared to mGFR.

**Methods:** This analysis is a cross-sectional evaluation of a prospective cohort of cancer patients in treatment at the ICESP. mGFR was determined by plasma clearance of 

\( \text{Cr-EDTA} \) indexed for body surface area.

**Results:** A group of 1,200 patients recruited between April 2015 and September 2017. Patients were 60 (51 – 68) y, 50.8% male. The most common cancer sites were breast (22.6%), prostate (19.8%) and gastrointestinal (13.4%). All eGFRcr equations overestimated mGFR with varying bias. CG had the lowest precision and was least accurate. eGFRcys underestimated mGFR and eGFRcr-cys had minimal bias and was the most accurate of all equations (Table).

**Conclusions:** All eGFRcr equations overestimated mGFR in our study. CG was the least accurate and should not be preferred over CKD-EPI. eGFRcr-cys is more accurate and can be used as a confirmatory test.

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**TH-OR42**

**Spatial Transcriptomics (ST): Integrating Molecular Profiles with Histomorphology in Kidney Tissue Sections**

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**Background:** Advances in sequencing methods have increased available molecular information on dissociated cells and tissues. Spatially linking this molecular information with histomorphology is needed to understand a complex organ like the kidney, in both health and disease.

**Methods:** Here we used the commercially available 10x Genomics ST platform to investigate the spatially resolved transcriptome expressions in fetal (n=2), adult male (n=3) and female (n=3) mouse kidney and a healthy human cortical frozen kidney tissue sections. We utilized Space Ranger (10x Genomics), Seurat and stLearn analysis pipelines to explore the spatial transcriptome expression within the kidney tissue sections. Furthermore, we confirmed the robustness of our ST data against matched publicly available mouse and human kidney scRNA-seq data.

**Results:** We identified a unique transcriptome plasticity in fetal and adult mouse kidneys, and healthy human cortical kidney tissue. Further dimensional reduction identified transcriptome clusters which correlated with distinct developing kidney structures in fetal mouse kidney tissue, functional cortical and medulla regions in adult mouse kidney tissue, and scarred and non-scarred regions in human cortical kidney tissue.

**Conclusions:** ST is a non-dissociative sequencing and imaging method which allows molecular profiles to be integrated with histomorphology of frozen kidney tissue sections. This provides a novel opportunity to inform physiological and non-physiological conditions at the cell, nephron and tissue levels.

**Funding:** Government Support - Non-U.S.
Sudhir Perincheri, Randy L. Luciano, Gilbert W. Moeckel, Richard Torres.
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**Background:** Digitization of clinical renal biopsy histology is motivated by the importance of early intervention in acute kidney conditions, assessment by remotely-based experienced nephropathologists, and application of emerging computerized quantitative evaluation tools. Despite the interest, image quality and workflow impact are concerns for digital renal pathology. A newly developed tool for rapid, slide-free microscopic image preparation called clearing histology with MultiPhotonic Microscopy (CHIMP) has demonstrated high efficiency and high quality morphology for diagnostic review in renal disease in a research environment. We sought to commence clinical validation of CHIMP for remote review using effects on downstream traditional special stains and ability to detect a broad range of clinically relevant pathological lesions in renal biopsies.

**Methods:** Kidney core biopsies were procured from 50 consented individuals undergoing renal biopsy for any reason and CHIMP processing was integrated into the routine clinical workflow, using previously-described methods. Images were obtained through entire core biopsies with a prototype fast, high resolution, multiphoton microscopy system (Applitek Technologies, Washington, DC) and visualized with web-based software. Samples were subsequently processed using standard methods for clinical interpretation under transmitted-light microscopy, including special stains. A subset of 20 core biopsies underwent detailed morphologic feature analysis and quantitative lesion comparison.

**Results:** Diagnostic quality remotely-reviewable renal images of 10-16 digital slices were available within ~3 hours of receipt. CHIMP detected morphologic findings were equally detectable in digital images compared to physical, paraffin-embedded sections including cases showing tubular injury, proliferative glomerulonephritis, glomerular deposition disease, and interstitial nephritis. No significant negative effects on downstream processing were identified.

**Conclusions:** CHIMP can be used in rapid morphologic evaluation of kidney biopsies integrated into clinical work enabling rapid rendering of preliminary diagnoses while simultaneously making digital images available for remote expert evaluation and digital analysis. Continuing validation will test ability to augment detection of rare lesions and quantitative precision.

**Funding:** NIDDK Support

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**Underline represents presenting author.**

**TH-OR44**

A Deep-Learning Approach to Kidney Biopsy Frozen Sections

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**Background:** Pre-implant assessment of donor kidney biopsies to determine allograft viability is often performed by non-renal pathologists, and carries limited accuracy and reproducibility. The purpose of this work is to develop a deep learning (DL) method for the classification of relevant histologic primitives from donor biopsies as an aid to pathologists. In this article, we report the development and validation of a deep learning system that allows for the recognition of histologic primitives in kidney biopsies.

**Methods:** A total of 268 frozen sections stained with hematoxylin and eosin (H&E) from cadaveric donor kidney biopsies (128 performed at Duke and 140 at outside institutions) were scanned into whole slide images (WSI) at 40x (Leica Biosystems AT2 iScan). The WSIs were divided into the training, validation, and test datasets (0.8:0.1:0.1). Mallory trichrome stained sections were used as ground-truth for training and validation cohorts. The DL algorithms reduced the time required for atubular glomeruli assessment, provided data correlating well with human manual-based assessment, and correlated well with relevant morphology data. This methodology can be extended to 3D glomerular phenotype analysis.

**Funding:** NIDDK Support

**TH-OR45**

Evaluation of a Direct-to-Digital Histology Method for Rapid Evaluation of Kidney Biopsies

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Yale University School of Medicine, New Haven, CT.

**Background:** Pre-implant assessment of donor kidney biopsies to determine allograft viability is often performed by non-renal pathologists, and carries limited accuracy and reproducibility. The purpose of this work is to develop a deep learning (DL) method for the classification of relevant histologic primitives from donor biopsies as an aid to pathologists. In this article, we report the development and validation of a deep learning system that allows for the recognition of histologic primitives in kidney biopsies.

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**Funding:** NIDDK Support

**TH-OR46**

Kidney Biopsy Transcript Patterns Offer a Novel Approach to Distinguishing Etiologies of Acute Interstitial Nephritis

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**Background:** One of the challenges in renal pathology is distinguishing causes of acute interstitial nephritis (AIN). Based on encouraging results from renal allografts, we sought mRNA transcript profiles of checkpoint inhibitor associated AIN (CPI), drug induced AIN (Drug), AIN in diabetes (DM), IgG4-related renal disease (IgG4) and T cell rejection type 1 (TCMR1).

**Methods:** Three 20 um sections were obtained from 65 FFPE blocks: 9 controls, 46 AIN types (10 CPI, 13 DM, 14 Drug, 9 IgG4 and 10 TCMR1). mRNA was extracted and hybridized with NanoString HOT Panel of 770 probes and analyzed on an nCounter Max instrument. The gene list is available at nanostring.com. Pathway analysis, differential expression and cell type scores were analyzed from normalized mRNA counts using nSolver.

**Results:** Similarities were found across AIN however each had one or more distinct patterns of transcripts. CPI AIN was distinguished from the other causes of AIN by higher IFNγ signaling pathway scores (Fig 1). CPI AIN had more exhausted CD8 cells (p<0.05) and NK cells (p<0.001) than drug induced AIN. DM AIN differed from histologically indistinguishable Drug AIN by several genes (e.g. higher TGFβ2, p=0.007). IgG4 AIN showed the highest levels of B cell receptor signaling, MAPK and mTOR pathways, and highest Th17 and Treg differentiation scores. TCMR1 had lower scores for TGFβ and TNF pathways and lower Treg scores compared with the other causes of AIN. TCMR1 had the most favorable scores for AKI and pathways related to outcome (eGFR later, GoCAR progression).

**Conclusions:** Our initial findings suggest that once extended to customized algorithms and validated, this approach may prove fruitful in distinguishing the underlying diagnosis and pathogenesis of diverse causes of AIN.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline represents presenting author.**

| Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
| **Underline represents presenting author.**
of histopathologic lesions. We tested the associations of each biomarker with clinicopathologic diagnoses, histopathologic lesions, and the risks of kidney disease progression (a ≥40% decline in estimated glomerular filtration rate (eGFR) or end-stage kidney disease) and death.

Results: After multivariable adjustment and correction for multiple testing, 39 proteins were independently associated with clinicopathologic diagnoses and 53 with different histopathologic lesions. Kidney-injury molecule-1 (KIM-1) associated with diabetic nephropathy and glomerular and tubulointerstitial diseases. The top performing markers for acute tubular injury and interstitial fibrosis and tubular atrophy were KIM-1 and tumor necrosis factor receptor superfamily member-9 (TNFRSF-9), respectively. Thirty proteins were significantly associated with kidney disease progression and 35 with death (Figure 1 A, B). The top performing markers for kidney disease progression were placental growth factor (PGF; HR 5.4, 95% CI 3.4 to 8.7) and BMP and Activin Membrane Bound Inhibitor (BAMBI; HR 3.0, 95% CI 2.1 to 4.2); the top performing markers for death were TRAIL-receptor-2 (TRAIL-R2; HR 2.9, 95% CI 2.0 to 4.0) and CUB Domain Containing Protein-1 (CDCP1; HR 2.4, 95% CI 1.8, 3.3). Five proteins were significantly associated with decreased risks of death (Figure 1 B).

Conclusions: We identified several biomarkers of kidney disease histology, pathology, and prognosis—many of which have not been reported previously and may represent important avenues for future research.

Funding: NIDDK Support, Private Foundation Support

Figure 1: Percentage of area per image stained for C5b9 with 95% CI after treatment with patient serum.
FR-OR01
Terlipressin Improves Renal Replacement Therapy–Free Survival in Hepatorenal Syndrome Type 1
Juan Carlos Q. Velez,1 Alex Befek,1 Ira Kurtz,2 Juan F. Gallegos-Orozco,3 Hugo E. Vargas,3 John M. Vierling,2 S. Chris Pappas,2 Kharram Jani.2
1Ochsner Health System, New Orleans, LA; 2Malinckrodt Pharmaceuticals Speciality Brands Principal Office, Bedford, NJ; 3Mayo Clinic, Phoenix, AZ; 4Saint Louis University, Saint Louis, MO; 5University of Utah Health, Salt Lake City, UT; 6Orphan Therapeutics, Lebanon, NJ; 7Baylor College of Medicine, Houston, TX; 8UCAL Medical Center, Los Angeles, CA.

Background: Hepatorenal syndrome type 1 (HRS-1) is an ominous form of acute kidney injury in patients with cirrhosis. Recently, the results of the randomized placebo (PBO)-controlled trial (CONFIRM) demonstrated that terlipressin (TERLI) is effective in reversing HRS-1 and in reducing the cumulative need for renal replacement therapy (RRT). However, whether TERLI reduces the need for RRT among survivors has not been determined.

Methods: CONFIRM (NCT02770716) was a North American RCT (n=300) that compared HRS-1 reversal rates between patients treated with albumin plus TERLI (n=199) or albumin plus PBO (n=101) (2:1). We conducted a post hoc intention-to-treat analysis to assess the incidence of RRT among CONFIRM survivors. We also conducted a pooled analysis of the 3 TERLI RCTs in HRS-1 (OT-0401 [NCT00089570], REVERSE [NCT01143246], and CONFIRM) to examine 90-day RRT-free survival rates.

Results: In CONFIRM, the cumulative incidences of need for RRT for TERLI at day 14, 30, and 90 were 23%, 26%, and 29% compared with 35%, 36%, and 39% for patients assigned to PBO (P=0.03, 0.07, and 0.1, respectively). Among survivors, significantly fewer TERLI-treated patients remained dependent on RRT at day 14, 30, and 90 (22%, 26%, and 30%, respectively) compared with PBO (39%, 43%, and 46%; P=0.01, P=0.03, and P=0.05, respectively). The 90-day RRT-free survival rate was 35% in the TERLI group vs 30% in the PBO group (P=0.08), with a numerically longer median number of days in the TERLI group (20 vs 11). Pooled analysis of the 3 RCTs revealed a greater 90-day RRT-free survival rate for TERLI-treated (n=352) compared with PBO-treated (n=256) patients (37% vs 29%, P=0.03; OR [95% CI], 1.47 [1.04, 2.07]).

Conclusions: Treatment with TERLI added to albumin decreased the rate of RRT and improved RRT-free survival in patients with HRS-1. This is the first pharmacological intervention proven to reduce the need for RRT in patients with HRS-1. Because of the significant impact of RRT on quality of life, this observation expands the clinical benefit of TERLI and enhances the reported efficacy of TERLI in inducing HRS-1 reversal.

TH-OR50
Immunotactoid Glomerulopathy: A Rare Entity with Monoclonal and Polyclonal Variants
Sanath H. Nasr,1 Satoru Kudose,2 Samar M. Said,1 Dominick Santoriello,2 Sanjeev Sethi,1 Mary E. Fidler,2 Nelson Leung,1 Vivette D’Agati,2 Glen S. Markowitz,3 Mayo Foundation for Medical Education and Research, Rochester, MN; 2Columbia University Medical Center, New York, NY.

Background: Immunotactoid glomerulopathy (ITG) is a rare disease currently classified as an MGRS lesion for which our understanding is limited.

Methods: 73 patients with ITG were identified by retrospective review of all native renal biopsies received at two large renal pathology laboratories from 1993-2019.

Results: ITG biopsy incidence was 0.04%. Median age at diagnosis was 61 years, 86% were Caucasian, and there was no gender predilection. Patients presented with proteinuria (median 6.6 g/day, 58% with full nephrotic syndrome), hematuria (86%), and renal insufficiency (median creatinine 1.6 mg/dl). Hematologic disorders were classified as an MGRS lesion for which our understanding is limited.

As compared to polyclonal ITG, monoclonal ITG had a higher incidence of lymphoma (11% vs. 6%), multiple myeloma (8% vs. 0), and MGRS (22% vs. 0). On follow up (median 47 months), 31% had complete remission, 11% partial remission, 35% persistent renal dysfunction, and 24% progressed to ESRD. The median survival (not reaching a plateau) was 123 months. Monoclonal ITG was more commonly treated with immunosuppression, and 24% progressed to ESRD. The median survival (not reaching a plateau) was 123 months. Monoclonal ITG was more commonly treated with immunosuppression, and 24% progressed to ESRD (53% vs. 11%), multiple myeloma (8% vs. 0), and MGRS (22% vs. 0). On follow up (median 47 months), 31% had complete remission, 11% partial remission, 35% persistent renal dysfunction, and 24% progressed to ESRD. The median survival (not reaching a plateau) was 123 months. Monoclonal ITG was more commonly treated with immunosuppression, and 24% progressed to ESRD.

Conclusions: As compared to polyclonal ITG, monoclonal ITG had a higher incidence of lymphoma (11% vs. 6%), multiple myeloma (8% vs. 0), and MGRS (22% vs. 0). On follow up (median 47 months), 31% had complete remission, 11% partial remission, 35% persistent renal dysfunction, and 24% progressed to ESRD. The median survival (not reaching a plateau) was 123 months. Monoclonal ITG was more commonly treated with immunosuppression, and 24% progressed to ESRD.

FR-OR02
A Parsimonious Model for Diagnosis of Biopsy-Proven Acute Intestinal Nephritis Using Electronic Health Record Data
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Background: Due to its atypical clinical features and difficulty in establishing diagnosis without a biopsy, acute intestinal nephritis (AIN) diagnosis is delayed or missed. We developed a predictive model for AIN using clinical data from all patients who underwent a kidney biopsy available through the electronic health record.

Methods: We obtained data on all patients who underwent a native kidney biopsy at two centers between 2013-18 and obtained corresponding information of demographics, comorbidities, and all laboratory tests collected up to one year before biopsy. We used least absolute shrinkage and selection operator (LASSO) method to select features associated with AIN and performed area under received operating characteristics curve (AUC) analysis in temporally-split training (70%) and test (30%) sets. We also applied this model to a separate cohort of kidney biopsies with AIN diagnosis adjudicated by 3 pathologists and compared it to the clinician’s prebiopsy impression of AIN obtained through chart review.

Results: Among 551 patients who underwent native kidney biopsies, 60 (11%) had AIN on clinical pathology diagnosis. We evaluated 163 potential features for their association with AIN. The five features with the highest AUC were last creatinine at the time of biopsy (AUC, 0.73), BUN to creatinine ratio (0.70), urine specific gravity before biopsy (0.67), serum bicarbonate (0.62), and urine protein (0.62). The top 4 variables picked using LASSO had an AUC of 0.76 in the test set (table). Applying this model to a separate cohort of participants with adjudicated AIN, we noted an AUC of 0.80 (0.73, 0.87), which was higher than the clinician’s pre-biopsy impression of AIN (0.61 (0.52, 0.70), P=0.001).

Conclusions: We noted four variables associated with AIN and the model containing these showed a modest AUC but was an improvement on clinician’s pre-biopsy impression of AIN.

Funding: NIDDK Support
FR-OR03
Development and Validation of a Convolutional Neural Network Model for Intensive Care Unit AKI Prediction
Jacob Calvert,1 Angier O. Allen,1 Sidney H. Le,1 Paul M. Palevsky,2 Gregory L. Breden,1 Shariad Patel,1 Emily Pellegrini,1 Abigail Green-Saxena,1 Jana Hoffman,1 Ritanark Das,1 Dascena, Oakland, CA; 2VA Pittsburgh Healthcare System, Pittsburgh, PA; 1Baystate Medical Center, Springfield, MA; 3Cooper University Health Care, Camden, NJ.

Background: Acute kidney injury (AKI) is common among hospitalized patients and has a significant impact on morbidity and mortality. While early prediction of AKI has the potential to reduce adverse patient outcomes, it remains a difficult condition to predict and diagnose. The purpose of this study was to evaluate the ability of a machine learning algorithm to predict for AKI KDIGO Stage 2 or 3 up to 72 hours in advance of onset using convolutional recurrent neural nets (CNN) and patient Electronic Health Record (EHR) data.

Methods: A CNN prediction system was developed to continuously and automatically monitor for incipient AKI. 7122 patient encounters were retrospectively analyzed from the Medical Information Mart for Intensive Care III (MIMIC-III) database. The CNN machine learning-based AKI prediction model was compared to an established XGBoost AKI prediction model and the Sequential Organ Failure Assessment (SOFA) scoring system. AKI onset was used for the outcome. The model was trained on routinely-collected patient EHR data.

Results: On a hold-out test set, the algorithm attained an Area Under the Receiver Operating Characteristic (AUROC) of 0.85 and PPV of 0.25, relative to a cohort AKI prevalence of 5.21%, for long-horizon AKI prediction at a 72-hour window prior to onset. The ROC curve comparison of 72-hour prediction on the 10% hold-out test set is shown in Figure 1. The CNN model, which was provided text data through Doc2Vec input, outperformed the XGBoost model and the SOFA score.

Conclusions: A CNN and autotagging-based AKI prediction model outperforms XGBoost and the SOFA scoring system, demonstrating superior performance in predicting acute kidney injury 72 hours prior to onset, without reliance on changes in serum creatinine.

Funding: Other NIH Support - This work was supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) [grant ID: R01AA02767401]

FR-OR04
Outcomes from the Use of the Selective Cytopheretic Device (SCD) in Critically Ill Children Receiving CRRT: A Report of the Multicenter Pediatric SCD (pSCD) Study
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Background: Critically ill children who develop acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT) are at increased risk of death. The SCD promotes an immunomodulatory effect in a hypocalcemic environment (ionized Ca (ionCa) < 0.4 mmol/L) in animal models of inflammation. In a randomized trial, adult ICU patients on CRRT treated with the SCD, who maintained CRRT ionCa < 0.4 mmol/L, had improved survival/dialysis independence. We conducted an FDA grant sponsored safety evaluation (adverse and serious adverse events) of the SCD in 16 critically ill children.

Methods: 4 center US study of the SCD in children (<15 kg, ±22 years) with AKI and multigener failure receiving CRRT. The SCD was integrated post CRRT membrane, changed daily, and circuit ionCa maintained <0.4 mmol/L. Pts received SCD treatment for up to 7 days or CRRT discontinuation.

Results: 16 pts (8F/8M) completed the study from 12/2016 thru 2/2020. Mean pt age was 12 yr (range 4-21 yr), weight was 53 kg (range 19-111 kg) and PRISM 2 score was 7 (range 2-19). Two pts received ECMO. The most common ICU diagnosis was shock. Circuit ionCa were maintained at <0.4 mmol/L for 90.2% of assessments. Median SCD duration was 6 days (range 1 to 7). 15/16 pts survived SCD therapy, 12/16 patients survived to ICU discharge. All 12 ICU survivors were dialysis independent at 60 days. No SCD related adverse events were noted.

Conclusions: Our data suggest the SCD is safe in critically ill children who require CRRT. While we cannot make efficacy claims, the 7% survival rate and 100% renal recovery rate in surviving children suggest a favorable benefit to risk ratio.

Funding: Other U.S. Government Support

FR-OR05
Nicotinamide Riboside with Pterostilbene Increases NAD+ in Patients with AKI: A Randomized, Double-Blind, Placebo-Controlled, Stepwise Safety Study of NRPT in Patients with AKI
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Background: Preclinical studies have identified both NAD+ and sirtuin augmentation as potential strategies for the prevention and treatment of AKI. Nicotinamide riboside (NR) is a NAD+ precursor vitamin and pterostilbene (PT) is potent sirtuin activator found in blueberries. Here, we tested the effect of combined NR and PT (NRPT) on whole blood NAD+ levels and safety parameters in patients with AKI.

Methods: We conducted a randomized, double-blind, placebo-controlled study of escalating doses of NRPT in 24 hospitalized patients with AKI. The study was comprised of four Steps during which NRPT (5 subjects) or placebo (1 subject) was given twice a day for two days. NRPT dosing was increased in each Step: Step 1 250/50mg, Step 2 500/100mg, Step 3 750/150mg and Step 4 1000/200mg. Blood NAD+ levels were measured by liquid chromatography-mass spectrometry and safety was assessed by history, physical exam, and clinical laboratory testing.

Results: AKI resulted in a 50% reduction in whole blood NAD+ levels at 48 hr compared to 0 hr in patients receiving placebo (p=0.05). There was a trend for increase in NAD+ levels in all NRPT Steps individually at 48 hr compared to 0 hr, but only the change in Step 2 reached statistical significance (47%, p=0.04), and there was considerable interindividual variability in the NAD+ response to treatment. Considering all Steps together, NRPT treatment increased NAD+ levels by 37% at 48hr compared to 0hr (p=0.002). All safety laboratory tests were unchanged by NRPT treatment, including creatinine, estimated glomerular filtration rate (eGFR), electrolytes, liver function tests, and blood counts. Three of 20 patients receiving NRPT reported minor gastrointestinal side effects.

Conclusions: NRPT increases whole blood NAD+ levels in hospitalized patients with AKI. In addition, NRPT up to a dose of 1000mg/200mg twice a day for two days is safe and well tolerated in these patients. Further studies to assess the potential therapeutic benefit of NRPT in AKI are warranted.

Funding: Commercial Support - Elysium Inc
FR-OR06
Role of Angiopoietins in CKD Progression After Hospitalization
Sherry Mansour,1 Steven G. Coca,2 Yaqi Jia,2 Vernon M. Chinchilli,4 Wassim Obeid,6 Francis P. Wilson,1 Samir M. Parikh,6 Edward D. Siew,2 Talat Alp Ikizler,7 Jonathan Himmelfarb,2 Paul L. Kimmel,1 Chirag R. Parikh.3
ASSESS-AKI Consortium 1Yale University School of Medicine, New Haven, CT; 2Icahn School of Medicine at Mount Sinai, New York, NY; 3John Hopkins University, Baltimore, MD; 4Pennsylvania State University, University Park, PA; 1Beth Israel Deaconess Medical Center, Boston, MA; 6University of Texas Southwestern Medical Center at Dallas, Dallas, TX; 7Vanderbilt University Medical Center, Nashville, TN.

Background: The factors determining chronic kidney disease (CKD) progression after an episode of acute kidney injury (AKI) are poorly understood. Angiopoietins play a role in vessel remodeling after AKI, where Angiopoietin-1 (Angpt-1) maintains vessel stability and Angiopoietin-2 (Angpt-2) destabilizes quiescent vessels. We investigated whether the balance of Angpt-1 and -2 was prognostic of CKD and mortality after hospitalization in patients with and without AKI.

Methods: Using plasma samples from ASSESS-AKI, we measured Angiopoietins 3 months after hospitalization. We assessed the ratio of Angpt-1:Angpt-2 with CKD progression (composite of incident and progression of CKD, and end stage kidney disease), and all-cause mortality.

Results: Angiopoietins were measured in 1503 hospitalized patients, among whom 746 (49.6%) had AKI. Median (IQR) age was 65.8 (56.6, 73.9) years, 555 (37%) were female, and 196 (13%) were black. Median times to CKD progression, and all-cause mortality were 4.4 (2.5, 5.7), and 4.9 (3.6, 6.0) years, respectively. CKD progression developed in 293 (19%) and mortality in 314 (21%) participants. The highest quartile of Angpt-1:Angpt-2 ratio was independently associated with 50% reduced risk of CKD progression and 77% reduced risk of mortality as compared to the lowest quartile. Stratified analyses by AKI status revealed stronger associations between Angpt-1:Angpt-2 ratio and both outcomes in the AKI group (Figure).

Conclusions: A higher Angpt-1:Angpt-2 ratio was strongly associated with lower risk of CKD progression and mortality after hospitalization, particularly in patients with AKI. Angiopoietins may help risk stratify patients with AKI after discharge for those in need of close follow-up and CKD management.

Funding: Private Foundation Support

FR-OR07
Determinants of Major Adverse Kidney Events (MAKE) in Extra Corporeal Membrane Oxygenation (ECMO) Survivors
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Background: The majority of ECMO patients develop acute kidney injury (AKI) and 40-60% require renal replacement therapy (RRT). Little is known about the effects of AKI on long-term renal outcomes after ECMO. The aim of this study was to examine the determinants of MAKE in ECMO survivors.

Methods: Patients who were admitted to a single-center between 2008 and 2017, were on ECMO for more than 24 hours & survived to hospital discharge were included. MAKE was defined as either doubling of serum creatinine (Scr), incident ESRD or death. USRDS and NDI databases were used to obtain information about ESRD and death. AKI was defined as KDIGO stages 2-3. Complete AKI recovery was defined as a return to 50% of baseline Scr and partial recovery as an improvement in the AKI stage without a return to 50% of baseline Scr. Survival analysis plots & Cox regression models were fitted to examine the associations of AKI status, AKI recovery and other factors with MAKE.

Results: Among 188 ECMO patients who survived until hospital discharge, 63% had AKI, and 41% required RRT. The mean follow-up time was 3.4 years. Patients with AKI were more likely to be on ECMO for a cardiac rather than respiratory indication and had a longer length of stay compared to patients with no AKI. Kaplan-Meier survival curves showed that patients with no/partial recovery from AKI had a higher rate of MAKE compared to those with no AKI (Figure 1). Results of the unadjusted analysis showed that ECMO type and timing of initiation of RRT were associated with MAKE. Multivariate analysis showed that AKI [aHR=1.79 (95%CI=1.00-3.21)], no/partial recovery from AKI [aHR=2.94 (95%CI=1.46-5.92)] and initiation of RRT after ECMO [aHR 5.4 (95%CI=1.14-25.6)] were significant determinants of MAKE after adjustment for potential confounders.

Conclusions: AKI, AKI recovery status, and timing of initiation of RRT are determinants of major adverse kidney events in patients who received ECMO.

FR-OR08
AKI Among African Americans with Sickle Cell Trait and Disease
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Background: Sickle cell trait (SCT) and disease (SCD) are independent risk factors for estimated glomerular filtration rate (eGFR) decline among African Americans (AA). However, our understanding of the risk for acute kidney injury (AKI) and the role of AKI in eGFR decline in patients with SCT/D remains limited. We aimed to describe the relative risk for AKI in SCT/D and the effect of AKI on eGFR decline in patients with SCT/D.

Methods: We performed a multi-center observational study of adult AA patients with a baseline eGFR ≥ 15 ml/min, and ≥ 1 year follow-up between 2005-2018. The presence of SCT/D (exposure) and normal hemoglobin phenotype (reference) was determined by hemoglobin electrophoresis. Outcomes of interest (incident All AKI [Kidney Disease: Improving Global Outcomes criteria], incident Severe AKI [doubling of baseline creatinine] and incident Sustained AKI [AKI persisting for ≥ 2 hours]) were adjudicated by chart review and evaluated by Cox regression. Only first AKI events were used. The effect of All AKI on eGFR decline (mixed linear models) was also investigated. Models were adjusted for predictors of AKI.

Results: We identified 8868 reference, 1279 SCT, and 254 SCD patients with a median follow-up of 7.6 years and mean serum creatinine of 0.8 mg/dl. SCT was associated with Sustained AKI (adjusted hazard ratio [aHR] 1.42; 95% CI, 1.08-1.88) compared to the reference. SCD was associated with All AKI (aHR 3.13; 95% CI, 2.33-4.21), Severe AKI (aHR 3.04; 95% CI, 1.90-4.87) and Sustained AKI (aHR 2.10; 95% CI, 1.24-3.53) compared to the reference. Effect of AKI on eGFR is shown in Figure 1.
**Conclusions:** The risk for AKI is increased in both SCT (Sustained) and SCD (all forms) and may contribute to faster eGFR decline in SCD/T. Further studies are needed to understand the mechanisms of AKI in SCT/D. Such studies will inform best practices that will help attenuate the burden of kidney disease in SCT/D.

**Funding:** Private Foundation Support

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**FR-OR09**

**Assessment of Kidney Proximal Tubular Secretion in Critical Illness**

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**Background:** Serum creatinine concentrations (SCr) are used to determine the presence and severity of acute kidney injury. SCr is primarily eliminated by glomerular filtration; however, most mechanisms of kidney injury in critical illness involve kidney proximal tubules, where tubular secretion occurs. Proximal tubular secretion is thought to currently measured in the ICU. To estimate the kidney clearance of solute clearance in critically ill adults.

**Methods:** We collected matched blood and spot urine samples from 170 ICU patients and from a comparison group of 70 adults with normal kidney function. We measured seven endogenously produced solutes using liquid chromatography-tandem mass spectrometry. We computed a composite secretion score incorporating all seven endogenously produced solutes using liquid chromatography-tandem mass spectrometry. We computed a composite secretion score incorporating all seven endogenously produced solutes using liquid chromatography-tandem mass spectrometry.

**Results:** The urine/plasma ratio of six of seven secretory solutes were lower in critically ill patients compared with normal individuals after adjustment for SCr. The composite secretion score was moderately correlated with SCr and cystatin C (r = -0.53, r = 0.53, respectively). Each standard deviation higher composite secretion score was associated with a 52% lower risk of MAKE and albuminuria (P = 0.004) and albuminuria (P = 0.007) remained in the final model for the non-AKI group. In the AKI group, PRO-C6 had a stronger association with mortality than eGFR, as only age (P = 0.005), albuminuria (P = 0.04) and PRO-C6 (P = 0.004) remained in the final model. When stratified into tertiles, patients with higher levels of PRO-C6 at year 1 were significantly more likely to die (P = 0.009).

**Conclusions:** In this study, we compared levels of PRO-C6 in patients with and without AKI, and show that PRO-C6 levels measured in plasma can predict mortality in patients with AKI. Our findings may indicate that PRO-C6 identifies patients with active fibrogenesis after AKI, suggesting that long-term renal injury after AKI is important for patient outcome.

**Funding:** NIDDK Support

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**FR-OR10**

**Endotrophin, Released During Collagen Type VI Formation, Predicts Long-Term Mortality After AKI**

Nadja Sparding,1,2 Daniel Guldager Kring Rasmussen,3 Federica Genovese,1 Morten A. Karsdal,1 Rebecca A. Packington,3 Nicholas M. Selby,3 Fibrosis, Renal and Cardiovascular Research. Nordic Bioscience, Herlev, Denmark; 2Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark; 3Centre for Kidney Research and Innovation, University of Nottingham, Nottingham, United Kingdom.

**Background:** Acute kidney injury (AKI) is defined as a rapid decrease in kidney function which may be associated to structural damage. Early markers predicting AKI are emerging, but tools to monitor patients subsequent to AKI are still lacking. The novel biomarker PRO-C6 reflects formation of collagen type VI (COL6) and levels of endotrophin, a bioactive molecule derived from COL6. Here we evaluated the potential of PRO-C6 as a biomarker of mortality in AKI patients.

**Methods:** We measured PRO-C6 in plasma samples collected 1 year after the episode of AKI, using a novel ELISA in 801 patients from the AKI Risk in Derby (ARID) study, who were then followed prospectively until year three. 393 of the patients had been hospitalized for an episode of AKI, and 408 patients who did not sustain AKI were included as controls (non-AKI). The groups were matched for age, baseline renal function and diabetes.

**Results:** PRO-C6 levels were significantly higher in the AKI compared to the non-AKI group (median (m): 10.85 vs 9.23 ng/mL, P < 0.0001). By year 3, a total of 70 patients died; 43 in the AKI group and 27 in the control group. In the AKI group, patients who died had significantly higher PRO-C6 levels than the patients who did not die (m: 12.66 vs 10.68 ng/mL, P < 0.004), whereas there was no difference between patients who died and did not die in the non-AKI group (m: 9.97 vs 9.21 ng/mL, P = 0.234). In a Multivariable Cox regression analysis with backwards elimination including age, gender, baseline CKD and diabetes status, albuminuria, serum creatinine, eGFR and PRO-C6, only age (P = 0.04) and albuminuria (P = 0.007) remained in the final model for the non-AKI group. In the AKI group, PRO-C6 had a stronger association with mortality than eGFR, as only age (P = 0.005), albuminuria (P = 0.04) and PRO-C6 (P = 0.004) remained in the final model. When stratified into tertiles, patients with higher levels of PRO-C6 at year 1 were significantly more likely to die (P = 0.009).

**Conclusions:** In this study, we compared levels of PRO-C6 in patients with and without AKI, and show that PRO-C6 levels measured in plasma can predict mortality in patients with AKI. Our findings may indicate that PRO-C6 identifies patients with active fibrogenesis after AKI, suggesting that long-term renal injury after AKI is important for patient outcome.

**Funding:** NIDDK Support

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**FR-OR11**

**Association of Use of Kidney Disease Education Benefit with ESKD-Related Outcomes**


**Background:** ESKD onset in the US is marked by poor outcomes, including little use of home dialysis, widespread catheter dependence among patients on hemodialysis, and high mortality. Consequently, in 2010, the Centers for Medicare and Medicaid Services (CMS) initiated a new kidney disease education (KDE) benefit to ensure that beneficiaries with stage 4 CKD are informed about the effects and treatment of kidney disease, diet and nutrition, transplantation, dialysis modalities, and vascular access. Following the US president’s Executive Order on Advancing American Kidney Health in 2019, CMS plans to expand KDE. However, the current use and efficacy of KDE have not been examined.

**Methods:** We used USRDS data to identify eligible patients and to ascertain KDE and ESKD outcomes. We examined use of KDE in the 2 years prior to ESKD onset in 2013-2017 among 106,465 individuals aged ≥67 years who had CKD stage 4. We compared use and ESKD outcomes. We examined use of KDE in the 2 years prior to ESKD onset in 2013-2017 among 106,465 individuals aged ≥67 years who had CKD stage 4. We examined use and ESKD outcomes among patients with stage 4 CKD are informed about the effects and treatment of kidney disease, diet and nutrition, transplantation, dialysis modalities, and vascular access. Following the US president’s Executive Order on Advancing American Kidney Health in 2019, CMS plans to expand KDE. However, the current use and efficacy of KDE have not been examined.

**Results:** 3171 patients (3%) received KDE, 56% of whom received a single session. 49.5% of KDE sessions were delivered by nephrologists and 42% by physician extenders. Younger patients, men, and non-Hispanics were more likely to receive KDE. There was substantial regional variation in KDE utilization, and rural residents were less likely to receive KDE. In the matched cohort, receipt of KDE was associated with higher odds of transplant waiting before dialysis initiation, pre-emptive transplantation, home dialysis, or pre-center HD initiation with an AVF or AVG (vs. catheter, Table). Can be sustainably relevant to structural damage. Early markers predicting AKI are emerging, but tools to monitor patients subsequent to AKI are still lacking.

**Conclusions:** A very small percentage of eligible patients reaching dialysis receive Medicare-reimbursed KDE within the previous 2 years. KDE was associated with favorable outcomes, at least among those who advanced to ESKD.

**Funding:** NIDDK Support

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**Table:** Use of KDE and ESKD Outcomes among Patients With Stage 4 CKD Among patients with stage 4 CKD are informed about the effects and treatment of kidney disease, diet and nutrition, transplantation, dialysis modalities, and vascular access.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>KDE</th>
<th>No KDE</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant waiting prior to ESKD</td>
<td>0.88</td>
<td>0.95</td>
<td>1.41 (1.15 - 1.74)</td>
</tr>
<tr>
<td>Pre-emptive transplant</td>
<td>1.9</td>
<td>1.3</td>
<td>1.34 (1.00 - 1.80)</td>
</tr>
<tr>
<td>Home dialysis</td>
<td>11.8</td>
<td>17.1</td>
<td>1.70 (1.39 - 2.08)</td>
</tr>
<tr>
<td>Home dialysis with AVG or AVF</td>
<td>0.65</td>
<td>0.83</td>
<td>2.10 (1.84 - 2.39)</td>
</tr>
</tbody>
</table>

*Pre-emptive transplant or home dialysis or in-center HD with AVG or AVF

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Underline represents presenting author.
FR-OR12
Correlation Between Patient Activation and Quality of Life Among Patients with CKD
Penn State College of Medicine, Hershey, PA.

Background: Quality of Life (QOL) is an important outcome in patients with chronic kidney disease (CKD). We have previously demonstrated that online peer mentoring (PM) improves patient activation and QOL. In this study, we evaluate the correlation between patient activation and QOL among patients with CKD who received online PM.

Methods: We randomized 155 patients with stage 4 or stage 5 CKD to one of 3 groups: online PM, face-to-face (FTF) PM, or usual care. Participants in all 3 groups received a book that contained detailed information about kidney disease. Participants assigned to intervention groups received 6 months of PM, either FTF or through a secure online platform. At baseline and at 18 months, the participants completed the Patient Activation Measure® (PAM) and the Kidney Disease QOL-36 (KDQOL-36) instrument. We used linear mixed effect models to estimate the slope of change of PAM and subsets of KDQOL over time. Then we calculated the correlation between PAM and individual subscales of KDQOL by Pearson’s Correlation Coefficient. We used SAS, version 9.4 (SAS Institute Inc., Cary, NC) for data analysis.

Results: Baseline KDQOL-36 and PAM scores, as well as demographic characteristics were similar among the 3 groups. Among the online PM group, there was a statistically significant improvement in: 1. The mean PAM score between baseline and 18 months (Slope estimate [SE]: 5.65, 95% confidence interval [CI]: 2.75, 8.52; P= 0.0001). 2. The following components of the KDQOL-36 score: Effects of Kidney Disease (EKD) (SE: 4.13; CI: 3.67, 4.56; P= 0.01); Burden of Kidney Disease (BKD) (SE: 5.44; CI: 4.29, 6.59; P= 0.01); Symptoms and Problems of Kidney Disease (SPKD) (SE: 6.00; CI: 3.09, 8.91; p= 0.006); SF-12 Physical Composite Score (PCS) (SE: 2.50; CI: 0.95, 4.06; P= 0.002); SF-12 Mental Composite Score (MCS) (SE: 3.46; CI: 1.78, 5.13; P=0.0001). Among the online PM group, the improvement in PAM was correlated with improvements in 4 components of the KDQOL-36: EKD (Pearson Coefficient [PC]: 0.36; P=0.04); BKD (PC: 0.44; p=0.01); SPKD (PC: 0.47; P=0.005); PCS (PC: 0.35; p=0.04). There was no correlation between PAM and MCS.

Conclusions: Among CKD patients who receive online PM, there is a correlation between the improvements in PAM and KDQOL, suggesting that improved QOL may be a result of improved activation. Funding: PCORI

FR-OR13
Breath Ammonia Is a Useful Biomarker Predicting Kidney Function in CKD Patients
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Background: Chronic kidney disease (CKD) is a public health problem and its prevalence has increased worldwide; patients are commonly unaware of the condition. Early identification and immediate intervention are crucial to delay CKD progression. Finding a tool to predict kidney function without visiting hospitals is an attractive method for CKD monitoring in COVID-19 pandemic. The present study aimed to investigate whether exhaled breath ammonia measurement could be used for rapid CKD screening.

Methods: CKD patients (n=121), including CKD stage 1-5 patients, were enrolled and breath ammonia was detected. Correlation between breath ammonia and blood urea nitrogen (BUN) levels, serum creatinine levels, estimated glomerular filtration rate (eGFR) were determined. The predictive value of breath ammonia for the presence of CKD was assessed.

Results: Correlation analysis demonstrated a good correlation between breath ammonia and blood urea nitrogen levels (R=0.756, p<0.0001), serum creatinine levels (R=0.735, p<0.0001), eGFR (R=-0.535, p<0.0001) and inversed eGFR (R=-0.685, p<0.0001). Breath ammonia concentration was significantly elevated with increased CKD stage compared with the previous stage (CKD stage 1/2:34/4: 636±54; 102±120; 1943±326, 442±1042; 1278±1807 ppb, p<0.05). The receiver operating characteristic curve analysis showed an area under curve (AUC) of 0.835 (p<0.0001) for distinguishing CKD stage 1 from other CKD stages at 974 ppb (sensitivity, 69%; specificity, 95%, positive predictive value [PPV] 0.99; negative predictive value [NPV], 0.36). The AUC was 0.831 (p<0.0001) for distinguishing between patients with/without eGFR ≥60 mL/min/1.73 m2 (cut-off 1187 ppb: sensitivity, 71%; specificity, 78%; PPV, 0.84; NPV, 0.61). At 886 ppb, the sensitivity increased to 80% but the specificity decreased to 69%. For a non-life threatening and non-serious CKD, breath ammonia at a cut-off concentration of 886 ppm is a good screening tool for detection of patients with potential CKD and suitable for kidney function monitoring.

Conclusions: Because CKD is non-life threatening and breath ammonia detection was conducted in real-time, inexpensive, easy to administer, and had an acceptable diagnostic accuracy, breath ammonia can be used as a good surrogate for kidney function and a reliable tool for CKD screening.
Funding: Government Support - Non-U.S.

FR-OR14
Estimated Glomerular Filtration Rate Equations: Do We Need to Use the Ethnicity Correction Factor in People of African Ancestry Outside of the United States?
Rouvik Gama, Amanda Clery, Kieran R. Palmer, Henry A. Kibble, Hugh Cairns, Claire C. Sharpe, Adrien M. Peters, Neil Heraghthy, Kate Bramham, King’s College Hospital, London, United Kingdom; King’s College London, London, United Kingdom.

Background: Recent African studies suggest ethnicity factors in estimated glomerular filtration rate (eGFR) equations is not required.

Methods: To assess accuracy of eGFR equations, with and without ethnicity factors compared with gold standard 4Cr-ethylenediaminetetraacetic acid (4Cr-EDTA) clearance assays. Patients with albumin <30g/dl, hepatology referrals, <18 years old, non-white or black, mixed ethnicities were excluded. Accuracy of CKD-EPI and MDRD eGFR compared to 4Cr-EDTA GFR were assessed with and without correction factor.

Results: 2,776 4Cr-EDTA studies were identified (Mean age: 54yrs; 43% female; 12% Black ethnicity). In Black patients, CKD-EPI and MDRD eGFR equations significantly overestimated GFR compared to White (p<0.001) but without ethnicity correction factor estimates were considerably improved (p<0.001)(Table 1). Accuracy was superior for GFRs60ml/min/1.73m2 compared to <60ml/min/1.73m2 using CKD-EPI equation for both White and Black patients (p=0.001).

Conclusions: Overestimation of measured GFR with eGFR equations using ethnicity correction factors identified in this study may lead to reduced rates of CKD diagnosis and under-recognition of CKD severity in people of Black ethnicity in the UK. These findings require prospective validation in other countries.

Table 1: Estimated Glomerular Filtration Equations bias, precision and accuracy compared with 4Cr-EDTA clearance for people of Black and White ethnicities according to 4Cr-EDTA GFR categories

FR-OR15
Mechanism of Higher Incidence of ESKD Among Blacks and Hispanics vs. Whites in the United States
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Background: In the U.S., Blacks and Hispanics have higher incidence of ESKD than Whites. Whether this is driven by lower mortality prior to ESKD or inherently faster progression to ESKD has not been clearly determined because most studies used prevalent cohorts that created survival bias. We examined this issue using a newly constructed national cohort of patients with new-onset CKD.

Methods: We identified 834,270 individuals with new-onset CKD in the US Veterans Health Administration (VHA) between 2002 and 2015, followed through 2016. CKD onset was defined as the first occurrence when there were two eGFR values (CKD-EPI equation) <60 mL/min/1.73 m2 that were >90 days apart, not in ESKD. We excluded patients in VHA for <2 years follow-up. The time of study entry should be close to the CKD onset for each individual. We examined jointly the cause-specific (CS) hazards ratios for two competing events, occurrence of ESKD and pre-ESKD death.

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Results: Upon study entry, 704,557 Whites, 98,082 Blacks, and 31,631 Hispanics had similar mean eGFRs (49.50 ml/min/1.73m²). Ten years after CKD onset, fractions of patients entering ESKD were 1.3-2.5 times greater for Blacks and Hispanics vs. Whites across six age groups (Table). CS hazards for ESKD was 2.1-2.9 times greater for Blacks and 1.2-2.7 times greater for Hispanics vs. Whites. CS hazards for pre-ESKD death were similar for Blacks and only modestly lower for Hispanics vs. Whites across ages.

Conclusions: More Blacks and Hispanics to ESKD were driven by their greater hazards for ESKD due to more rapid decline in kidney function, not through lower mortality prior to ESKD. Delineation and elimination of the causes of faster kidney function declines are therefore the appropriate strategies to improve clinical outcomes in Blacks and Hispanics with CKD, instead of attributing the higher incidence to pre-ESKD survival bias.

Funding: NIDDK Support

Crude CS hazards ratios and 95% confidence intervals (CI) for ESKD and for pre-ESKD death

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<th>Age group</th>
<th>Black/White</th>
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<th>Pre-ESKD death hazard ratio (95% CI)</th>
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FR-OR16
Incidence of CKD and Environmental Inequities: An Integration of Ecological and Spatial Approaches in US Veterans
Yun Han,1 Jennifer L. Bragg-Gresham,1 Diane Steffick,1 Xiaosong Zhang,1 April Wyncott,1 Tiffany C. Veint,2 V. G. Vinod Vydiswaran,2 Brenda W. Gillespie,2 William Weitzel,1 Karandeep Singh,1 Susan T. Crowley,4 Rajiv Saran,1 1University of Michigan Medical School, Ann Arbor, MI; 2University of Michigan, Ann Arbor, MI; 3Veterans Health Administration, Ann Arbor, MI; 4Veterans Health Administration, West Haven, CT.

Background: Disparities in chronic kidney disease (CKD) can be linked to social and environmental determinants of health, which vary geographically across the US. We assessed geographic variation and the impact of environmental factors on incident CKD in US veterans.

Methods: We used a linked dataset from Veterans Health Administration (2014-18), the American Community Survey (2018); National Environmental Public Health Tracking Network (2018); EPA(2019) and Reference USA(2017). Incident cases of CKD were assessed geographic variation and the impact of environmental factors on incident CKD and environmental determinants of health, which vary geographically across the US. We applied to investigate the relationship between environmental factors and incidence rate of CKD.

Results: Average of incident rate of CKD was 34.8/1000 person-years (SD=12.3, n=2,718). Incident rate was higher in the rust-belt area and Appalachian region (Fig 1.b). PM2.5 was associated with higher incident rate (Fig 1.c).

Conclusions: Different environmental factors were associated with incident CKD in US counties. This highlights the potential importance of allocating resources for varied approaches to preventing and slowing the progression of CKD based on residence.

Funding: Veterans Affairs Support

FR-OR17
Chlorthalidone and Bumetanide in Advanced CKD: HEBE Trial
Fabio Solis-Jime涅z, L. M. Perez-Navarro, Rafael Valdez-Ortiz. Hospital General de Mexico Dr Eduardo Liceaga, Ciudad de Mexico, Mexico.

Background: Current treatment for hypertension and volume overload in chronic kidney disease consists of loop diuretics, nevertheless, chronic use leads to adaptive changes at the distal nephron, which in turn decreases their efficacy. The use of thiazide diuretics could be another treatment option in these patients, notwithstanding, there’s not enough evidence to justify their use in this population.

Methods: To evaluate the efficacy and safety of treatment with bumetanide plus chlorthalidone in patients with advanced chronic kidney disease a double-blind randomized controlled trial was conducted.

Results: Thirty-two patients with hypertension, chronic kidney disease stage IV/V, and chronic loop diuretic use where divided in two groups. The dual treatment group received bumetanide (2 mg BID) plus chlorthalidone (50 mg BID), while the control group was given chlorthalidone (2 mg BID) plus placebo, both for twenty-eight days. There was a decrease of systemic blood pressure in the dual treatment group when compared with the control group; systolic blood pressure -26.1±15.3 vs. -10±23.3 mmHg (p=0.028), diastolic blood pressure -13.5±10.7 vs. -3.4±11.9 mmHg (p=0.018), and mean arterial pressure -18.1±8.7 vs. -5.4±14.3 mmHg (p=0.006). There was also a decrease of volume overload in the dual treatment group when compared to the control group: total body water -4.3±3.29 vs. -0.7±0.78 liters (p=0.001), extracellular water -2.5±1.1 vs. -0.15±1.2 liters (p=0.001), and extracellular water to total body water ratio -2.9±2.76 vs. -0.24±2.42 (p=0.039).

Conclusions: In advanced chronic kidney disease plus hypertension patients whose treatment with loop diuretics is insufficient, combined use of bumetanide plus chlorthalidone can be useful for systemic blood pressure and volume overload control.

Funding: Commercial Support - Senosian

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Underline represents presenting author.
FR-OR18
Benefits of Icosapent Ethyl Across a Range of Baseline Renal Function in Patients with Established Cardiovascular Disease or Diabetes: Results of REDUCE-IT RENAL
Arjun Maithia,1 Deepak L. BHATT,2 Allan N. Friedman,2 Michael Miller,3 Philippe Gabriel Sieg,4 Eliot A. Brinton,5 Terry A. Jacobson,6 Stephen B. Ketchum,7 Rebecca A. Kettula,5 Licia Jiao,8 Ralph T. Doyle,9 Craig B. Granowitz,10 Matthew J. Badoff,10 Preston Mason,10 Jean-Claude Tardif,10 William E. Boden,4 Christie Ballantyne.4 REDUCE-IT Investigators 1Brigham and Women’s Hospital, Boston, MA; 2Indiana University School of Medicine, Indianapolis, IN; 3University of Maryland School of Medicine, Baltimore, MD; 4Hopital Bichat - Claude-Bernard, Paris, France; 5University of California Los Angeles, Los Angeles, CA; 6Baylor College of Medicine, Houston, TX; 7VA Puget Sound Health Care System, Seattle, WA; 8Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; 9VA Boston Healthcare System, West Roxbury, MA; 10Amarin Pharma Inc, Cambridge, MA.

Background: Chronic kidney disease is associated with adverse outcomes among patients with established cardiovascular disease (CVD) or diabetes. Medications for treatment of CVD among patients with low estimated glomerular filtration rate (eGFR) may be ineffective.

Methods: The Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) randomized patients with CVD or diabetes and one additional risk factor to treatment with icosapent ethyl or placebo. Patients from REDUCE-IT were categorized by prespecified eGFR categories for analysis of the effect of icosapent ethyl (IPE) on the primary endpoint (composite of cardiovascular (CV) death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina) and key secondary endpoint (a composite of CV death, nonfatal MI, or nonfatal stroke). In post hoc analysis, patients were categorized by additional eGFR cutoffs consistent with current medical guidelines.

Results: Among the 8179 REDUCE-IT patients, median baseline eGFR was 75 mL/min/1.73m² (range: 17 to 123 mL/min/1.73m²). There were no meaningful changes in median eGFR for IPE versus placebo across study visits. IPE benefit was consistent across baseline eGFR for the primary (Figure) and key secondary endpoints. The numerical reduction in CV death was greatest in the eGFR <60 mL/min/1.73m² group (IPE: 7.6%; placebo: 10.6%; HR 0.70, 95%CI 0.51, 0.95, p=0.02). The rate of microalbuminuria in adverse event reporting was lower among IPE-treated patients (0.1% versus 3.3%, p=0.01).

Conclusions: In REDUCE-IT, icosapent ethyl reduced fatal and nonfatal ischemic events across the broad range of baseline eGFR categories.

Funding: Commercial Support - Amarin

FR-OR19
Dapagliflozin Reduces the Risk of Hyperkalaemia in Patients with Heart Failure and Reduced Ejection Fraction: A Secondary Analysis from DAPA-HF
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Background: Hyperkalaemia often limits the use of mineralocorticoid receptor antagonists (MRAs) in patients with heart failure and reduced ejection fraction (HFrEF), denying these patients a life-saving therapy.

Methods: In a double-blinded randomized trial (NCT02252081), 50 patients with DAPA Stage 3, and MS and/or pre-diabetes, received either metformin or placebo for 16 weeks. Dosing was initiated at 500 mg and up-titrated over 7-14 days based on GI tolerance up to 1500 mg/day in CKD Stage 3a and 1000 mg/day in CKD 3b. Co-therapies for optimal CV risk reduction were continued. The co-primary outcomes included change in brachial artery flow-mediated dilation (FMD), aortic pulse-wave velocity (aPWV), and carotid intima-media thickness (CIMT) in common (CCA) and internal (ICA) carotid arteries, at 16 weeks. Lactic acid was obtained throughout the study for safety.

Results: Participants were 65 ± 10 years old and 80% were men. Mean (SD): BMI 31.4 ± 5.1 kg/m²; SBP 130.5 ± 16 mmHg; DBP 74 ± 9 mmHg; HDL 46.4 ± 15 mg/dl; fasting glucose (FG) 92.3 ± 10.3 mg/dl; Hba1c 5.7 ± 0.24%; HOBA-IR 2.4±1.5, and eGFR was 50 ± 7 ml/min/1.73 m². There were 18 patients (16%) in CKD Stage 3b, 3 in the metformin and 5 in the placebo group. Compared with placebo, metformin improved FMDbaseline (6.24% ± 4.5% [mean±SD], 16 weeks: 12.06% ± 8.4% [mean±SD]) with metformin and baseline: 6.12% ± 3.34% [mean±SD], 16 weeks: 7.6% ± 4.6% [mean±SD] with placebo, P=0.03 (Fig 1), without changing aPWV (P=0.84) or CIMT: R CAA (P=0.01) L CCA (P=0.96) R ICA (P=0.74) L ICA(P=0.44).

Conclusions: Treatment with metformin improved FMDbaseline but not aPWV or CIMT in patients with CKD and IR. Studies of larger sample size and longer duration are required to further evaluate the effects on cardiovascular outcomes.

Funding: Veterans Affairs Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

FR-OR20
Metformin Improves Vascular Function in CDK Patients with Metabolic Syndrome
Everly Ramos,1 Melis Sahinoz,1 Carlos O. Pena,2 Elvis A. Akwo,2 Christianne Romaine,2 Zhihong Yu,1 Edward D. Siew,2 Talat Alp Ikizler,2 Adriana Hung,2,3 Vanderbilt University Medical Center, Nashville, TN, 2Tennessee Valley Healthcare System, Nashville, TN, 3Universidad Central de Venezuela, Caracas, Venezuela, Bolivarian Republic of.

Background: Cardiovascular (CV) risk is increased in CKD. Insulin resistance (IR), highly prevalent in CKD patients, contributes to endothelial dysfunction and arterial stiffness, leading to poor CV outcomes. It remains unknown if insulin sensitization with metformin improves CV risk, in patients with CKD Stage 3-4 and metabolic syndrome (MS).

Methods: In a double-blinded randomized trial (NCT02252081), 50 patients with CKD Stage 3, and MS and/or pre-diabetes, received either metformin or placebo for 16 weeks. Dosing was initiated at 500 mg and up-titrated over 7-14 days based on GI tolerance up to 1500 mg/day in CKD Stage 3a and 1000 mg/day in CKD 3b. Co-therapies for optimal CV risk reduction were continued. The co-primary outcomes included change in brachial artery flow-mediated dilation (FMD), aortic pulse-wave velocity (aPWV), and carotid intima-media thickness (CIMT) in common (CCA) and internal (ICA) carotid arteries, at 16 weeks. Lactic acid was obtained throughout the study for safety.

Results: Participants were 65 ± 10 years old and 80% were men. Mean (SD): BMI 31.4 ± 5.1 kg/m²; SBP 130.5 ± 16 mmHg; DBP 74 ± 9 mmHg; HDL 46.4 ± 15 mg/dl; fasting glucose (FG) 92.3 ± 10.3 mg/dl; Hba1c 5.7 ± 0.24%; HOBA-IR 2.4±1.5, and eGFR was 50 ± 7 ml/min/1.73 m². There were 18 patients (16%) in CKD Stage 3b, 3 in the metformin and 5 in the placebo group. Compared with placebo, metformin improved FMDbaseline (6.24% ± 4.5% [mean±SD], 16 weeks: 12.06% ± 8.4% [mean±SD]) with metformin and baseline: 6.12% ± 3.34% [mean±SD], 16 weeks: 7.6% ± 4.6% [mean±SD] with placebo, P=0.03 (Fig 1), without changing aPWV (P=0.84) or CIMT: R CAA (P=0.01) L CCA (P=0.96) R ICA (P=0.74) L ICA(P=0.44).

Conclusions: Treatment with metformin improved FMDbaseline but not aPWV or CIMT in patients with CKD and IR. Studies of larger sample size and longer duration are required to further evaluate the effects on cardiovascular outcomes.

Funding: Veterans Affairs Support
FR-OR21
Associations Between Enrollment in ESRD Special Needs Plans and Outcomes
Bryan N. Becker,1 Jiacong Luo,2 Kathryn S. Gray,3 Carey Colson,4 Dena E. Cohen,1 Stephen D. McMurry,1 Bryan W. Gregory,1 Nathan Lohmeyer,5 Steven M. Brunelli,2 DaVita Integrated Kidney Care, Denver, CO; 2DaVita Clinical Research, Minneapolis, MN; 3DaVita Inc, Denver, CO.

Background: Chronic condition special needs plans (C-SPNs) are Medicare Advantage plans that offer care coordination and specialized services for patients with conditions such as end-stage renal disease (ESRD) via specific benefits packages and provider networks. Although ESRD C-SPNs have been offered for over 10 years, an understanding of their impact on patient outcomes is lacking.

Methods: This observational study considered dialysis patients receiving care at a large dialysis organization who enrolled in a C-SPN from January 2013 to September 2017; study data were derived from deidentified medical records. As of C-SPN enrollment date (or matched date for controls), enrollees and controls were matched on the basis of index month, sex, race, etiology, and dialysis modality, as well as a propensity score. Eligible controls were patients who (1) did not enter into the same facility as the C-SPN patient but had not enrolled in the C-SPN, (2) dialyzed in counties with no C-SPN but that were otherwise socio-demographically similar to C-SPN counties. Outcomes were evaluated from enrollment date through the first of study end (31 Dec 2018) or censoring for death, insurance change, or loss to follow-up. Within each matched cohort, outcomes were compared using generalized linear or Fine and Gray subdistribution hazard models.

Results: Hospitalization rates were 10% to 24% lower among C-SPN enrollees compared to controls, with an incidence rate ratio of 0.90 (95% confidence interval [CI] 0.84, 0.97) for patients in the same facility and 0.76 (95% CI 0.70, 0.83) for patients in similar counties. The mortality rate for C-SPN enrollees was approximately 23% lower than that of controls, with a hazard ratio of 0.77 (0.68, 0.88) for patients in the same facility and 0.77 (0.68, 0.88) for patients in similar counties. No meaningful differences were observed between groups with respect to serum calcium, phosphate, potassium, parathyroid hormone levels, or Kidney Disease Quality of Life scores.

Conclusions: C-SPN enrollment is associated with markedly lower rates of hospitalization and mortality, compared to non-enrollment.

FR-OR22
Organizational Characteristics Associated with High Performance in Medicare’s ESRD Seamless Care Organizations
Kelsey M. Dreyer1, Amal Trivedi,2 Adam S. Wilk,3 Emory University, Atlanta, GA; 4Brown University, Providence, RI.

Background: In 2016, the 1% of beneficiaries with end-stage renal disease (ESRD) constituted >7% of Medicare spending ($35 billion). To improve the value of care for the ESRD population, CMS implemented an alternative payment model (APM) for ESRD care, the ESRD Seamless Care Organization (ESCO), which shares savings with provider groups that reduce spending for ESRD patients below a defined benchmark. This study evaluated the relationship between key organizational, provider, and community characteristics, and ESCO performance.

Methods: We constructed a novel ESCO-level dataset capturing key information for Wave 2 (2017) ESCOs using data from CMS reports, the National Provider Identification registry, and the Area Health Resource File. After describing all 37 ESCOs, we performed bivariate comparisons of high- and low-performing (above vs below median) ESCOs based on gross savings/losses, composite quality score, and standardized mortality ratio (SMR). We then estimated generalized logistic regression models of ESCO performance as a function of organizational, provider, and community characteristics.

Results: ESCO composition and performance were highly varied (ranges: savings/losses −3.9 to 10.2%; quality 76.4-100%; SMR 0.75-1.14). Bivariate analysis showed that ESCOs with above (vs below) median savings had more aligned physicians (58 vs 29, p<0.006), fewer dialysis facilities (8.7 vs 17, p=0.07), a smaller non-Hispanic Black population (14% vs 22%, p<0.006), and a higher median household income ($55k vs $49k, p<0.001). Facilities reporting a quality score of 100% (vs <100%) had fewer practices (22 vs 43, p=0.05) and smaller non-Hispanic Black (16% vs 21%, p=0.06) and Medicaid eligible (6.5% vs 8.9%, p=0.14) populations. Low (vs above-median) SMR was associated with a higher median household income ($58k vs $46k, p<0.001). Regression model results were consistent with these findings, though small sample size prevented statistically significant estimates.

Conclusions: Our findings offer the first evidence of the impact of organizational composition and social disparities on ESCO performance. We show that the diversity in ESCO composition and settings partially explained the high variation in performance. This study provides crucial evidence that will inform the design and implementation of APMs in nephrology and the decisions of providers considering participation.

FR-OR23
Progress in Preventing Bloodstream Infections in Hemodialysis: Data from the National Healthcare Safety Network, 2014-2018
Shannon Novosad, Lucy V. Fike, Minn Soe, Shunte Moon, Preeti Ravindranith, Erika J. Woolfolk, Lauren Moccia, Duc B. Nguyen, Priti R. Patel. Centers for Disease Control and Prevention, Atlanta, GA.

Background: Patients on hemodialysis are at high risk of bloodstream infections (BSIs) and associated morbidity and mortality. National prevention efforts have resulted in widespread practice changes, including central venous catheter (CVC) care. We analyzed Dialysis Event Surveillance data submitted to the National Healthcare Safety Network (NHSN) to describe BSI rates among hemodialysis outpatients from 2014 to 2018.

Methods: Outpatient hemodialysis facilities report BSIs (positive blood cultures collected in the outpatient setting or within 1 day after hospital admission) and the number of hemodialysis patients treated during the first 2 working days of each month to NHSN. For each BSI, the suspected source and vascular access type [e.g., CVC, arteriovenous fistula (AVF) or arteriovenous graft (AVG)] are indicated. Pooled mean rates (per 100 patient-months) were calculated. Annual BSI rate trends were evaluated using a negative binomial regression model including access type, year, and an access-year interaction variable.

Results: More than 6,000 outpatient hemodialysis hemodialysis facilities reported 134,961 BSIs from 2014 to 2018. Of these BSIs, 102,505 (76%) were categorized as access-related. Pooled mean BSI rates decreased 27% from 0.64 to 0.47 per 100 patient-months. Significant decreases in rates occurred across vascular access strata (Table); the reduction was most pronounced among patients with CVCs. BSI rates in patients with CVCs decreased 32% from 2.16 per 100 patient-months to 1.46 (annual average decrease 9.5%).

Conclusions: Substantial reductions in BSI rates among hemodialysis patients occurred during this 5-year period. Improvements in infection prevention practices, including CVC care, have likely contributed. Efforts to increase uptake of known prevention practices and implementation of new strategies might contribute to continued decreases in infections.

Funding: Other U.S. Government Support

BSI rates per 100 patient-months and annual trends, by access type, NHSN 2014-2018

FR-OR24
Efficacy and Safety of Difelikefalin for Moderate-to-Severe CKD-Associated Pruritus: A Global Phase 3 Study in Hemodialysis Patients (KALM-2)
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Background: Chronic kidney disease (CKD)-associated pruritus (CKD-aP) is a common and distressing condition in CKD patients (pts) and has a serious negative impact on quality of life (QoL). Difelikefalin (DFK), a novel, peripherally restricted and selective kappa opioid receptor agonist, demonstrated efficacy in a US phase 3 study (KALM-1) in hemodialysis (HD) pts with CKD-aP. Here we report primary results from the global phase 3 study of DFK in HD pts with CKD-aP (KALM-2; NCT03632609).

Methods: HD pts with CKD-aP were randomized to receive intravenous DFK 0.5 mg/kg (N=237) or placebo (PBO; N=236) after dialysis sessions. The primary endpoint was the proportion of pts who achieved a ≥3-point improvement from baseline (BL) in the weekly mean of the daily Worst Itching Intensity Numerical Rating Scale (WI-NRS) score at wk 12. Secondary endpoints were the proportion of pts who achieved an ≥4-point improvement in WI-NRS score and mean change in itch-related QoL scores (5-D Itch and Skinindex-10) from BL to wk 12.

Results: BL mean weekly WI-NRS scores were 7.3 and 7.1 in the DFK and PBO groups. The primary endpoint was met, with 54% of pts who received DFK achieving ≥3-point improvement from baseline (BL) in the weekly mean of the daily Worst Itching Intensity Numerical Rating Scale (WI-NRS) score at wk 12. Secondary endpoints were the proportion of pts who achieved an ≥4-point improvement in WI-NRS score and mean change in itch-related QoL scores (5-D Itch and Skinindex-10) from BL to wk 12.

Results: BL mean weekly WI-NRS scores were 7.3 and 7.1 in the DFK and PBO groups. The primary endpoint was met, with 54% of pts who received DFK achieving ≥3-point improvement from baseline (BL) in the weekly mean of the daily Worst Itching Intensity Numerical Rating Scale (WI-NRS) score at wk 12. Secondary endpoints were the proportion of pts who achieved an ≥4-point improvement in WI-NRS score and mean change in itch-related QoL scores (5-D Itch and Skinindex-10) from BL to wk 12.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Online
Underline represents presenting author.

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a ≥3-point improvement in WI-NRS score vs 42% in the PBO group (P < 0.020). The proportion of pts who achieved a ≥4-point improvement in WI-NRS score was also significantly greater with DFK vs PBO (41 vs 28%, P < 0.010). Itch reduction was evident at wk 1 and was sustained through wk 12. Improvement in itch-related QoL assessed by 5-D Itch and SkinIndex-10 was observed. Treatment-emergent AEs ≥5% in DFK vs PBO were generally similar: 8.1% vs 5.5%, fall (6.6% vs 5.1%), dizziness (5.5% vs 5.1%), vomiting (6.4% vs 5.9%), and nausea (6.4% vs 4.2%). The incidence of serious AEs was similar across the groups.

Conclusions: In this phase 2 study, IV DFK demonstrated rapid and sustained itch reduction in HD pts with CKD-aP in multiple regions of the world. DFK was generally well tolerated, safety was consistent with findings in prior studies. With no approved therapies for CKD-aP in the US or Europe, DFK is a potential therapeutic that may address this unmet need.

Funding: Commercial Support - This study was funded by Cara Therapeutics

FR-OR25

Efficacy and Safety of Roxadustat in Patients with Dialysis-Dependent CKD and Anemia on Hemodialysis

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Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Dialysis modality in patients with ESRD may impact clinical outcomes and survival. Thus, evaluation of safety and efficacy of roxadustat in patients on hemodialysis (HD) is of clinical importance.

Methods: Pooled data from three pivotal, phase 3, randomized, open-label, epoetin alfa-controlled studies of roxadustat for the treatment of anemia in patients with dialysis-dependent CKD were assessed in the subgroup of patients on HD. Endpoint evaluations were: mean change from baseline (CBF) in hemoglobin (Hb) averaged over Weeks 28–52 regardless of rescue therapy and Hb CBF averaged over Weeks 28–36 for all adverse events (TEAEs).

Results: In the DD-CKD study population, 90% (3515/3887) of patients were on HD (roxadustat=1761, epoetin alfa=1754). Baseline characteristics were generally similar between treatment groups. Mean (SD) Hb levels (mg/dL) at baseline were 9.64 (1.31) in the roxadustat (SD) CKD group and 9.3 (1.31) in the epoetin alfa group. Patients achieved a larger mean (SD) CBF to Weeks 28–52 in HD with roxadustat vs. epoetin alfa (1.27 [1.49] vs. 0.98 [1.51]), corresponding to a least-squares mean (LSM) difference of 0.25 (95% CI: 0.16, 0.33) (p<0.0001). TEAE rates were comparable between treatment groups.

Conclusions: Roxadustat was efficacious vs. epoetin alfa for increasing and maintaining Hb levels in patients with HD on CKD on HD. The safety and tolerability profiles were similar to the overall population and consistent with that observed in this patient subgroup.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

FR-OR26

Stroke and Bleeding Risk Among US Veterans with Preexisting Atrial Fibrillation Transitioning to ESRD

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Background: Anticoagulation has been the mainstay of stroke prevention in patients with atrial fibrillation (AF). However, end stage renal disease (ESRD) patients on hemodialysis are at higher risk of bleeding and stroke outcomes, even without anticoagulation. It is unclear if patients should be continued on anticoagulation at the time of transition to ESRD.

Methods: We retrospectively examined a cohort consisting of 29,054 pre-dialysis US veterans that had a diagnosis of AF prior to transition to ESRD without a history of anticoagulation. It is unclear if patients should be continued on anticoagulation at the time of transition to ESRD. Incidence Rate Ratios (IRR) for stroke and bleeding outcomes among other ESRD patients with AF transitioning to dialysis regardless of CHA2DS2-VASC and HAS-BLED scores.

Methods: We specified the US ESKD population in Dec. 2018 and used Markov chain Monte Carlo methods to randomly assign patients to a dialytic modality, transplant, or death each month until Dec. 2030, according to parameters that regulate the inflow and outflow of each state. Incident ESKD patients entered the cohort each month and were subject to the same transition parameters. We assessed how changing transition parameters affects projected dialytic modality distributions.

Results: By prevailing conditions, the simulation projects home dialysis will comprise 12% of the dialysis population in 2025. Increasing home hemodialysis (HD) and peritoneal dialysis (PD) utilization among incident ESKD patients from rates of 0.3% to 7.5% and from 11.5% to 37.5%, respectively, by 2025 results in home dialysis utilization of 25% in 2025 and 29% in 2030. Concurrently increasing the rate of conversion from in-center HD to home dialysis from 3.0 to 15.0 events per 100 patient-years by 2025 results in home dialysis utilization of 37% in 2025 and 44% in 2030, as displayed. Decreasing home dialysis attrition rates has a smaller effect on home dialysis utilization.

Conclusions: Substantial growth of home dialysis utilization in the next decade will require a two-pronged approach to inflow: higher utilization of home dialysis in incident patients, emphasizing PD, and increased conversion of patients from in-center HD to home dialysis.

Funding: Commercial Support - Fresenius Medical Care
The absolute number of hospitalizations for each day of the week was reported for each treatment type and differences in the distribution of hospitalizations were compared using the Chi-Square test.

**Results:** The cohort consisted of 36,334 individuals. Median age was 67 and 61% were of male sex. A total of 81% of patients were receiving hemodialysis at dialysis initiation and the cause of end-stage kidney disease was secondary to diabetes in 37%. Overall, there were 119,466 hospitalizations over the observation period. The cumulative number of hospitalizations was highest for conventional in-center HD (92,707) and lowest for conventional home HD (701). Day of the week the admissions for each treatment type are noted in Table 1 (P<0.001). Hospitalizations were least frequent on Saturday and Sunday for all groups. The proportion of admissions was highest on Monday or Tuesday for conventional HD (regardless of location) and frequent in-center HD. In contrast, frequent home HD had a higher proportion of admissions on Wednesday.

**Conclusions:** There are daily variations in hospitalization comparing dialysis modalities. Future planned analyses will evaluate whether there are adjusted differences in day of the week hospitalization across modalities accounting for differences in patient characteristics.

**FR-OR29**

Improving Supportive Care of Seriously Ill Dialysis Patients with Goals-of-Care Conversations

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**Background:** Dialysis patients are frequently known to receive unwanted high intensity end-of-life care. Families rate the quality of this care lower than families of patients with other chronic diseases. The purpose of this study was to test the feasibility of a supportive care intervention—the Pathways Project, an evidence-based change package of best practices—to identify seriously ill patients (SI), engage them in goals of care discussions, and track outcomes for patient goal concordance.

**Methods:** Pathways researchers recruited 10 dialysis centers with 1,546 patients. Dialysis staff screened patients with the surprise question (SQ): “Would you be surprised if this patient died in the next 6-12 months?” to identify those who were SI and recorded patient outcomes including the number screened, SI, goals of care conversations, hospitalizations, referred to hospice, death, and place of death. An odds ratio was calculated for the odds of SI dying versus those who were not SI, and one-sided Cochran-Armitage trend tests were used to assess for increasing goals of care conversations and deaths at home. The study was interrupted at 9 months due to COVID-19.

**Results:** On average, 98.8% of patients were screened monthly, and 18.4% were identified as SI. Of 114 patients who died, the SI constituted 66% of deaths though only 18.4% of patients. The mortality for the SI was 27% versus 3% for those who were not, and the odds ratio for SI dying was 11.22 (95% CI 7.42 to 16.98, P < .0001). Dialysis interdisciplinary teams implemented site-specific approaches to adding goals of care conversations into usual workflow; the number conducting conversations with SI within 30 days of hospital discharge increased from 30% to 80% (P = .02). The proportion of the patients who died at home in the last 2 months was higher than baseline (32.6% vs 18.8%), but a trend was not yet evident (P = .12).

**Conclusions:** The Pathways intervention is feasible to implement supportive care best practices into existing workflow of dialysis centers. It takes time for teams to get comfortable with new processes and communication approaches; after 9 months more centers were conducting goals of care conversations and more patients were dying at home. Future research is needed to determine if the Pathways intervention results in outcomes more aligned with patient preferences.

**Funding:** Private Foundation Support

**FR-OR30**

Implementation of a Decision Aid for Recognition and Correction of Volume Alterations (Recova®) in Hemodialysis

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**Background:** Chronic fluid overload is an independent predictor of mortality in hemodialysis. Clinical assessment of fluid status is subjective and unprecise, and 30% of the patients remain fluid overloaded at dry weight. This study evaluates the effects of implementing a recently developed decision aid, Recova®, which combines a systematized fluid status procedure with bioimpedance spectroscopy, for individualized dry weight determination in hemodialysis.

**Methods:** The study was a prospective implementation intervention carried out at two hemodialysis units. The impact of the intervention was measured as the proportion of participants at an adequate dry weight at the end of the study, assessed as change in symptoms, hydration status, and N-terminal pro-brain natriuretic peptide (NT-proBNP). Hemodialysis nurses were instructed to use Recova® every two weeks, assessing the study participants’ fluid status and adjusting their dry weights as appropriate. The process of the intervention was measured as frequencies of fluid status assessments, bioimpedance measurements, and dry weight adjustments.

**Results:** Forty-nine patients were enrolled. In participants with fluid overload (n = 10), both bioimpedance-measured overhydration and fluid overload symptom score decreased. In fluid-depleted participants (n = 20), dry weight adjustment frequency and dry weight increased. The post-dialytic negative overhydration was reduced, but NT-proBNP increased. In the remaining 19 participants, with low volume status scores, no significant changes were observed.

**Conclusions:** Recova® defines how and when dry weight should be evaluated in hemodialysis patients. Its purpose is to provide the multidisciplinary team with a common language, and thereby facilitate early recognition and appropriate response to fluid alterations. Implementation of Recova® in hemodialysis care increased the monthly frequencies of bioimpedance measurements and dry weight adjustments, and contributed to symptom reduction.

**Funding:** Clinical Revenue Support, Government Support - Non-U.S.

**FR-OR31**

Development of Alport-Syndrome-on-a-Chip to Study the Glomerular Filtration Barrier Pathophysiology

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**Background:** Alport Syndrome (AS) is a genetic disorder in which podocytes fail to correctly assemble the COL4a3c4a4c5 trimer, a major constituent of the GBM. Disruption of the GBM network leads to podocyte depletion and progressive kidney failure. While important advances in our understanding of AS progression have been made possible by animal models, we still lack an efficient and faithful in vitro model that can mimic the human AS disease. We have recently developed a glomerulus-on-a-chip system (GOAC) that replicates the features of the glomerular filtration barrier and generated AS chips by combining this novel tool with COL4-defective podocytes.

**Methods:** Podocytes derived from amniotic fluid of patients affected by AS (APD) were seeded with human glomerular endothelial cells (hGEC) on Organoplates in a barrier-free system to generate AS-GOAC. The system was assayed by confocal microscopy, WB, proteomics and RNA-seq. Permeability was assessed by measuring albumin leakage. Transcriptomics studies were performed on podocytes by RNA-seq and qPCR and results confirmed in vivo in a mouse model of AS. Primary human podocytes were used as control.

**Results:** We confirmed AS phenotype in AS-POD by RNA-seq and WB. GOAC generated with AS-POD show absence of COL4A3-4-5 confirmed by WB. AS-GOAC
present impaired permeability to albumin, due to a dysfunctional assembly of the GBM, typically with high-grade vesicoureteral reflux (VUR). Our research has identified key targets known to target key players in AS and CKD like WT1, osteopontin, vinculin as well as VEGF and TGFβ pathways. Results were confirmed in vivo in glomeruli of AS mice, further validating the AS-GOAC as an efficient tool for AS studies. Proteomics analysis of the filtrate and the collected urinary proteins showed a distinct signature in AS-GOAC, including presence of apolipoprotein A, α1-antitrypsin and β2-glycoprotein I.

Conclusions: We have successfully developed an Alport-on-a-chip system that closely mimics the GBM structure and provides a powerful tool for studying the effect of AS on the GBM at the molecular level. We have also identified some specific AS proteins, indicative of disease manifestation. This system has the potential to improve our knowledge on AS pathophysiology, allowing novel therapeutic targets and a transformative tool, thus ultimately benefiting patients affected by renal failure.

Funding: Private Foundation Support

FR-OR32

Development of a Personalized Medicine Platform for Non-stop RTD Therapy in Alport Syndrome

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Background: Alport syndrome (AS) is characterized by glomerular basement membrane (GBM) abnormalities leading to progressive glomerulosclerosis. Mutations in the COL4A3, COL4A4 or COL4A5 genes encoding type IV collagen α3(α4)5α5(α5) are responsible for AS. Nonsense mutations resulting in premature termination codons (PTCs) account for about 65% of AS cases. Type IV collagen chains have a C-terminal NC1 domain, which is essential for assembly of GBM and for network formation in the GBM. Truncated α3(α4)5α5 chains without an intact NC1 domain due to PTCs cannot assemble in the GBM. Therefore, achieving full-length protein expression is a potential therapy for AS due to nonsense mutations. Small compound-based nonsense readthrough therapies have been studied in other genetic diseases, but whether nonsense readthrough therapy is applicable to Alport syndrome is unexplored.

Methods: To investigate the feasibility of PTC readthrough in AS, we made a C-terminal NanoLuc-fusion COL4A5 reporter cDNA to monitor full-length translation. The full-length COL4A5-NLuc produces luminescence, but truncated forms do not. To screen for COL4A5 nonsense mutants susceptible to PTC readthrough therapy, we introduced 49 nonsense mutations found in X-linked AS patients into the COL4A5-NLuc gene. We transfected these individually into HEK293 cells and measured luminescence in individual wells. The GBM in the New Zealand Golden (NZ) rat is known to have high residual activity.

Results: The COL4A5-NLuc gene produced luminescence when wild type, but not when carrying COL4A5 nonsense mutations. Among 49 nonsense mutants, we found that 11 were susceptible to PTC readthrough. The efficacy of readthrough was higher for UGA nonsense codons than for UAG and UAA. Gentiamicin also induced readthrough of these same 11 PTCs.

Conclusions: We found 11 nonsense mutations in COL4A5 susceptible to PTC readthrough drugs. This luciferase-based COL4A5 translation reporter system will contribute to the development of PTC readthrough therapy in a personalized medicine approach to treating AS.

Funding: NIDDK Support

FR-OR33

A ROBO2 Fusion Protein (PF-06730512) Traps SLIT Ligands and Therapeutically Ameliorates Podocyte Injury

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Background: ROBO2/SLIT2 signaling negatively regulates nephrin-induced actin polymerization and destabilizes podocyte focal attachments and adherence to the glomerular basement membrane (GBM) by inhibiting non-muscle myosin II A. Lack of ROBO2 in podocytes are protected from podocyte injury. Based on these findings we hypothesized that blocking this pathway might have therapeutic potential in podocyte pathologies. Here, we present preliminary evidence to support our hypothesis from a case with a genetic defect in ROBO2 and a rodent model of podocyte injury.

Methods: We investigated a patient with a chromosomal translocation that disrupted the ROBO2 gene, produced transcripts encoding dominant negative proteins, and caused high-grade vescoureteral reflux (VUR). We designed a novel therapeutic ROBO2 fusion protein (ROBO2-Fc, PF-06730512) that inhibits the ROBO2/SLIT2 pathway. In vivo efficacy of ROBO2-Fc was tested in the rat Passive Heymann Nephritis (PHN) model. We also studied the molecular and cellular functions of SLIT2 in kidney glomeruli.

Results: In contrast to most adults with long-standing VUR that develop focal segmental glomerulosclerosis (FSGS) and proteinuria, the patient with a disrupted ROBO2 gene had stable renal function without proteinuria. In vitro, ROBO2-Fc bound to SLIT ligands with high affinity and dose-dependently inhibited SLIT binding to cell surface ROBO2, and it inhibited ROBO2-dependent cell migration ex vivo. ROBO2-Fc has a 35% half-life of about 8 hours in rats and 5 days in monkey. Treatment with ROBO2-Fc reduced proteinuria, shortened podocyte foot process width, and increased slit-diaphragm density in the rat PHN model. Mechanistically, we found that SLIT2 is localized to the GBM and binds to COL4A3/4 laminin to inhibit podocyte adhesion.

Conclusions: We have generated a novel therapeutic ROBO2 fusion protein that functions as a SLIT ligand trap to treat podocyte injury in a clinical model. Inhibiting the ROBO2/SLIT2 pathway therapeutically reduces proteinuria and improves podocyte ultrastructure. A phase 2 clinical trial to evaluate the safety and efficacy of ROBO2-Fc (PF-06730512) in patients with FSGS is currently ongoing (NCT03448692).

Funding: Other NIH Support - National Institute of Health (NIH), Commercial Support - Pfizer Inc.

FR-OR34

Semaphorin 3B-Associated Membranous Nephropathy

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Background: Membranous nephropathy (MN) results from subepithelial anti-β3 integrin complex deposition along the glomerular basement membrane (GBM). Although PLA2R, THSD7A, and NELL1 account for a majority (approximately 80%) of the target antigens, the target antigen in the remaining MN is not known.

Methods: We performed laser microdissection and mass spectrometry (MS) of glomeruli in kidney biopsies of 70 cases of PLA2R-negative MN. We detected high spectral counts of a unique protein Semaphorin 3B (Sema3B) in 3 cases. Immunohistochemistry (IHC) for Sema3B was then performed to confirm MS results. Next, we analyzed 332 Sema3B-positive cases and 118 PLA2R-negative MN cases by immunofluorescence microscopy (IF). Confocal microscopy studies were done to confirm colocalization of IgG and Sema3B along the GBM. Next, serum antibodies were detected by Western blotting (WB).

Results: MS identified a unique protein, Sema3B in 3 cases of PLA2R-negative MN. MS failed to detect Sema3B in the remaining 67 PLA2R-negative MN, in 23 PLA2R-associated MN, and 88 controls that included IgA nephropathy, diabetes, FSGS and undefined chronic disease. Semaphorin 3B antibody levels were significantly higher for Sema3B-positive cases compared to PLA2R-negative MN.

Conclusions: Semaphorin 3B-associated MN is a distinct type of MN, and is predominantly present in pediatric patients.

Figure 1 shows bright granular capillary wall staining for Sema3B in 3 cases of Sema3B-associated MN.

FR-OR35

High Temperature Recombinant Protein A1 (HTRA1): A Novel Antigen in Membranous Nephropathy

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Conclusions: Semaphorin 3B-associated MN is a distinct type of MN, and is predominantly present in pediatric patients.

Methods: We present a multi-approach approach using traditional and modern technologies to converge on a novel target antigen. Instead of a case-vs-control design, we capitalized on the temporal variation in autoantibody titer for our biomarker discovery. Western blotting (WB) of human glomerular extract (HGE) proteins followed by differential immunoprecipitation and mass spectrometry analysis was complemented by laser-capture microdissection / mass spectrometry as well as autoimmune profiling on a protein expressed sequence tag microarray. Commercial antibodies to the candidate antigen were used for immunostaining MN biopsies, and reactivity of patient sera with a recombinant HTRA1 (HTRA1) by WB and ELISA was assessed.

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Glomerular Diseases: Charting New Territory

Protocadherin 7-Associated Membranous Nephropathy

of PCDH7-associated MN, and negative staining in a case (D) of PLA2R-negative MN. Figure 1 shows bright granular capillary wall staining for PCDH7 in 3 cases (A, B, C) of PCDH7-associated MN, and negative staining in a case (D) of PLA2R-negative MN.

Results: Using these combined approaches, we identified HTRA1 as a novel antigen in a subset of patients with primary MN. Serum from these patients reacted with WB with a 51 kDa protein in non-reduced HGE as well as HTRA1, which correlated with clinical disease activity.(Fig A and B) Consistent with PLA2R and THSD7A, anti-HTRA1 antibodies were predominantly IgG4. HTRA1 specifically was detected in a capillary loop fine granular pattern. (Fig C) and colociliated with IgG4. Whole-proteome peptide microarrays detected significantly higher titer (6.9 SD) of anti-HTRA1 antibody in the active stage as opposed to the remission stage which was informative of its candidacy as a podocyte targeted protein. We have 3 confirmed cases of HTRA1-associated MN and are currently screening several large biopsy cohorts of MN that are negative for PLA2R, THSD7A, and NELL-1 to better assess the prevalence of this novel form of MN.

Conclusions: This report demonstrates the convergence of conventional with more modern techniques to identify HTRA1 as a target podocyte antigen in MN.

Funding: Private Foundation Support

FR-OR36
Protocadherin 7-Associated Membranous Nephropathy
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Background: Membranous nephropathy (MN) results from subepithelial antigen-antibody complex deposition along the glomerular basement membrane (GBM). Although PLA2R, THSD7A, and NELL-1 account for a majority (approximately 80%) of the target antigens, the target antigen in the remaining MN is not known.

Methods: We performed laser microdissection and mass spectrometry (MS) of glomeruli in kidney biopsies of 85 cases of PLA2R-negative MN. We detected high spectral counts of a unique protein Protocadherin 7 (PCDH7) in 8 cases. Immunohistochemistry (IHC) for PCDH7 was then performed to confirm MS results.

Results: MS identified a unique protein, PCDH7 in 8 cases (9.4%) of PLA2R-negative MN. MS failed to detect PCDH7 in remaining 77 PLA2R-negative MN, 23 PLA2R-positive MN, and 88 controls that included IgA nephropathy, diabetes, FSGS and minimal change disease. Among the 77 PLA2R-negative MN, MS detected NELL1 (14 cases), EXT1/EXT2 (6 cases), PLA2R (4 cases labeled PLA2R-negative on IF), Sema3B (3 cases), THSD7A (2 cases), and DNAJH9 (4 cases of fibrillary GN, misdiagnosed as MN as EM was not done). PCDH7 localized as granular deposits along the GBM by IHC (Figure 1). Kidney biopsy showed a grade II MN in 6 cases, grade I in 1 and grade III in 1 case. Immunofluorescence microscopy showed GBM staining for IgG and C3 in all cases. IgG subtyping done in 2 cases showed IgG4 in both. The mean age was 64 years (+/-11) and 7 of the 8 patients were males. The average serum creatinine and proteinuria was 1.28 mg/dL (+/-0.3) and 4.9 gm/L (+/-3.0), respectively. Interestingly, 3 of 8 cases had associated malignancies. Further studies including evaluation for circulating antibodies are ongoing.

Conclusions: Protocadherin 7-associated MN may represent distinct type of MN.

FR-OR37
Nefecon® (Budesonide) Selectively Reduces Circulating Levels of BAFF (BLYS) and Soluble BCMA and TACI in IgA Nephropathy
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Background: Evidence supports a pivotal role for gut-associated lymphoid tissue (GALT) as a major source of poorly O-galactosylated immunoglobulin A (IgA) 1 in patients with IgA nephropathy (IgAN). IgA synthesis in GALT is regulated by B-cell activating factor (BAFF) [B-lymphocyte stimulator (BLYS)] and APRIL, a proliferation-inducing ligand (APRIL). BAFF and APRIL bind to specific cell-surface receptors: transmembrane activator and calcium modulator and cyclophilin-Ligand (TACI), B-cell maturation antigen (BCMA), and the BAFF receptor. Elevated levels of BAFF and APRIL have been linked to worse clinical outcomes in IgAN. The therapeutic potential of targeting GALT was demonstrated in the NEFIGAN trial (NCT01738035), which assessed the efficacy of a novel targeted-receptor formulation of budesonide (Nefecon®), designed to deliver budesonide to the GALT-rich distal ileum in patients with IgAN. The trial comprised 6-month run-in, 9-month treatment, and 3-month follow-up phases: 48 patients received Nefecon® 16 mg/day, 51 patients received Nefecon® 8 mg/day, and 50 patients received placebo. As a result, Nefecon® 16 mg/day, added to optimised renin–angiotensin system blockade, reduced proteinuria and stabilized estimated glomerular filtration rate in patients with IgAN. This study investigated whether Nefecon® treatment altered serum levels of BAFF and APRIL and their receptors.

Methods: Serum levels of BAFF, APRIL, BCMA, and TACI were measured using Luminex technology. Changes in the levels of BAFF and APRIL were compared using a one-way analysis of variance. Significance was set as p<0.05.

Results: A significant, dose-dependent reduction in serum BAFF levels was seen with Nefecon®, which reversed on cessation of Nefecon®. There were similar significant reductions in the levels of soluble BCMA and TACI with treatment, but no effect was seen on circulating levels of APRIL. These changes were mirrored by parallel changes in soluble CD27 levels and were consistent with our previous reports on dose-dependent reductions in circulating IgA-IgG immune complexes, secretory IgA, and galactose-deficient IgA-IgG levels with Nefecon®.

Conclusions: Delivering budesonide to the GALT-rich distal ileum modules key regulators of GALT B-cell maturation and IgA class switch recombination in patients with IgAN.

Funding: Commercial Support - Calliditas

FR-OR38
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Background: Selective inhibition of the immunoproteasome blocks progression of nephritis in a mouse model of systemic lupus erythematosus (SLE). Here we describe the effects of KZR-616 in this model and in patients from MISSION (KZR-616-002; NCT03393013), an open-label study of KZR-616 in patients with SLE with and without nephritis.

Methods: 24-week old NZB/W mice were treated weekly with subcutaneous administration of 5 mg/kg KZR-616 for 11 weeks. SLE patients with active disease and stable background medication (N=34) were dosed subcutaneously with KZR-616 at 30, 45 or 60 mg weekly for 13 weeks with a 12-week follow-up. Clinical samples were evaluated for proteasome subunit binding, and immune cell profile was evaluated by flow cytometry. Gene expression analysis was performed by RNaseq in mouse tissue (whole blood, spleen, and kidneys) and patient (whole blood) samples.

Results: KZR-616 treatment resulted in complete resolution of proteinuria, prevention of glomerular damage, and absence of renal IgG deposition. Depletion of splenic activated T- and B-cells and short and long-lived plasma cells in treated animals was noted and correlated with decreased gene expression associated with inflammation, T helper (Th) 1 and Th17 pathways, interferon signaling, antibody secreting cells, and differentiation of plasma cells (PC). KZR-616 reduced kidney tissue transcripts associated with inflammation, cell and myeloid glomerulus trafficking and renal genes implicated in LN pathogenesis. In SLE patients, KZR-616 treatment was determined to be safe and tolerated at all dose levels and reductions in disease activity parameters were noted. KZR-616 treatment was associated with a reduction in class-switched memory B cells and PC in peripheral blood. Decreased expression of gene modules for PC, T-cell activation, inflammation, neutrophil, and type I IFN responses were seen in response to treatment.

Conclusions: KZR-616 resolves nephritis in a mouse model of SLE/LN by regulating immunoproteasome subunit gene expression and glomerular injury. In SLE patients, KZR-616 demonstrated broad anti-inflammatory activity across T, B, and innate immune effector cells. These results support further clinical evaluation of KZR-616 in patients with LN.

Funding: Commercial Support - Kezar Life Sciences
FR-OR39
NCAM1 Is an Autoantigen in Membranous Lupus Nephritis
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Background: Membranous lupus nephritis is a frequent cause of proteinuria in patients with systemic lupus erythematosus. In patients with membranous lupus nephritis, the target autoantigens are largely unknown. Determination of a target autoantigen can have diagnostic significance, inform prognosis, and enable non-invasive monitoring of disease activity. We utilized mass spectrometry to identify target autoantigens in membranous lupus nephritis and report cell neural adhesion molecule-1 (NCAM1) as a novel target podocyte antigen.

Methods: We utilized mass spectrometry for antigen discovery of laser capture microdissected (LCMD) glomeruli and protein G immunoprecipitation studies to interrogate immune complexes. Confocal microscopy was used to examine co-localization with IgG within glomerular immune deposits. Case series of biopsies from PLA2R-negative membranous nephropathy patients (n=101) and patients with membranous lupus nephritis (n=212) were used to determine the overall frequency of these antigens. Western blotting detecting patient sera against recombinant NCAM1 protein was used to detect circulating anti-NCAM1 antibodies.

Results: NCAM1 was uniquely identified in a subset of patients with membranous lupus nephritis in LCMD glomeruli and protein G immunoprecipitations by mass spectrometry. NCAM1 was co-localized with IgG within glomerular immune deposits. The prevalence of NCAM1 positivity by immunofluorescence was 6.1% of cases of membranous lupus nephritis and 2.0% of idiopathic membranous nephropathy cases. Additionally, serum from NCAM1 patients showed reactivity to NCAM1 recombinant protein, demonstrating the presence of circulating autoantibodies.

Conclusions: We propose that NCAM1, a cytoskeleton-linked transmembrane protein, is a target autoantigen in a subset of patients with membranous lupus nephritis and within rare cases of idiopathic membranous nephropathy. The presence of anti-NCAM1 antibodies in urine could allow for non-invasive monitoring.

Funding: Other NIH Support - SBIR funding from the National Institute on Minority Health and Health Disparities, awarded to Dr. Christopher Larsen

FR-OR40
Alpha1-Antitrypsin Diminishes Neutrophil Activation by PR3-ANCA
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Background: Neutrophil serine proteases (NSPs) contribute to ANCA-associated vasculitis (AAV). PR3 is a unique NSF family member because it is both a proteolytic enzyme and an ANCA antigen. Alpha1-antitrypsin (AAT) is the major natural NSP inhibitor. We hypothesized that AAT protects from ANCA-induced neutrophil activation and neutrophil-mediated glomerular endothelial cell injury.

Methods: We produced wild-type (wt) AAT and a mutant (μm) form that does not inhibit proteolytic NSP activity. We used flow cytometry to study membrane PR3 (mPR3) and MPO (mMPO), ferricchiochrome C assay for superoxide release, FRET assays for proteolytic NSP activity, human neutrophils and glomerular microvascular endothelial cells (gMVEC) for transcriptional and electron microscopy, and assessed ECs by phallodin staining and gene expression.

Results: Wt-AAT reduced mPR3 on TNF-primed neutrophils dose-dependently from 0.1 to 10 μM (n=3). Five μM wt-AAT, but not μm-AAT, reduced neutrophil mPR3 in suspension, on fibronectin, and on an EC monolayer to approximately 25% (n=3). Parallel comparisons in neutrophil-EC co-cultures using antibodies to different PR3 epitopes showed that 5 μM AAT reduced mPR3 but not mMPO. Importantly, reduced mPR3 by AAT resulted in significantly less superoxide release by TNFα-primed neutrophils that activated with PR3-, but not with MPO-ANCA IgG from AA V patients (n=4). Next, we studied the NSP transfer from activated neutrophils to gMVEC and found that gMVEC increased NSP concentrations, exemplified by PR3 from both cell-free supernatants (cf-SN) and under neutrophil-EC co-culture conditions. Importantly, wt-, but not μm-AAT abrogated the PR3 transfer from cf-SN. In contrast, AAT did not inhibit the PR3 transfer under neutrophil-EC co-culture conditions. Finally, we observed by RT-PCR that cf-SN from activated neutrophils increased two NF-kB dependent genes in gMVEC, namely IkBα and IL-8. This effect was reduced by wt-, but not by μm-AAT suggesting an NSF-dependent activation mechanism.

Conclusions: AAT has protective effects by reducing neutrophil activation in response to PR3-ANCA, and NSF-mediated glomerular microvascular endothelial cell injury. Disturbances of the AAT-NSP balance possibly contribute to neutrophil-mediated vascular injury in AAV, particularly, but not exclusively, in patients with PR3-ANCA.

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FR-OR41
Harnessing Expressed Single-Nucleotide Variation and Single-Cell RNA Sequencing to Define Immune Cell Chimerism in the Rejecting Kidney Transplant
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Background: In solid organ transplantation, donor derived immune cells are assumed to decline with time after surgery. Whether donor leukocytes persist within kidney transplants or play any role in rejection is unknown, however, in part because of limited techniques for distinguishing recipient and donor cells.

Methods: We performed paired whole exome sequencing of donor and recipient DNA and single cell RNA sequencing (scRNA-seq) of human kidney transplant biopsy cores. Exome sequences were used to define single nucleotide variants (SNV) across all samples.

Results: By analyzing expressed SNVs in the scRNA-seq dataset we could define recipient vs. donor cell origin for all 81,139 cells. The leukocyte donor to recipient ratio varied with rejection status for macrophages and with time post-transplant for lymphocytes. Recipient macrophages were characterized by inflammatory activation and donor macrophages by antigen presentation and complement signaling. Recipient origin T cells expressed cytotoxic and pro-inflammatory genes consistent with an effector cell phenotype whereas donor origin T cells are likely quiescent expressing oxidative phosphorylation genes relative to recipient T cells. Finally, both donor and recipient T cell clones were present within the rejecting kidney, suggesting lymphoid aggregation. Our results indicate that donor origin macrophages and T cells have distinct transcriptional profiles compared to their recipient counterparts and donor macrophages can persist for years post transplantation.

Conclusions: This study demonstrates the power of this approach to accurately define leukocyte chimerism in a complex tissue such as the kidney transplant coupled with the ability to examine transcriptional profiles at single cell resolution.

Funding: NIDDK Support, Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: We found 107 glomerular and 112 tubulointerstitial proteins significantly differentially expressed in AMR vs ACR (p<0.05). Similarly, 112 (glomerular) and 124 (tubulointerstitial) proteins were altered in AMR vs ATN. Basement membrane and extracellular matrix (ECM) proteins were decreased in both compartments in AMR, compared to ACR and ATN. We verified decreased glomerular and tubulointerstitial LAMA proteins expression, and decreased glomerular NPHS1 and PTPRO expression in AMR. Cathepsin-V (CTSV) was predicted to cleave ECM-proteins in the AMR glomeruli. We identified galectin-1, an immunomodulatory protein increased in AMR glomeruli and linked to the ECM. An external dataset (GSE36039) also demonstrated increased galectin-1 expression in anti-HLA class-I antibodies induced inflammation and significantly increased CTSV expression, and galectin-1 expression and secretion, in human glomerular endothelial cells. We also studied GSTO1, an ECM-modifying enzyme, increased in the AMR tubulointerstitium. GSTO1 expression was significantly increased in TGF-treated proximal tubular epithelial cells.

Conclusions: Baseline remodelling are often remodeled in chronic AMR, and we demonstrated that this remodelling begins early in glomeruli and tubulointerstitium. ECM-remodelling in AMR may represent a new therapeutic target.

FR-OR43

Interim Update of the MDR-101-MLK Phase 3 Trial: MERCURY Study

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Methods: Eligible adult pairs (donor/recipient) of a first kidney allograft from an ABO-compatible donor were randomized to receive ATG conditioning, low-dose total lymphoid irradiation (TLI) over 10 days and IS followed by 5 days before undergoing apheresis (1 or 2 cycles). IA recipients receive ATG (IA; n=20) or Control Arm (CA; n=10). Donors in the IA received G-CSF mobilization conditioning, low-dose total lymphoid irradiation (TLI) over 10 days and IS followed by 5 days before undergoing apheresis (1 or 2 cycles). IA recipients receive ATG

Conclusions: Administration of MDR-101 in HLA-identical LD Ktxp recipients eliminated the lifelong need for immunosuppressive (IS) drugs and to prevent graft loss due to rejection or drug toxicity. MDR-101 is a novel cellular immunotherapy, to produce persistent mixed chimerism without graft versus host disease (GvHD) to allow elimination of all IS therapy without rejection, and, thus, to produce operational tolerance. The randomized study evaluated the need for chronic IS therapy in recipients of HLA-matched living donor (LD) kidney transplants as compared to standard of care (SOC) (NCT03363945).

FR-OR44

Single-Cell RNA-sequencing Analysis of Kidney Transplant Biopsies Demonstrates a Proinflammatory Role for Renal Tubular Cells in Rejection

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Background: Antibody mediated rejection (AMR) remains one of the major causes of allograft failure and our understanding of this disease process is poor. CXCL12 is thought to contribute to allograft rejection through T cell recruitment and a CXCL12 promoter variant is associated with worse graft outcomes. We performed single cell RNAseq on biopsies from transplant patients to examine ligand expression in kidney cells.

Methods: The 10X Genomics platform was used to make libraries which were sequenced to a depth of ~50k reads/cell. Gene-cell matrices were obtained from CellRanger and the downstream analysis (clustering, integration analysis, expression analyses) were done using R and Seurat. This study had IRB approval.

Results: 81139 cells in total (avg = 1124 genes/cell) from 5 kidney transplant biopsy samples (2 non-rejecting, 3 ABMR) were included in the final integrated analysis using UMAP. All major kidney cell types were identified as well as macrophages, B cells and T cells. Renal epithelial cells from rejection samples differentially expressed ligands with cognate receptors found on immune cells. All renal tubular cell types increase HLA gene expression allowing allowing for ligation of macrophage and T cell cognate receptors LIRL and CD3, respectively. Interestingly, only loop of Henle cells increased expression of CXCL12 whereas stromal cells decreased CXCL12 expression in rejection samples.

Conclusions: Comprehensive single cell RNAseq of human kidney transplant biopsies suggests a role for loop of Henle cells in rejection though expression of CXCL12. We also demonstrate that stromal cells, known to express CXCL12, downregulate CXCL12 expression in rejection. These data suggest a pro-inflammatory role for tubular cells in rejection.

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FR-OR46
Modulated Immune Cell Infusion in Kidney Transplantation
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Background: We have shown that donor blood cells, modified in vitro by an alkylating agent (MIC, modified immune cells), induced specific immunosuppression against the allogeneic donor when administered prior to transplantation. An additional finding was an up to 60-fold increase in the frequency of immunosuppressive CD19CD24CD38hi Bregs compared to transplanted controls without MIC infusions. The question arises whether donor-specific immunosuppression and increased regulatory B lymphocytes (Breg) are permanently detectable in MIC-treated patients.

Methods: Four patients from a phase-I trial who had received 1.5x10^8 MIC per kg b.w. on day -7 before living donor kidney transplantation and who were not on immunosuppression were compared to 12 transplanted control patients without MIC infusions.

Results: MIC-treated patients showed an excellent clinical course with no donor-specific HLA antibodies or rejection. On day 1080 after transplantation, median serum creatinine was 1.59 mg/dL. Patients had absent in vitro lymphocyte reactivity against stimulatory donor blood cells while reactivity against third party cells was preserved as an indication of continued donor-specific unresponsiveness. CD19CD24CD38+ and CD10+CD19CD24CD38+ Breg were with 2.2 ± 0.84 and 1.0 ± 0.50 μL respectively, strikingly higher than the 0.0 ± 0.01 and 0.0 ± 0.01 μL (P<0.001) in transplanted controls and in the range of the numbers of healthy individuals (N=34, P=0.73 and P=0.60). In addition, significantly higher Breg numbers were found for CD1D CD19CD24CD38+ (P=0.0071), CD19CD25+CD73CD71 (P=0.0077), CD19CD25CD73CD71 (P=0.013), CD19CD25CD73CD71 (P=0.0011), CD19CD24CD27+ memory (P=0.029), and IL10+CD19CD24CD27+ memory Breg (P=0.042). No such differences were observed for CD4+CD25CD27FoxP3+ Treg (P=0.08) or different Treg subsets when comparing the four MIC-treated patients to transplanted controls without MIC infusions.

Conclusions: Donor-specific immunosuppression after MIC infusion is long-lasting and is associated with a striking increase in Breg at various stages of B cell development, including memory Breg.

FR-OR47
Normothermic Ex Vivo Kidney Perfusion in a Porcine Auto-Transplantation Model Preserves the Expression of Key Mitochondrial Proteins: An Unbiased Proteomics Analysis
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Background: Normothermic ex-vivo kidney perfusion (NEVKP) results in significantly improved graft function in porcine auto-transplant models of DCD injury compared to cold storage of the organ (CS). However, the molecular mechanisms underlying these beneficial effects remain unclear.

Methods: We performed an unbiased proteomics analysis of 28 kidney biopsies obtained at 3 timepoints from pig kidneys subjected to 30-minutes of warm ischemia, followed by 9 hours of NEVKP or CS, and auto-transplantation.

Results: Of 6593 proteins quantified, 70 were differentially expressed between NEVKP and CS groups (2-way ANOVA, q<0.05). Proteins increased in NEVKP mediated key metabolic processes including fatty acid β-oxidation, the TCA cycle and oxidative phosphorylation; expression of our findings with external datasets of ischemia-reperfusion, and other models of kidney injury confirmed that 47 of our proteins represent a common signature of kidney injury reversed or attenuated by NEVKP. We validated key metabolic proteins (ETFB, CPT2) by immunoblotting. Integrated transcription factor databases identified PPARC1A, PPARG/D and RXRA/B as the upstream regulators of our dataset, and we confirmed their increased expression in NEVKP with RT-PCR.

Conclusions: The proteome-level changes observed in NEVKP mediate critical metabolic pathways that may explain improved graft function with NEVKP compared to CS. These effects may be coordinated by PPAR-family transcription factors, and may represent novel therapeutic targets in ischemia-reperfusion injury.

FR-OR48
Cyclosporine-Induced Endothelial Injury and Complement Activation Is Caused by Impaired Complement Factor H Binding to the Glycoalkyly Chia Wei Teo,1 Carolina Ortiz,1 Magdalena Riedl Khursigara,2 Valentina Bruno, Lisa Robinson, Christoph Licht. The Hospital for Sick Children, Toronto, ON, Canada.

Background: Calcineurin inhibitors are associated with nephropotoxicity, endothelial cell (EC) dysfunction and thrombotic microangiopathy. Evolving evidence suggests a central role for complement dysregulation in the pathogenesis of CNI-induced thrombotic microangiopathy. However, the exact mechanism of calcineurin-induced complement-mediated injury remains unknown.

Methods: In an in-vitro model utilising Blood Outgrowth EC (BOEC) from healthy donors, we evaluated the effects of cyclosporine (CsA) on EC injury, complement activation (C3a, C9) and regulation (CD46, CD55 and complement factor H [CFH]) on EC surfaces, and on the EC glycoalkyly, utilising flow cytometry, Western blot, and immunofluorescence imaging. Functional activity of CFH was assessed via CFH co-factor assay. Co-immunosuppression of Angiopoietin-2 (Angpt-2), Angiopoietin-1 (Angpt-1) and Tie2 was assessed by Western blot.

Results: CSa resulted in a dose and time dependent enhancement of EC complement deposition and EC death. CsA (10 μg/ml) led to a 15-fold upregulation of CD46, CD55 and CD9 on EC surface. CsA led to Angpt-2 mediated breakdown of the EC glycoalkyly, which was mitigated by Angpt-1. This EC glycoalkyly breakdown led to decrease in CFH surface binding and surface co-factor activity.

Conclusions: Our findings confirm a role for complement in CsA-induced EC injury, and suggest Angpt-2 mediated glycoalkyly abolishment, induced by CsA, as a mechanism leading to complement alternative pathway dysregulation via decreased CFH surface binding. Insights into this mechanism may provide a potential therapeutic target that might lead to improved patient outcomes which is subject to further studies. It might also apply to other thrombotic microangiopathies, in which a role for complement has so far not been recognized.

FR-OR49
Epigenome-Wide Microarray Analysis of Pre- and Post-Transplant Methylation Profiles in Kidney Transplant Recipients
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Background: Kidney transplantation is the optimal treatment for suitable individuals with end-stage kidney disease (ESKD). Serious post-transplant complications include infections, cardiovascular events, malignancy, and new onset of diabetes after transplant (NODAT). Our regional nephrology centre has the highest living donor transplant rate per million population in Europe, and promotes research to improve patient outcomes. We compared pre and post-transplant methylation profiles in samples derived from matched participants.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: Epigenome-wide analysis was conducted using the Illumina Infinium MethylationEPIC array to interrogate 862,987 sites across the genome and identify any differentially methylated regions (DMR) in samples derived from peripheral blood mononuclear cells of age and sex matched pre (n=25) and post (n=25) kidney transplant recipients. DNA was extracted in a uniform manner and stored carefully undergoing minimal freeze thaw cycles. Samples were run on the same instrument and regression calibration was performed in R to estimate leukocyte cell proportions.

Results: Association analysis using Partek® GenomicsSuite® identified 53 DMR (FDR adjusted p<0.1 x 10^6, fold change +/-2). Within the top ranked CpG probes we identified DMR within genes dysregulated in melanoma (e.g. EXOC2, VEPH1), genes encoding extracellular matrix proteins that could influence structural glomerular changes (e.g. SPAM1) and genes with prior chronic kidney disease associations (e.g. FNTA). A DMR was also identified within the long intergenic non-protein coding RNA LINC01544, suggesting a possible regulatory function. Additionally, Partek®Pathway™ identified enrichment of DMR in the mitogen-activated protein kinase (MAPK) signaling pathway, primarily implicated in malignancy but also ESKD and cardiovascular disease. Gene ontology analysis identified enrichment of terms associated with localization and binding within cells.

Conclusions: This analysis provides a novel epigenomic perspective on molecular changes caused by kidney transplantation, and highlights markers that may be of relevance to post-transplant complications. We provide evidence supporting further methylation and transcriptomic analyses in larger cohorts to help identify epigenetic risk factors associated with post-transplant complications.

FR-OR50
Impact of Caspase-1 Deletion on Apoptosis and AKI in a Murine Transplant Model
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Background: Prolonged cold ischemia (CI) is a known risk factor for acute kidney injury (AKI) after kidney transplantation. However, the mechanism by which CI leads to AKI is unknown. Caspase-1 knockout mice (Casp1KO) are protected from AKI after warm ischemia/reperfusion injury. We hypothesized that Casp1KO mice would be protected from AKI following transplant.

Methods: Renal tubular cells (RTECs) were subjected to cold storage and rewarming (CS/REW). C57Bl/6J wild type or Casp1KO kidneys were subjected to CI for 30 min and then transplanted into wild type recipients (CI+Txp). The recipients underwent bilateral nephrectomy to assess transplant function. DNA was extracted in a uniform manner and stored carefully undergoing any differentially methylated regions (DMR) in samples derived from peripheral blood mononuclear cells of age and sex matched pre (n=25) and post (n=25) kidney transplant recipients. DNA was extracted in a uniform manner and stored carefully undergoing minimal freeze thaw cycles. Samples were run on the same instrument and regression calibration was performed in R to estimate leukocyte cell proportions.

Results: We observed significantly increased expression of NLRP1 inflammasome protein and Caspase-1 in cells subjected to CS/REW. Using Imagestream in a flow cytometer we observed spatial overlap between two different fluorescent labels of inflammasome protein and Caspase-1 in cells subjected to CS/REW. Using Imagestream in a flow cytometer we observed spatial overlap between two different fluorescent labels of inflammasome protein and Caspase-1 in cells subjected to CS/REW. Using Imagestream in a flow cytometer we observed spatial overlap between two different fluorescent labels of inflammasome protein and Caspase-1 in cells subjected to CS/REW.

Conclusions: Caspase-1 deletion improves tubular cell apoptosis following CI+Txp. Deletion of Caspase-1 improves tubular cell apoptosis following CI+Txp. Deletion of Caspase-1 improves tubular cell apoptosis following CI+Txp. Deletion of Caspase-1 improves tubular cell apoptosis following CI+Txp.

Funding: Veterans Affairs Support

Histological assessment of transplanted kidneys

**p<0.001 vs. WT-WT

SA-OR01
Studying Proteinuria in COVID-19 to Define Markers of Severity and New Treatments
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Background: The recent SARS-CoV-2 pandemic has led to ~375,000 fatalities worldwide as of June 1st. Nearly, 43% of COVID-19 patients have been reported to have proteinuria, which can result from direct podocyte injury, podocytopathy related to cytokine storm, or both. This association between respiratory viruses, proteinuria, and primary kidney disease has also been observed in the context of respiratory syncytial virus (RSV), where patients can develop nephrotic syndrome. Therefore, studying primary and virus-dependent models of proteinuria and podocyte injury is critical to shed light into COVID-19 pathobiology, severity of disease and potential treatments.

Methods: We accessed transcriptomic data (RNA-seq) for lung cell lines (A549) infected with three different viruses and identified differentially expressed genes (DEGs) for SARS-CoV-2, RSV and IAV. In parallel, we also investigated DEGs for FSGS and MCD using LIMMA R package. We investigated the statistical correlation between the log-fold change of DEGs (Nephropathic syndrome and SARS-CoV-2) using R. Pathway analysis was performed using WebGestalt. Possible drugs correcting the skewed gene expression in FSGS and SARS-COV-2 were identified using the Connectivity map (eMAP).

Results: 120 gene signatures were specific to SARS-CoV-2. By using gene expression data from glomeruli of FSGS/MCD we identified 902 DEGs for FSGS and 5 for MCD. Out of these, 6 were overlapping and upregulated in COVID-19 and FSGS/MCD (B2M, EIF2AK2, IFIT1, IFIT2, TC7M and UBE2L6). Strikingly, IFIT27 has been recently reported as a marker of disease severity in COVID-19. We found significant positive correlation between the log2 fold change of 94 FSGS/MCD genes intersecting with the 120 COVID-19. The results were specific to glomeruli and to high proteinuric diseases, supporting a common cellular response in lung and podocytes. We then searched the cramp data and identified 59 drugs significantly inversely associated with SARS-COV-2 and 72 for FSGS. Out of these, 7 drugs were in common, representing novel potential drugs for COVID-19 and podocytopathies.

Conclusions: Overall, our results suggest transcriptional congruency between NS and SARS-COV-2 which can possibly be used to design novel therapies treat these diseases.

SA-OR02
Machine Learning for Prediction of Severe AKI in Hospitalized Patients with COVID-19
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Background: Preliminary reports indicate that acute kidney injury (AKI) is common in coronavirus disease (COVID-19) patients and is associated with worse outcomes. Identification of patients at high risk for developing severe AKI in hospitalized COVID-19 patients in the United States is not well-described.

Methods: This is a retrospective observational study of patients aged ≥18 years with laboratory confirmed COVID-19 admitted to the Mount Sinai Health System between February 27 and April 15, 2020. We trained and tested a machine learning algorithm, extreme gradient boosting (XGBoost), a boosted decision-tree based machine learning (ML) model, with 5-fold cross validation to predict AKI requiring dialysis. Patients from the Mount Sinai (MSS) were randomly split into a training and validation set for the model. To increase model generalizability and help minimize bias, the model’s performance was assessed on a test set composed entirely of patients from the other hospitals in the Mount Sinai Health System (MSSH). Input features for the model included demographics, laboratory values, and vital signs that occurred in the first 48 hours of admission.

Results: Of 3,235 hospitalized patients with COVID-19, AKI occurred in 1406 (46%) patients and 280 (20%) with AKI required dialysis. In the training set (n=1,317 patients), the classifier achieved good performance with an area under the receiver operating characteristic curve (AUROC) of 0.79 and area under the precision recall curve (AUPRC) of 0.38 for predicting AKI requiring dialysis. Performance was similar in the testing set (n=1,918) with 0.79 AUROC and 0.36 AUPRC. The features that had a larger impact on the model included serum creatinine, age, potassium, and heart rate.

Conclusions: A machine-learned model using admission features had good performance for dialysis prediction and could be used for resource allocation.

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Underline represents presenting author.

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SARS-CoV-2 Detection in Urine Suggests Infection of Kidneys and Correlates with Risk of AKI and Poor COVID-19 Prognosis

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Background: Since the emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), most of the focus has been on the respiratory failure caused by the resulting disease, COVID-19. However, the effects of COVID-19 in the kidney are increasingly recognized. Acute kidney injury (AKI) has been identified with varying prevalence around the world with higher rates (37-46%) reported in the USA. It is debatable whether AKI is an indirect consequence of systemic inflammation or a consequence of viral renal cell infection and tropism. We hypothesize that SARS-CoV-2 directly infects kidney tissue and increases the risk of developing AKI, worsening prognosis of COVID-19 patients.

Methods: We studied 88 COVID-19 patients admitted to the Henry Ford Hospital, Detroit after April 15, 2020. Demographics were: mean age 60, 71% African American, 55% male. We quantified viral copies by RT-PCR (S and N) in urine samples from 52 PCR-confirmed COVID-19 patients. We performed immunofluorescence for Membrane and Spike viral proteins in two COVID-19 biopsies.

Results: The prevalence of AKI was 72%, with 32% of patients admitted to the ICU. The overall mortality rate was 14%, with no deaths in non-AKI patients. Viral proteins M and S were detected in the glomerulus, parietal cells and tubules of COVID-19 patients. In some tubules, SARS-CoV-2 overlapped with ACE2, the receptor for viral entry. Virus was detected in 61% of urine specimens, with 6-fold greater viral load in AKI patient urines (copies/ng RNA: AKI, 742±1338 vs No-AKI: 1523 ± 404; p<0.05, n=52). The highest viral loads were detected three weeks post-AKI in 11,374±2248 copies/ng RNA (p<0.01). Among COVID-19 AKI-patients who died, the urine viral load exceeded 8000 copies/ng RNA. Above this threshold, the mortality rate was 55%.

Conclusions: Our data support that direct viral renal cell infection occurs in COVID-19 AKI patients with urinary viral genome detection. Greater urinary viral loads portend increased mortality. Urinary viral detection can facilitate management and treatment of COVID-19 and more extensive research should focus on studying whether urine contains infective virus or sheds non-infective genomic fragments.

Funding: NIDDK Support

SA-OR04
SARS-CoV-2 Receptor Networks in Diabetic Kidney Disease, BK Virus Nephropathy, and COVID-19 Associated AKI

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Background: COVID-19 shows increased disease burden in patients with diabetic kidney disease (DKD). SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) for host cell entry, so ACE2 levels may influence SARS-CoV-2 susceptibility. We investigated how pre-existing conditions and drug treatments alter receptor expression for host cell entry, so ACE2 levels may influence SARS-CoV-2 susceptibility. We

Methods: Single cell RNA profiling of 7 healthy living donor kidneys, 44 DKD, 3 BK virus nephropathy (BKVN) and a urine COVID19 patient with acute kidney injury (COV-AKI) revealed ACE2 expression primarily in proximal tubular epithelial cells (PTEC).

Results: ACE2 mRNA expression levels were higher in proximal tubule epithelial cells (PTEC) in DKD versus LD, but unaltered by exposures to renin angiotensin aldosterone system inhibitors. Bayesian integrative analysis of public -omics datasets identified molecular network modules induced in ACE2 positive versus negative PTEC in DKD and BKVN (hb.flatiron institute.org/covid-kidney), that were linked to viral entry, immune activation, endomembrane reorganization, and RNA processing. Similar programs were seen in COV-AKI ACE2-positive PTEC, and overlapped with programs in SARS-CoV-2 infected cells.

Conclusions: A consistent ACE2-correlated expression program in PTEC may interact with SARS-CoV-2 infection processes. These networks can seed further research into developing therapeutic strategies and assessing risk in patients with COVID-19.

Funding: NIDDK Support, Private Foundation Support
Results: Of 5,449 patients admitted with Covid-19, AKI developed in 1,993 (36.6%). The peak stages of AKI were stage 1 in 46.5%, stage 2 in 22.4% and stage 3 in 31.1%. Of these, 14.3% required renal replacement therapy (RRT). AKI was primarily seen in Covid-19 patients with respiratory failure, with 89.7% of patients on mechanical ventilation developing AKI compared to 21.7% of non-ventilated patients. 276/285 (96.8%) of patients requiring RRT were on ventilators. Of patients who required ventilation and developed AKI, 52.2% had the onset of AKI within 24 hours of intubation (Figure and Table). Risk factors for AKI included older age, diabetes mellitus, cardiovascular disease, black race, hypertension and need for ventilation and vasopressor medications. Among patients with AKI, 1,136 died (57%), 519 (26%) were discharged and 338 (17%) were still hospitalized.

Conclusions: AKI occurs frequently among patients with Covid-19 disease. It occurs early and in temporal association with respiratory failure and is associated with a poor prognosis.

SA-OR07
A Multicenter Observational Study of Clinical Features and Outcomes of AKI in Critically Ill Patients with COVID-19
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Background: Acute kidney injury (AKI) is emerging as an important sequela of COVID-19 infection. Existing data on the incidence and clinical features of AKI in patients with COVID-19 are mainly limited to single-center studies. Given the high incidence of severe AKI among patients with COVID-19 and its strong association with mortality in other settings, we conducted a multicenter nationally representative cohort study to examine the incidence, clinical features, risk factors, and outcomes of AKI in critically ill patients with COVID-19.

Methods: We used data from a multicenter observational study that collected granular, patient-level data from >3,000 critically ill adults with laboratory-confirmed COVID-19 admitted to participating ICUs from 67 centers across the United States. Using multivariable logistic regression, we examined risk factors for the primary composite outcome, AKI requiring renal replacement therapy or death (RRT/death) in the 14 days following ICU admission.

Results: Among 3099 patients, 1205 (38.9%) developed the primary outcome of RRT/death (n=637 required RRT, n=792 died within 14 days, and n=224 both required RRT/death) in the 14 days following ICU admission. Independent risk factors for RRT/death included chronic kidney disease (odds ratio [OR], 5.02; 95% CI, 3.55-7.10 for eGFR<30 vs. ≥60; OR 1.90; 95% CI, 1.55-2.33 for eGFR 30-59 vs. ≥60), as well as older age, male sex, higher body mass index, and greater severity of hypoxemia on ICU admission (Figure). Patients admitted to hospitals with higher degrees of strain also had a greater risk of RRT/death (OR 1.49; 95% CI, 1.06-2.06 for highest versus lowest quintile of hospital strain). Patients requiring RRT and died within 14 days). Independent risk factors for RRT/death included chronic kidney disease (odds ratio [OR], 5.02; 95% CI, 3.55-7.10 for eGFR<30 vs. ≥60; OR 1.90; 95% CI, 1.55-2.33 for eGFR 30-59 vs. ≥60), as well as older age, male sex, higher body mass index, and greater severity of hypoxemia on ICU admission (Figure). Patients admitted to hospitals with higher degrees of strain also had a greater risk of RRT/death (OR 1.49; 95% CI, 1.06-2.06 for highest versus lowest quintile of hospital strain).

Conclusions: This multicenter study identifies several key insights into the risk factors for RRT/death in critically ill patients with COVID-19.

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SA-OR08
Screening for SARS-CoV-2 (COVID) Infection in Chronic Dialysis Patients: A Nonprofit Provider’s Experience
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Background: The CDC recommends screening of all patients for COVID exposure history and or signs and symptoms prior to treatment. In order to limit the spread of COVID within our facilities, Dialysis Clinic Inc. screens all patients prior their in-center hemodialysis treatment or peritoneal dialysis visit consistent with recommendations.

Methods: We describe the outpatient screening process of our dialysis patients having a positive screen as patients under investigation (PUI) to activate local protocols for isolation and testing. We determined the frequencies of positive screening parameters and rate of identifying COVID patients.

Results: From 2/17 to 5/20, 2020, facilities screened 15,602 patients over 402,002 in-person visits, identifying 959 PUI’s (6%). Among PUIs, 61 of 351 (17%) COVID+ patients were correctly triaged prior to COVID+ diagnosis. In the subset of 788 PUIs screened prior to 4/11/20 where we were able to catalogue reasons for positive screening, 149 (19%) had exposure only and 639 exhibited symptoms (81%), of which 15 had exposure; 34 resided in group home (GH) and 7 had both exposure and GH residence. It was determined 41 (6.4%) were COVID+. Frequency of symptoms elicited by PUI are shown below.

Conclusions: 959 PUIs were identified and isolated by our screening process, resulting in the successful preemptive triage of 61 COVID+ (6%) patients before testing positive, potentially limiting infection spread in the facility. Cough and fever were the most common reasons for positive screen, and fever was most commonly associated with COVID+ diagnosis. However, the majority (83%) of COVID+ patients were primarily asymptomatic and hence not captured by screening.

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SA-OR13
Screening for SARS-CoV-2 Infection among Hemodialysis Staff: A Rural Hospital’s Experience
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Background: Staff were encouraged to pursue local or state testing. With limited local and state testing availability, staff needed an alternative rapid method for COVID-19 screening. MUSC conducted an anonymous employee screening program.

Methods: We describe the staff screening experience at MUSC.

Results: From 3/1-5/20, 2936 employees were tested. In the initial testing periods (3/1-4/4), 10% of employees were tested in person and 90% were tested at home. In the later testing periods (4/4-5/20), 30% were tested in person and 70% home. Staff were isolated if COVID+ and paid for 2 weeks. Staff who tested positive were not allowed back to work until negative test results were received. Staff who were asymptomatic were tested after 2 weeks. To date, no COVID+ staff were identified.

Conclusions: Staff screening is feasible. Staff were isolated if COVID+ and paid for 2 weeks. Staff who tested positive were not allowed back to work until negative test results were received. Staff who were asymptomatic were tested after 2 weeks. To date, no COVID+ staff were identified.
SA-OR09
Urgent Peritoneal Dialysis Catheter Placement at a New York City Hospital During the COVID-19 Pandemic
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Background: During the COVID-19 pandemic, there has been an unparalleled burden on nephrology services to provide kidney replacement therapy to patients admitted to the hospital with COVID-19, who develop severe AKI. Given the unprecedented surge in COVID-19 admissions, ability to provide inpatient hemodialysis and continuous kidney replacement therapy (CRRT) was quickly saturated. We present data from our acute peritoneal dialysis (PD) program that was quickly assembled to provide kidney replacement therapy due to shortage of hemodialysis and CRRT resources.

Methods: Patients admitted to an academic NYC hospital during COVID-19 pandemic with AKI requiring kidney replacement therapy were evaluated for candidacy for bedside PD catheter placement via cut-down method with the majority having COVID respiratory failure. A dedicated surgery team was assembled to place PD catheters within 12-24 hours of request by the nephrology team. Catheters were placed in patients with BMI up to 51. Patients requiring proning were not excluded. Exclusion criteria were prior lower abdominal surgery, known varices, or imminent death.

Results: Thirty-eight PD catheters were placed during the 4 week period from April 8 to May 8, 2020. Majority of the catheters were placed bedside in an ICU setting (36/38 - 95%), with 2 being placed laparoscopically in the OR. There were no episodes of peritonitis. Three catheters required revision due to poor flows. Six catheters required floseal for bleeding along the catheter tract, which resolved without additional intervention. There were no major bleeding complications during PD catheter placement despite many patients being on systemic anticoagulation. Dwell volumes of up to 2.2L did not appear to have negative effects on the ability to ventilate patients. One patient required transition to hemodialysis due to catheter malfunction.

Conclusions: Acute peritoneal dialysis successfully allowed kidney replacement therapy for patients with severe AKI during the peak phase of the COVID-19 pandemic at our hospital in NYC. There were no major complications with acute PD catheter placements.

SA-OR10
Recovery from AKI and Acute Respiratory Distress Syndrome (ARDS) with the Use of Low-Dose Steroids During COVID-19 Infection in an African American Population: A Retrospective Analysis
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Background: Corona Virus Disease-19 (CoVID-19) infection associated with AKI and ARDS results in a mortality of 80%. In AA population COVID 19 presentations and outcomes are worse. NIH and Interim WHO guidelines suggest against steroids use unless in the context of clinical trials. We conducted a retrospective analysis on the impact of 2 different doses of IV steroids in AA adult population.

Methods: 75 patients between March 1 and April 30, 2020 were enrolled. Primary outcomes (21-day mortality) and secondary outcomes (improvement in lung function and renal function) were analyzed. Comparisons between the steroid doses (methylprednisolone 1 mg/kg/day or 2 mg/kg/day) and no-steroid groups were performed with the Wilcoxon, Kruskal-Wallis, and Chi-Square tests. Factors affecting the recovery of AKI or ARDS were analyzed. AKI recovery was defined as 50% increase of GFR, and cessation of RRT; lung function recovery was defined as improved oxygenation by P/F ratio > 200 and extubation.

Results: 38 out 75 patients received steroids. Survival in the steroids group reached 73% at 21 days compared to 36% in the non-steroids group (p=0.0006). Steroids improved the likelihood of renal function improvement by 300% (p=0.06). Lung function was 73% in the steroids group versus 45% in the other (p=0.01). Use of anticoagulants (16% vs 51%, p= 0.001) seemed to be interacting with steroids on outcomes. Low dose steroids had the most beneficial impact.

Conclusions: In patients with COVID-19 infection and ARDS with AKI, low dose IV methylprednisolone was associated with a significantly lower incidence of mortality and higher likelihood of renal and lung function recovery. Further investigation with a randomized control trial consisting of low dose steroids seems warranted.

Mortality in steroids and non-steroids groups

SA-OR11
p53/MicroRNA-214/ULK1 Axis Impairs Renal Tubular Autophagy in Diabetic Kidney Disease
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Background: The pathogenesis of diabetic kidney disease (DKD) is unclear. Dysregulation of autophagy in DKD has been reported, but the underlying mechanism and its pathogenic role in DKD remain elusive.

Methods: Autophagy changes in DKD were investigated in high glucose treated renal tubular cells in vitro and in Akita mice and streptozotocin (STZ)-induced diabetic mice in vivo. Autophagy-related gene 7 (Atg7), microRNA-214 (miR-214), or p53 were ablated specifically from kidney proximal tubules to elucidate the pathogenic role and underlying mechanism of autophagy dysregulation in DKD. The expression of autophagy-related proteins, miR-214, and p53 were analyzed in human diabetic kidney tissues along with renal pathologies to determine their correlations.

Results: Autophagy was inhibited in DKD models and in human diabetic kidneys. Ablation of Atg7 from kidney proximal tubules led to autophagy deficiency and worsened renal hypertrophy, tubular damage, inflammation, fibrosis, and albuminuria in diabetic mice, indicating a protective role of autophagy in DKD. Autophagy impairment in DKD was associated with the downregulation of ULK1, a key serine/threonine protein kinase for the initiation of autophagy. ULK1 downregulation in DKD involved miR-214, which was induced in diabetic kidney cells and tissues to repress ULK1 expression. Expression of miR-214 from kidney proximal tubules prevented ULK1 decrease and autophagy impairment in diabetic kidneys, resulting in less renal hypertrophy and albuminuria. Furthermore, blockade of p53 attenuated miR-214 induction in DKD, leading to higher levels of ULK1 and autophagy, accompanied by the amelioration of DKD. Compared to non-diabetic samples, renal biopsies from human diabetic patients showed the induction of p53 and miR-214, associated by the downregulation of ULK1 and autophagy. There was a significant positive correlation between p53/miR-214 and renal fibrosis, whereas a negative correlation between ULK1/miR-214 and renal fibrosis in diabetic patients.

Conclusions: Autophagy dysfunction occurs in renal tubules in DKD, and contributes to renal hypertrophy and related pathologies. Mechanistically, p53 is activated in DKD to induce miR-214, which represses ULK1 resulting in autophagy dysfunction. The results identify the p53/miR-214/ULK1 axis of autophagy impairment for the development and progression of DKD.

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SA-OR12
Podocyte-Derived Extracellular Vesicles Mediate Renal Proximal Tubule Cell De-differentiation via MicroRNA 221 in Diabetic Nephropathy

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Background: Podocyte injury is a key event in the initiation of diabetic nephropathy (DN), and the proximal tubule has been regarded as a target of injury. Evidence suggests that cross-talk between podocytes and tubular epithelium is a key component in the pathogenesis of DN, but the mechanisms are not fully understood.

Methods: The podocytes and proximal tubular epithelial cells (PTECs) were co-cultured in high glucose conditions to detect the intercellular communication. Podocytes-derived extracellular vesicles (EVs) was isolated and identified by specific morphology and surface markers. Immuno-fluorescence, PCR, western blot, electron microscope, and transwell were conducted to assess the de-differentiation of PTECs. The expression level of miRNA in EVs was detected and C3-treated mice was used to demonstrate its direct transfer into target cells. A dual-luciferase reporter system was utilized to confirm the binding of miRNA to its target gene. The roles of miRNA and target gene were assessed using specific miRNA inhibitors, mimics and shRNA. In addition, Streptozotocin-induced diabetic mice and a models mice were construct, and miRNA antagonist were used to explore its role in proximal tubule injury.

Results: Podocytes induced de-differentiation of PTECs in high-glucose conditions and mediated the intercellular interaction. The podocytes-derived EVs were extracted and identified as exosomes, and the EVs treatment induced PTECs injury. miR-221 was remarkably increased in EVs and could be directly transferred into target cells, moreover, this miRNA was shown to play a key role in PTECs de-differentiation. The dual-luciferase reporter assay confirmed that miR-221 target DKK2, and miR-221 positively regulated β-catenin activation. Importantly, inhibition of β-catenin markedly diminished the EVs and miRNA induced PTECs de-differentiation. Furthermore, inhibition of miR-221 in diabetic mice reversed the PTECs injury and relative β-catenin activation.

Conclusions: Podocyte-derived EVs in diabetes acted as key mediators of proximal tubule cell injury and the exosomal miR-221 mediated the cells damage through Wnt/β-catenin signaling. These findings provide unique insights in the mechanisms of proximal tubule cell injury in diabetic nephropathy, and miR-221 can be used as a new target for the treatment of renal fibrosis in DN.

Funding: Government Support - Non-U.S.

SA-OR13
Whole-Genome Sequencing Identifies a Dominant Negative ADIPOQ Mutation in a Type 2 Diabetic Family Enriched for ESRD

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Background: Diabetic nephropathy (DN) is a complex, heterogeneous complication of diabetes. Despite evidence of its strong genetic predisposition, identification of the genetic factors that contribute to DN and the risk of end-stage renal disease (ESRD) has been challenging.

Methods: We performed whole genome sequencing (WGS) in a multi-generational family enriched for both type 2 diabetes and ESRD followed by unified linkage analysis and rare variant association testing using gVAST.

Results: Using WGS to evaluate this family, we identified a rare loss-of-function mutation in adiponectin (ADIPOQ) c.245_247delCTG; seen only once among 56,810 Finnish Europeans included in the gnomAD database) observed among 6 ESRD cases in this family. This 10-nucleotide deletion results in a premature termination codon and a complete loss of adiponectin’s globular domain. We found that carriers of this mutation have low circulating adiponectin (15% of normal levels) and dramatically high ceramide levels (double the level of C16 ceramides as compared with wt diabetic patients). Individuals have low circulating adiponectin (15% of normal levels) and dramatically high ceramide levels (double the level of C16 ceramides as compared with wt diabetic patients). This 10-nucleotide deletion results in a premature termination codon and a ADIPOQ mutation in adiponectin (Gly93GlufsTer73; seen only once among 56,810 non-family members). This family is enriched for both type 2 diabetes and ESRD followed by unified linkage analysis.

Conclusions: This family has been followed for 6 wk. Results: Using WGS to evaluate this family, we identified a rare loss-of-function mutation in adiponectin (ADIPOQ c.245_247delCTG; seen only once among 56,810 Finnish Europeans included in the gnomAD database) observed among 6 ESRD cases in this family. This 10-nucleotide deletion results in a premature termination codon and a complete loss of adiponectin’s globular domain. We found that carriers of this mutation have low circulating adiponectin (15% of normal levels) and dramatically high ceramide levels (double the level of C16 ceramides as compared with wt diabetic patients). Individuals have low circulating adiponectin (15% of normal levels) and dramatically high ceramide levels (double the level of C16 ceramides as compared with wt diabetic patients). This 10-nucleotide deletion results in a premature termination codon and a ADIPOQ mutation in adiponectin (Gly93GlufsTer73; seen only once among 56,810 non-family members). This family is enriched for both type 2 diabetes and ESRD followed by unified linkage analysis.

Conclusions: Podocytes/Derived EVs in diabetes acted as key mediators of proximal tubule cell injury and the exosomal miR-221 mediated the cells damage through Wnt/β-catenin signaling. These findings provide unique insights in the mechanisms of proximal tubule cell injury in diabetic nephropathy, and miR-221 can be used as a new target for the treatment of renal fibrosis in DN.

Funding: Government Support - Non-U.S.

SA-OR14
Enhancing Kidney DDAH-1 Expression by Adenovirus Delivery Reduces Asymmetric Dimethylarginine and Ameliorates Diabetic Nephropathy

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Background: Endothelial dysfunction, characterized by reduced bioavailability of nitric oxide and increased oxidative stress, is a hallmark characteristic in diabetes and diabetic nephropathy (DN). High levels of asymmetric dimethylarginine (ADMA) are observed in several diseases including DN and are a strong prognostic marker for cardiovascular events in patients with diabetes and end-stage renal disease. ADMA, an endogenous endothelial nitric oxide synthase (NOS3) inhibitor, is selectively metabolized by dimethylarginine dimethylaminohydrolase (DDAH). Low DDAH levels have been associated with cardiac and renal dysfunction, but its effects on DN are unknown. We hypothesized that enhanced renal DDAH-1 expression would improve DN by reducing ADMA and restoring NOS3 levels.

Methods: DBA/2J mice injected with multiple low doses of vehicle or streptozotocin were subsequently injected intraretraally with adenovirus expressing DDAH-1 (Ad-h-DDAH-1) or vector control (Ad-green fluorescent protein (GFP)), and mice were followed for 6 wk.

Results: Diabetes was associated with increased kidney ADMA (p<0.05) and reduced kidney DDAH-1 activity (p<0.05) and DDAH-1 expression (p<0.05) compared to normal mice but had no effect on kidney DDAH-2 expression. Ad-GFP-treated diabetic mice showed significant increases in albuminuria (p<0.005), histological changes (p<0.005), glomerular macrophage recruitment (p<0.001), inflammatory cytokine (p<0.01) and fibrinotic markers (p<0.01), kidney ADMA levels (p<0.05), and urinary thiobarbituric acid reactive substances excretion (p<0.005) and fibrotic markers (p<0.01) and inflammatory cytokine (p<0.01) and fibrinotic markers (p<0.01), kidney ADMA levels (p<0.05), and urinary thiobarbituric acid reactive substances excretion (p<0.005) and fibrotic markers (p<0.005). These data indicate, for the first time, that DDAH-1 mediates renal tissue protection in DN via the ADMA-NOS3 interaction. Enhanced renal DDAH-1 activity could be a novel therapeutic tool for treating patients with diabetes.

Funding: NIDDK Support

SA-OR15
Cell Type Specificity of Hypoxia Signaling in Early Diabetic Kidney Disease (DKD)

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Background: Chronic hypoxia is considered a driver of kidney disease progression. Given the spatial heterogeneity of hypoxia, we evaluated the cell type specificity of Hypoxia Related Genes (HRG) in DKD along the nephron and the association of HRG with structural parameters.

Methods: Cell-specific expression and normalized gene signatures (Z scores) were calculated for 237 HRG in single cell RNA profiles of 44 kidney biopsies from American Indians with Type 2 Diabetes (T2D) and 7 healthy living donor kidneys (LD), and replicated in 49 independent micro-dissected biopsies of T2D with DKD (DN).

Results: Mean measured glomerular filtration rate was 159 ml/min (SD 54) in T2D and 147 ml/min (SD 45) in DN, and mean urine albumin/creatinine ratio was 304 mg/g (SD 1542) for T2D and 35 mg/g (SD 90) for DN. Average HgA1c was 9.2 for T2D and 9.3 for DN. HRG expression showed highly cell-type specific elements in both LD and T2D (Figure 1). HRG signature in stressed proximal epithelial cells (pSPEC), unique to T2D, was dominated by apoptosis and glycosylation signals, while endothelial cells (EC) signatures expressed more genes involved in fibrosis in T2D compared to LD. In DN, Z score of the EC signature was associated with increased mesangial volume (R 0.33, p-value 0.02) and Z score of SPEC signature was associated with interstitial fibrosis (R 0.35, p-value 0.02), which are strong predictors of long-term outcomes in this cohort.

Conclusions: HRG expression varies by cell type in LD and DKD, suggesting transcriptional regulation changes of HRG in diabetes and DKD. Association of HRG signatures with morphometrics that are associated with progressive GFR loss implicate chronic hypoxia processes in early DKD.

Funding: NIDDK Support
Conclusions: Loss of SCO2 and mutant SCO2 reduced glomerular endothelial injury, oxidative stress, and early diabetic injury in the kidney with improved mice survival in a murine model of DKD.

Funding: NIDDK Support, Veterans Affairs Support, Private Foundation Support

SA-OR17

Reversal of Diabetic Nephropathy After 10 Years of Pancreas Transplantation Occurs Despite Parallel Podocyte Loss

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Background: Diabetic nephropathy (DN) is associated with podocyte (PC) injury and loss. PC injury is believed to play important role in DN progression. DN reversal following 10 years (10Y) of euglycemia after pancreas transplantation (PTx) is documented (N Engl J Med 2017;376:69-75). We hypothesized that PC loss would continue, DN reversal would be associated with PC regeneration and improvement in PC structure.

Methods: Paired kidney biopsies prior to PTx (BL) and 10Y after PTx were compared for classical DN lesions, PC number and foot process width (FPW) using electron microscopy morphometry in 10 type 1 diabetic (T1D) patients with age 33 (30-54) years [median (range)], diabetes duration 23 (16-33) years and albumin excretion rate (AER) 134 (0-951) μg/min at BL. The results were compared with biopsies from 10 age matched living donor biopsies [controls (C)].

Results: Glomerular basement membrane (GBM) width, fractional volume of mesangium/glomerulus [Vv(Mes/glom)] and fractional volume of mesangial/glomerulus [Vv(MM/glom)] and FPW were all increased at BL compared to C (data not shown). There were significant reductions in GBM width (30%, p=0.0002), Vv(Mes/glom) (21%, p=0.001), Vv(MM/glom) (30%, p=0.002), and glomerular volume (27%; p=0.02) at 10Y compared to BL. However, while PC number density did not change from BL to 10Y, there was a significant decrease in PC number/glomerulus (31%; p=0.049), FPW in T1D patients at BL (p=0.0088) or 10Y (p=0.002) was greater than C with no significant change from BL to 10Y. No relationship was found between change in GBM width, Vv(Mes/glom) or Vv(MM/glom) and PC number density, PC number per glomerulus or FPW. Creatinine clearance was reduced by 25% from BL to 5y post PTx in these calcineurin treated patients, and remained stable between 5 and 10Y. AER did not change significantly.

Conclusions: Substantial reversal of GBM and mesangial extracellular matrix (ECM) accumulation in T1D occurs following long term PTx despite decrease in PC number, persistence of foot process widening and no change in PC density. This study does not support PC loss to be an important mediator of glomerular extracellular dynamics in DN in T1D. Moreover, despite long-term normoglycemia, PC do not regenerate and PC injury does not regress in T1D patients.

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SA-OR18

Urinary Proteomics Identifies Proteins Associated with Rapid eGFR Decline in Type 1 Diabetes

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Background: Varying rates of eGFR decline have been observed in patients with type 1 diabetes (T1D), the pathophysiologic mechanisms of which remain poorly understood.

Methods: We performed a case-control study nested within four T1D cohorts (EDC, CACTI, STENO, FinnDiame) to identify urinary proteins associated with rapid eGFR loss. Cases and controls were defined by annual eGFR decline ≥3ml/min/1.73m² and <1ml/min/1.73m², respectively. We developed a targeted liquid chromatography-tandem mass spectrometry assay to measure 38 peptides of 20 proteins implicated in diabetic kidney disease. Peptide associations with rapid eGFR loss in discovery and validation sets were compared using logistic regression. Associations of significant peptides with rapid eGFR loss were then evaluated in the Nephroseq transcriptomic database.

Results: 1271 participants (508 cases, 763 controls) with baseline median eGFR 95ml/min/1.73m² and ACR ≥30mg/gCr in 36% were included. Over 8 years mean follow-up, mean eGFR slope was −5.65 and 0.57ml/min/1.73m² per year for cases and controls, respectively. Out of 38 urine peptides, 2 cathespin D (CatD) peptides were associated with rapid eGFR loss adjusting for demographic and clinical variables with a false discovery rate of <5% in the discovery set (fully-adjusted OR per SD 1.52, 95%CI 1.22-1.88; 1.41, 95%CI 1.14-1.74). In the validation set, CatD peptides were associated with rapid eGFR decline adjusting for demographic but not clinical variables (1.26, 95%CI 0.99-1.60; 1.15, 95%CI 0.91-1.46). When stratified by baseline urine albumin creatinine ratio (UACR), CatD peptides were associated with rapid eGFR loss among those with UACR 30-300mg/g in both discovery (2.36, 95%CI 1.39-4.03; 2.28, 95%CI 1.32-3.92) and validation (1.93, 95%CI 1.10-1.39; 1.84, 95%CI 1.08-3.13) sets.

Conclusions: Loss of functional SCO2 attenuates diabetic kidney disease in db/db mice.

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Background: Synthesis of Cytochrome C Oxidase 2 (SCO2), a Cu2+ metallochaperone located in the inner mitochondrial membrane, is essential for the assembly of Complex IV (COX IV) of the electron transport chain, maintenance of the proton gradient, and redox signaling. Altered COX activity and reduced mitochondrial function have been reported in diabetic kidney disease (DKD), but the mechanism mediating this process remains to be explored.

Methods: db/db mice were bred with Sco2 mutant mice (E129K, most common human missense mutation in the Cu2+ binding domain) to generate Sco2−/−;db/db and Sco2+/-;db/db mice. Sco2+/-, Sco2+/-;db/db, and wildtype mice served as controls. All mice were euthanized at 24 weeks of age and assessed for functional and histological changes in the kidney.

Results: Data mining in Nephroseq showed that SCO2 expression was increased in micro-dissected glomeruli in human DKD kidney biopsies (Ju et al. 2013), which we confirmed by immunostaining in human kidney biopsies with DKD as compared to healthy donor nephrectomies. Since SCO2−/− mice are embryonally lethal, we ascertained the role of mutant and heterozygous knockout SCO2 in DKD (SCO2−/−, SCO2+/−). As compared to db/db mice, SCO2−/−;db/db and SCO2+/−;db/db mice had a significant reduction in albuminuria, serum creatinine, glomerular hypertrophy, glomerular oxidative stress (8-oxoG staining) with an increase in podocyte number (WT 1+ cells per glomerular cross-sectional area), synaptopodin expression, and overall survival. SCO2−/−;db/db and SCO2+/−;db/db mice also exhibited less glomerular endothelial injury with a decrease in glomerular capillary loop dilatation and a trend towards decrease in Fcan and Vcan1 and an increase in Angpt1, Vegfa, Kdr and KIf2 expression as compared to db/db mice.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Conclusions: Among patients with TID and largely normal kidney function, differences in renal lysosomal function as suggested by increased urine CatD may represent a mechanism of rapid eGFR loss early in the course of TID.

Funding: Private Foundation Support

SA-OR19

Reduction in the Rate of eGFR Decline with Semaglutide vs. Placebo: A Post Hoc Pooled Analysis of SUSTAIN 6 and PIONEER 6

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Background: The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated that once-weekly (OW) subcutaneous (s.c.) semaglutide may have beneficial effects on kidney function in subjects with type 2 diabetes (T2D) at high CV risk. SUSTAIN 6 and the PIONEER 6 CVOT (once-daily [OD] oral semaglutide) had similar designs and populations, and both evaluated the effects of semaglutide vs placebo (PBO) on macro- and microvascular outcomes. This post hoc analysis of pooled data from the two trials evaluated the effects of semaglutide vs PBO on kidney function decline.

Methods: Data for 6,480 subjects with T2D from SUSTAIN 6 (OW s.c. semaglutide 0.5 and 1.0 mg or PBO, N=3,297; median follow-up 2.1 years) and PIONEER 6 (OD oral semaglutide 14 mg or PBO, N=3,183; median follow-up 1.3 years) were pooled into two groups: semaglutide and PBO. Annual change in estimated glomerular filtration rate (eGFR) was compared (semaglutide vs PBO) in the overall population and subgroups by baseline (BL) eGFR (≥45 mL/min/1.73 m²) and at each level of additional risk (baseline eGFR <45 mL/min/1.73 m² or baseline eGFR ≥45 mL/min/1.73 m² and at least one additional CV risk factor). Changes in eGFR from BL during trial were analyzed using a linear random regression model with individual intercept and time slope. The estimated treatment difference (ETD) at 1 year between annual rates of eGFR slope from BL was calculated; an interaction p-value <0.05 indicated difference between subgroups.

Results: In the overall population, the annual rate of eGFR change was 0.60 mL/min/1.73 m² (p<0.0001) lower with semaglutide vs PBO. In the eGFR ≥45 mL/min/1.73 m² and at least one additional CV risk group, the ETDs for semaglutide vs PBO were, respectively, 1.07 and 0.48 mL/min/1.73 m²/year, with a non-significant interaction p-value (Figure).

Conclusions: Semaglutide was associated with a significantly smaller decline in kidney function than PBO in subjects with T2D at high CV risk across tested BL eGFR categories; the data suggest the main benefit might be observed in those with kidney disease.

Funding: Commercial Support - Novo Nordisk

SA-OR20

Patrionomer to Enable Spironolactone in Patients with Resistant Hypertension and CKD (AMBER): Results in the Prespecified Subgroup with Diabetes

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Background: Spironolactone (SPIRO) reduces BP in patients (pts) with resistant hypertension (RHTN); however, its use in pts with advanced chronic kidney disease (CKD) is often limited by hyperkalemia (HK). In AMBER, patrionomer (PAT) enabled more persistent use of SPIRO in pts with RHTN and CKD. As SPIRO is recommended in RHTN and diabetes mellitus (DM) increases HK risk, we report results in prespecified subgroups with Type 1 or 2 DM.

Methods: Randomized, double-blind, placebo (PBO)-controlled trial in adults with RHTN and eGFR 25 to 60 mL/min/1.73 m². Pts were assigned (1:1) to PBO or PAT, and SPIRO 25 mg QD, with dose titrations permitted after 1 wk for PAT/PBO and 3 wks for SPIRO. The primary endpoint, between-group difference at Wk 12 in 45 mL/min/1.73 m² and more persistent use of SPIRO in pts with RHTN and CKD. As SPIRO is recommended for pts with RHTN and CKD, we were assessed prospectively in prespecified DM subgroups.

Results: 295 pts were randomized, 145 (49%) DM+ and 150 (51%) DM-. Baseline mean (SD) serum K+ (mEq/L) was 4.76 (0.34) in DM+ and 4.67 (0.39) in DM-. Significantly more pts treated with PAT than with PBO remained on SPIRO at Wk 12 in both subgroups (Figure). LS Mean (SE) cumulative SPIRO dose was higher with PAT than PBO, by 438.7 (177.7) mg in DM+ and 317.8 (175.0) mg in DM-. Adverse events occurred in 61% (PBO) and 60% (PAT) of DM+ pts and in 46% (PBO) and 51% (PAT) of DM- pts. 4 pts had serum magnesium (Mg2+) <1.4 mg/dL between baseline and Wk 12 (none <1.2 mg/dL), including 3 DM+ (1 PBO, 2 PAT) and 1 DM- (PAT) pt. None of these pts had cardiac arrhythmias temporally associated with low Mg2+ levels, neuromuscular abnormalities, or serum K+ below the LLN (3.5 mEq/L).

Conclusions: PAT enabled more pts with advanced CKD and RHTN to continue treatment with SPIRO, regardless of DM status.
Kidneyomics: From Cysts to Populations
Oral Abstract/Saturday

SA-OR24

Single-Cell RNA Sequencing Provides Insights into the Mechanism Through Which Adaptive Immune Cells Promote Injury-Induced Cyst Formation

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Backgrounds: Inducible deletion of cilia related genes in adult mice results in slow progressing cystic disease, which can be greatly accelerated by renal injury. However, cells that promote accelerated cystogenesis following renal injury are poorly understood.

Methods: To identify cells that may be responsible for driving rapid, injury induced cystic disease, we performed single cell RNA sequencing on cells isolated from sham operated control and 48 hour ischemia-reperfusion (IR) injured kidneys. IR injured, cilia mutant mice were 56 days post injury, a time point in which injured cilia mutant mice had mild cystic disease.

Results: Single cell RNA sequencing data from sham- and injured- cilia mutant mice indicate that renal injury in the setting of cilia loss results in alterations in T cells clusters with limited differences in other cell populations. In contrast, single cell RNA sequencing data comparing injured cilia mutant mice and normal cilia mutant mice revealed that loss of primary cilia in the setting of IR injury resulted in major changes in clusters of tubular epithelia and macrophages with minimal effects on T cells. These data suggest that accelerated cystogenesis in cilia mutant mice requires both injury induced changes in T cells as well as cilia-dependent alterations in the injured epithelium and macrophages. Using WicNet to identify ligand-receptor-gene regulatory networks, we show that T cells from injured cilia mutant mice produce ligands that cause alterations in the gene expression signature of the cilia mutant epithelium and macrophages suggesting that these cells are master regulators of injury induced cystic disease. In agreement with this hypothesis, our data indicate that loss of adaptive immune cells (including T cells) significantly reduced injury induced cystic disease. In contrast, loss of adaptive immune cells did not affect cyst progression in the absence of injury in multiple cystic models, even when animals were aged out several months.

Conclusions: Collectively, our data indicate that IR injury creates a unique population of ligand-producing T cells that crosstalk with macrophages and epithelium of cilia mutant mice to drive rapid, injury induced cystogenesis.

Funding: NIDDK Support, Other NIH Support - University of Alabama at Birmingham (UAB) Hepato/Renal Fibrocystic Disease Core Center P30-DK-074038, R01-DK-099724 (M.M), 1R01DK1002298 from the Office of Research and Development, Biomedical Research Service, Department of Veterans Affairs (M.M) and by the Detraz Endowed Research Fund in Polycystic Kidney Disease (to M. M.). Additional support was provided by the Polycystic Kidney Disease Research Foundation grant 214g16a (M.M.), a Pilot and Feasibility grant from the University of Alabama (UAB) School of Medicine AMC21 grant (B.K.Y., M.M.); the National Institutes of Health T32 training grant in Basic Immunology and Immunologic disease 2T32AI007051-38 (to K.A.Z); an NIH R01 DK115752 (B.K.Y., M.M), a PKD Foundation Research Award (to K.H.), and the Zell Family Foundation (to K.H.), Veterans Affairs Support, Private Foundation Support

SA-OR23

Activation of AMP-Activated Protein Kinase In Vivo Leads to a Polycystic Kidney Disease

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Background: Polycystic kidney disease (PKD) is a genetic disorder in which numerous fluid-filled cysts form in the kidney. Despite having identified the causative genetic mutations in PKD1 and PKD2, our understanding of the molecular signalling pathways involved in cystogenesis is limited, hindering PKD drug discovery. In this project, we generated a mouse model of AMP-activated protein kinase (AMPK) activation and observed a polycystic kidney phenotype, reminiscent of PKD. AMPK is known for its role in controlling energy homeostasis and is activated in response to cellular stress. It is currently unknown whether AMPK could play a role in PKD pathogenesis.

Methods: AMPK activation mouse models were generated by expressing the AMPKα1 isofrom with a D316A mutation under the control of β-actin (global) and Ksp (kidney-specific) promoters using the Cre-LoxP system. A constitutively active form of AMPK is produced when AMPKα1-D316A is incorporated into the enzyme complex. Renal function was assessed using metabolic caging, serum and urine samples were collected for analysis. Kidneys were collected and snap-frozen for biochemical studies or were embedded for histological studies.

Results: Global activation of AMPKα1 resulted in a striking polycystic kidney phenotype. Tubule dilations were evident from 11 days of age, which progressed to heavily cystic kidneys by 3 weeks of age. Adult mice showed signs of polyuria associated with increased urine osmolarity, kidney damage and compromised renal function. Cysts were observed in the collecting ducts of these mice, consistent with the distal neobrain being mostly affected in PKD. Mechanistically, the cystic kidneys had increased AMPK levels and ERK activation (a pathway known to be dysregulated in PKD), increased PKD1 expression and altered lysosomal protein expression. Kidney specific activation of AMPKα1 also produced polycystic kidneys in mice, demonstrating that AMPK activation within the kidney was causative.

Conclusions: These results show that activation of AMPK causes polycystic kidneys to form, raising the possibility that AMPK activation could be a contributing factor in PKD pathogenesis. Disregulation of the cAMP-ERK pathway in this model suggests a possible mechanism for how AMPK activation could be implicated in renal cystogenesis. Future studies should investigate whether AMPK has a pathogenic role in other PKD models.

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SA-OR24

CUB062, the Product of the C2orf62 Gene, Is a Polycystin-1 Ligand

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Background: The PKD1 gene, encoding the protein polycystin-1 (PC1), is responsible for 85% of cases of mutation positive autosomal dominant polycystic kidney disease (ADPKD) and is the most common genetic cause of renal failure (1:800). CUB062 has been shown to be present on easily accessible urinary exosome-likes (ELVs) and to be decreased in individuals with PKD1 mutations. Label-free mass spectrometry comparison of ELVs from normal and PKD1 urine showed that several other proteins were decreased to a degree similar to PC1, including a small signal peptide bearing protein of unknown function, CUB062, the product of the C2orf62 gene.

Methods: To determine whether this novel protein is involved in cystogenesis, we applied a genetic approach and deleted the entire C2orf62 open reading frame in c57Black6j mice. We also investigated the ability of CUB062 to interact with the entire 4302 aa ORF of PC1 and mapped the interacting domains. Furthermore, we probed its ability to rescue injury induced PC1/PKD1 knock-out (KO) murine cilia mutant phenotype.

Results: A TALEN induced deletion of the entire C2orf62 ORF generated mice that were grossly phenotypically normal, and both sexes were fertile. Close inspection of the kidney showed that about 25% of the homozygous null animals had mild tubular dilation in the loop of Henle and collecting duct. The C2orf62- allele exacerbated the fibrocystic disease phenotype in mice using primary cilia patch clamp.

Conclusions: Our data indicate that CUB062 activated cystogenesis in vivo in cilia mutant mice to drive rapid, injury induced cystogenesis.

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SA-OR25

Interconnected Cells and the Transmission Factor FOXIN1 Drive the Kidney Cystogenesis in Tuberous Sclerosis Complex

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Background: Tuberous sclerosis complex (TSC) is caused by mutations in either the TSC1 or TSC2 gene and affects multiple organs, including the kidney. Patients can present with benign tumors (angiomylipomas) and cysts, which can lead to kidney failure. Factors that promote cyst formation and tumor growth in TSC are poorly understood.

Methods: Mice with principal cell specific inactivation of Tsc1 were generated. In addition, mice with double deletion of Fox1 and Tsc1 (Fox1/Tsc1 double KO) or ERT2+ Ift88 f/f (hereafter referred to as cilia mutant mice), ischemia-reperfusion was performed and renal tissue was analyzed for cyst number and size. RNA-seq studies demonstrated a 3-fold enhanced expression of Fox1, which is critical to the development of IC cells and regulation of V H+-ATPase. RNA-seq studies demonstrated a 3-fold enhanced expression of Fox1, which is critical to the development of IC cells and regulation of V H+-ATPase. The expression of Fox1 was significantly increased in FOXIN1 knock-out mice. FOXIN1 knock-out mice showed significantly reduced cyst burden and increased longevity vs. Tsc1 KO mice.

Conclusions: These data suggest that CUB062 might be a circulating ligand for PC1 and carbonic anhydrase 2 (CAII) and Tsc1 (CAII/Tsc1 double KO) were generated based on RNA-seq and expression studies. Results: Tsc1 KO mice showed numerous kidney cortical cysts, which were overwhelmingly comprised of A-intercalated (A-IC) cells that showed strong expression of apical V H+-ATPase. RNA-seq studies demonstrated a 3-fold enhanced expression of Fox1, which is critical to the development of IC cells and regulation of V H+-ATPase and CAII. The expression of Fox1 in Pkd1 mice remained unchanged vs. WT mice. Deletions Fox1 completely abrogated the cyst burden in Fox1/Tsc1 dko mice (Kidney MRK, p=0.0017) and caused a profound reduction in V H+-ATPase expression in the A-IC cells. Mice with double deletion of Tsc1 and CAII, a regulator of V H+-ATPase, showed significant reductions in cyst burden and increased longevity vs. Tsc1 KO mice.

Funding: Veterans Affairs Support, Private Foundation Support

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Underline represents presenting author.
SA-OR26

Genome-wide Analyses Provide Insights into the Architecture of Kidney Function and CKD in African Americans in the Million Veteran Program (MVP)

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Background: End-stage kidney disease (ESKD) incidence rates for African Americans are more than 3 times higher than for European-Americans. This disparity has been only partly explained by known determinants of ESKD and the presence of high-risk APOL1 variants. The identification of “second hit” triggers may explain kidney outcome disparities observed in African Americans.

Methods: We performed a GWAS of eGFR among 84,544 African Americans from the MVP at or closest to enrollment. Exclusion criteria were: dialysis, kidney transplant, and BMI>18. We evaluated the association of common (minor allele frequency >1%) SNPs with linear eGFR (by CKD-EPI equation), adjusted for age, sex, BMI, and the top ten principal components of ancestry. Analyses were performed by strata of diabetes and estimates were aggregated with fixed-effects meta-analysis.

Results: We identified 2,275 SNPs in 22 independent loci associated with eGFR (p<5x10^-8). The SNP with the strongest signals replicated previously detected associations at SPTASL1/GATM (rs2486272, p = 1.7 x 10^-10). Of these, 19 were identified previously reported loci from GWAS of kidney function or CKD. Known CKD genes from case-control studies such as APOL1 (rs73885319 p=9.08x10^-28) were included in the known loci. Three were novel loci for the association with kidney function in African Americans. Of the novel variants, we discovered SNPs in ABCA1 (rs10091574 p = 2.97x10^-10) associated with accelerated atherosclerosis and lipid metabolism through PPPAR alpha, PRKCI/ps564767p = 3.1x10^-8 associated with leskocyte count and BLK(rs6964029 p=2.49 10^-8) associated with colorectal adenoma. Some of the strongest signals previously reported for kidney phenotypes included: DAB2 (rs25427131 p=1.5 x 10^-10), OCT2 (rs2279463, p=1.98 10^-10), UNCG (rs62435145 p=1.97 10^-10) and PRKAG2 (rs10253736 p=3.0x10^-10). 70 SNPs were exonic variants overall. SNPs within UMOD/PDILT, the top hits for kidney function GWAS and CKD progression among European-Americans, did not reach genome-wide (p=9.19x10^-10) significance.

Conclusions: In this large GWAS of eGFR among African Americans to date, we replicate over 19 previously identified loci, identify 3 novel loci associate with kidney function.

Funding: Veterans Affairs Support

SA-OR27

3D Genome Architecture of Human Renal Cortex and Medulla

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Background: Genomic DNA is organized in a non-random manner within the mammalian nucleus. How this three-dimensional genome architecture influences cell-type specific phenotypes is poorly understood. Genome-wide methods such as Hi-C or massively sequenced Hi-C architecture maps can only be used if the tissue can be dissociated. We developed a novel machine learning algorithm used in the domain of computer vision to identify significant contacts in our Hi-C data.

Methods: We performed global genome conformation (Hi-C) analysis on macrodissected human renal cortex and medulla from the same individual. Since existing algorithms to identify intra and inter-chromosomal interactions in Hi-C sequencing data are plagued by low concordance, we developed a novel machine learning algorithm used in the domain of computer vision to identify significant contacts in our Hi-C data.

Results: Each kidney Hi-C sample was deep sequenced to >400 million mapped contacts enabling visualization of topologically associated domains (TADs) and contacts at 10kb resolution. Comparing even these highly similar samples, our novel algorithm identified significantly different genome conformation at multiple intra-chromosomal contacts in renal cortex (n=1789) and medulla (n=1841) (figure). Further validation by DNA-FISH and comparison to orthogonal functional genomic data sets (ATAC-seq, RNA-seq) are ongoing.

Conclusions: These high-resolution chromatin conformation maps of intact human kidney tissues will provide a valuable resource for the study of kidney genome regulation. Our novel loop-calling algorithm enabled identification of fine genome architectural differences between renal cortex and medulla. Our data can also be used to link genetic risk loci to target genes in genome-wide association studies.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

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complement system, also cause aHUS. In the glomeruli, DGKE is expressed in endothelial cells and podocytes. The molecular mechanisms by which DGKs cause aHUS are not known. Phosphatidylinositol bisphosphate [PtdIns(4,5)P2] levels are reduced in Dgke knockout cells. Since the disruption of vascular endothelial factor A (VEGFA) signaling in humans and mice results in glomerular lesions that resemble those in humans with loss-of-function mutations in DGKE, we hypothesized that loss of Dgke may impair VEGFA signaling in endothelial cells due to shortage of PtdIns(4,5)P2.

**Methods:** To test this hypothesis, we performed in vitro studies on Dgke knockdown human umbilical vein endothelial cells (HUVECs) and generated endothelial-specific Dgke2 conditional knockout mice.

**Results:** We found that signaling downstream of VEGFA receptor 2 (VEGFR2) is compromised in Dgke knockdown HUVECs due to decreased activation of Akt, a phenotype that is rescued by supplementation the culture medium with PtdIns(4,5)P2. Endothelial-specific Dgke2 conditional knockout mice spontaneously developed thrombocytopenia, scistocytosis, and renal insufficiency, indicating that the endothelium is the cellular compartment responsible of the DGKE disease. Remarkably, these mice also developed albuminuria at later times, indicating that the impairment of the glomerular barrier, which is characteristic of the DGKE disease, is a later and secondary event.

**Conclusions:** Our data indicate that loss of Dgke compromises signalling downstream of VEGFR2 in endothelial cells by decreasing cellular levels of PtdIns(4,5)P2, inducing aHUS and, secondarily, disruption of the glomerular barrier. These results also implicate that pharmacological manipulation of the VEGFA signaling may be used to modify the clinical course of other forms of aHUS.

**SA-OR30**

**Re-Envisioning the APOL1 Cation Channel Structure**

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**Background:** Apolipoprotein L-I (APOL1) is a channel forming protein that protects humans and other primates from African trypanosome infection. African Americans have inherited common APOL1 variants with increased trypanolytic potential; however, these variants are responsible for an increased risk of kidney disease compared with other variants. Human APOL1 forms non-selective cation channels in a strictly pH dependent manner: channel formation requires acidic pH, whereas channel opening requires pH neutralization. Current APOL1 structural models rely on tenuous comparisons with neutralization.

**Methods:** We recently identified by high-throughput screening and subsequent medicinal chemistry, small molecule TMEM16A inhibitor TMinh-23 that inhibits TMEM16A current fully, with IC50 ~ 30 nM. Here we tested TMinh-23 pharmacokinetics in rodents and its effects on vascular smooth muscle contraction (via wire myograph) and BP in spontaneously hypertensive rats (SHR) and wild type rodents.

**Results:** TMinh-23 pretreatment blocked maximum in vitro vascular smooth muscle contractions induced by a thromboxane mimetic (U46619) in rat mesenteric arteries by 90%. Intraperitoneal (ip) administration of TMinh-23 to rodents at 10 mg/kg produced sustained systemic effects in concentrations of ~10 μM for >4 hours. BP measurements by tail-cuff and telemetry showed a maximum ~45 mmHg reduction in SBP in spontaneously hypertensive rats (SHR) after a single dose TMinh-23 (~10 mg/kg, ip) compared to vehicle administration, with BP gradually returning to baseline values within 6-8 hours after TMinh-23 pretreatment. Minimal effect on BP (less than 10 mmHg decrease in SBP) was seen in wild-type rats and mice with TMinh-23 treatment (10 mg/kg, ip). Chronic 5-day treatment of SHR with TMinh-23 (~10 mg/kg, ip, twice daily) caused sustained decreases (~25 mmHg) in daily average SBP, DBP and MAP during the treatment period. TMinh-23 action was reversible, with BP returning to baseline (~170/115 mmHg) by 3 days after discontinuation of treatment.

**Conclusions:** These studies provide validation for TMEM16A as a target for hypertension therapy, and demonstrate the proof-of-concept for efficacy of TMinh-23 as an antihypertensive with a novel mechanism of action.

**Funding:** NIDDK Support, Private Foundation Support

**SA-OR32**

**Intravitral Imaging of Affenter Arteriole Calcium Dynamics and the Role of Connexin 45**

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**Background:** The glomerular afferent (AA) and efferent (EA) arterioles are the most critical resistance vessels in the autoregulation of renal blood flow and glomerular filtration rate. Calcium dynamics of vascular smooth muscle cells (VSMC), in part mediated by gap junction communication via connexin 45 (Cx45), are important regulators of AA contractility and myogenic tone. We aimed to study the role of Cx45 in renal hemodynamics in vivo.

**Methods:** Intravitreal imaging with multiphoton microscopy (MPM) of renal functional parameters was performed in mice expressing a genetically encoded calcium indicator (GCaMP3 or GCaMP5) in cells of renin lineage with or without connexin 45 knockout (KO). Suramin treatment was used to test the effects of purinergic receptor blockade.

**Results:** Compared to the uniform upstream AA segment, high baseline and A(a-), were observed in a few AA VSMCs at the glomerular entrance, which appeared to function as sphincter cells. The diameter of the AA (25±1.27μm WT, vs. 11.3±0.37μm KO) and EA (7.18±0.36μm WT, vs. 8.58±0.30μm KO) were larger in KO animals, although no difference was found in SBP, snGFR and glomerular diameter. Blood flow in AA was also increased (1.42±0.15μm/min WT, vs. 2.0±0.12μm/min KO). AA myogenic tone was visualized 3-4 weeks after unilateral ureteral obstruction (UUO). In WT animals, regular AA contractions were observed uniformly in all AAs with an average frequency of 0.12±0.01 Hz, with large magnitude A(a-), in VSMCs during every contraction (A(a-)) ~ 556±635 AU). In contrast, KO animals showed highly heterogeneous and irregular vascular activity. In those AAs that did exhibit some myogenic tone-like contractions, a higher frequency was observed (0.28±0.02 Hz), however the magnitude of A(a-)) in AA VSMCs was much lower than in the WT (A(a-)) ~ 395±249 AU). In both WT and KO animals, treatment with suramin rapidly blocked AA VSMC calcium influx and the myogenic contractions, and the AA became dilated.

**Conclusions:** AA sphincter cells have robust effects on AA (Ca(a-)), dynamics and contractility in vivo, and Cx45 and purinergic signaling are essential components of AA calcium signaling and vascular contractility. Cx45 and purinergic signaling in the AA regulate the myogenic response and renal blood flow, and may be culprit and potential target in vascular pathologies.

**Funding:** NIDDK Support
SA-OR33
Inorganic Nitrate Supplementation Improves Endothelial Function with Age: Translational Evidence for Suppression of Mitochondria-Derived Oxidative Stress
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Background: We previously observed improvements in vascular endothelial function with inorganic nitrate supplementation in old mice, which we translated to older humans in a pilot study of sodium nitrite supplementation. Methods: Here, we sought to confirm the efficacy of sodium nitrite in humans and determine mechanisms of action using: 1) a randomized, placebo-controlled, parallel-group clinical trial with sodium nitrate (80 mg/day, 12 weeks) in older adults (n=49, 68±1 yr) and 2) reverse translation experiments in young (6 mo) and old (27 mo) male C57BL/6 mice.

Results: In humans, sodium nitrite increased plasma nitrite (p<0.05) and was well-tolerated over 12 weeks. Endothelial function (brachial artery flow-mediated dilation) was increased by 28% vs. baseline after nitrite supplementation (p<0.05), but unchanged with placebo. Serum from nitrite-treated subjects reduced whole-cell (CellROX) and mitochondria (mito)-specific (MitoSOX) reactive oxygen species (ROS) in human umbilical vein endothelial cell culture (p<0.05), whereas serum from placebo-treated subjects had no effect. Old mice (OC, n=9) had ~30% lower ex vivo carotid artery endothelium-dependent dilation (EDD) vs. young mice (YC, n=9) due to reduced nitrite oxide (NO) bioavailability (p<0.05). Nitrite supplementation (drinking water, 50±8 mg/L, 8 weeks) restored EDD and NO bioavailability in old mice (ON, n=10). MitoROS suppression of EDD was present in OC (increased EDD with a mito-targeted antioxidant, p<0.05), but not in Y or ON. A mito stressor (rotenone) further impaired EDD in OC (p<0.05), whereas Y and ON were protected.

Conclusions: Nitrite supplementation improves age-related endothelial dysfunction and is associated with increased NO, reduced mito ROS and improved mitochondrial stress resistance. Funding: NIDDK Support, Other NIH Support - NIH RO1 AG103308, NIH/NCCATS Colorado CTSA Grant Number UL1 TR002535

SA-OR34
Paracrine FGF-23 Signaling in the Heart Causes Cardiac Hypertrophy
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Background: Elevated serum levels of the phosphaturic hormone, fibroblast growth factor (FGF) 23, contribute to cardiac hypertrophy in chronic kidney disease (CKD). FGF23 directly targets cardiac myocytes via FGF receptor (FGFR) 4 to induce hypertrophic growth and FGFR4 blockade not only protects rodent models of CKD from cardiac hypertrophy but also from fibrosis. Our cell culture studies indicate that cardiac fibroblasts do not directly respond to FGF23. It is known that a miscommunication between cardiac myocytes and fibroblasts contributes to pathologic cardiac remodeling. It has been shown that in rodent models and patients with CKD, as well as in mice on high phosphate diet without kidney injury, the heart starts to produce FGF23. Here, we studied if by targeting cardiac myocytes FGF23 promotes paracrine signaling that drives fibrosis. We aimed to determine the cardiac cell type(s) that act as FGF23 source and study if FGF23 serves as a novel paracrine signal mediator between cardiac cell types.

Methods: We treated cultured cardiac myocytes with FGF23 and determined expression levels of established paracrine signal mediators (IL6, LIF, TGFβ, FGF2), or with high phosphate and analyzed FGF23 expression, all by qPCR. We isolated cardiac fibroblasts from wildtype mice on a high phosphate (2%) diet or control chow (0.7%) for 12 weeks. We analyzed paracrine signal mediators by qPCR, as well as FGF23 by qPCR and ELISA. After plating cardiac fibroblasts for 24 and 48 hours, we transferred cell supernatants to myocytes and analyzed hypertrophy.

Results: FGF23 did not increase the expression of paracrine signal mediators in cardiac myocytes, or fibroblasts. Phosphate elevations induced FGF23 expression in cardiac fibroblasts, but not in myocytes. Cardiac fibroblast-derived supernatants showed pro-hypertrophic activity when transferred to myocytes, which could be inhibited by co-administration of blocking antibodies for FGF23 or FGFR4.

Conclusions: FGF23 does not affect cardiac fibroblasts by regulating paracrine signal mediators in myocytes. However, FGF23 acts as a novel fibroblast-derived paracrine signaling mediator that induces hypertrophic growth of cardiac myocytes in an FGFR4-dependent manner in scenarios of hyperphosphatemia, such as CKD.

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SA-OR35
A Renal Potassium-Switch Prioritizes Dietary Potassium Over Sodium, Driving Salt-Sensitive Hypertension
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Background: Reducing dietary salt (NaCl) is well appreciated to lower blood pressure, but what a growing body of evidence indicates that increasing dietary potassium (K) intake is equally important. A ‘renal K switch’ that turns on the thiazide-sensitive NaCl cotransporter (NCC) in response to low dietary K intake and off in response to high K intake has been implicated. Here we test this idea in genetically engineered mice (CA-SPAK) in which the K switch is ‘locked on.’

Methods: Kinase-activating mutations were introduced in SPAK, Expression of the constitutively active (CA) SPAK mutant was limited to the early DCT and results in NCC hyperactivation. BP responses to small changes in plasma [K+] in CA-SPAK were compared to control mice. Dietary K content was varied over 4 days to titrate [K+] over a narrow range (3.7 mLK, 4.4mM K, and 5.1mM HK). Blood pressure was monitored by telemetry at each [K+] level in mice consuming control or high salt diet (HNa). At the end of each treatment, the BP response to hydrochlorothiazide (HCTZ) was measured to assess the contribution to BP.

Results: BP decreased by ~10 mmHg when [K+] increased from 3.7 to 5.1 m in control mice, coincident with the inactivation of NCC. When the switch was on (LK and MK groups), HNa significantly elevated BP but had no effect when the switch was inactivated by HK. HCTZ significantly reduced BP in the LK/HNa and MK/HNa groups but had no effect on BP in the HK/HNa group, supporting the low K switch hypothesis. HCTZ activation of NCC exacerbates the effects of Na. Studies in CA-SPAK mice reveal a causal relationship between switch activation and BP responses to Na and HK. In contrast to control mice, increasing [K+] in CA-SPAK mice had no effect on BP under control salt conditions and failed to blunt the significant hypertensive effects of HK. HCTZ significantly decreased BP in all CA-SPAK groups to near control levels, consistent with NCC-driven salt reabsorption. Thus, locking on the K switch prevents the anti-hypertensive effects of HK. No sex differences were found.

Conclusions: In summary, low K consumption, common in modern diets, presses the switch pathway to turn on to conserve K at the expense of increasing Na retention, even in the face of high dietary Na, and this elevates BP. Thus, switch activation can drive salt-sensitive hypertension.

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SA-OR36
Risk of Cardiovascular Events Is Higher in Patients with Glomerular Disease Compared with the General Population
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Background: Cardiovascular (CV) disease is a recognized cause of morbidity and mortality in chronic kidney disease; however, understanding of CV risk in patients with glomerular disease (GN) is limited. We sought to define CV risk in GN patients and compare incidence rates to the general population.

Methods: A centralized kidney pathology registry (2000-2012) was used to capture all incident cases of focal segmental glomerulosclerosis (FSGS, n=540), IgA nephropathy (IgAN, n=759), membranous nephropathy (MN, n=387), and minimal change disease (MCD, n=226) in British Columbia, Canada. The primary outcome was a composite of major CV events, ascertained from a hospital discharge registry and evaluated using the Kaplan-Meier method. Hazard ratios (HR, 95% CI) were determined using Cox proportional hazards regression. Event rates were age and sex standardized to the general adult population to generate standardized incidence ratios (SIR, 95% CI).

Results: Over a median follow-up of 6.5years there were 338 CV events; 10-year risk (95% CI) was 16.0% (13.8-18.3) and differed by GN type(Figure): IgAN=7.7% (5.4-10.4), MCD=13.2% (7.6-20.4), MN=19.4% (14.3-25.0), and FSGS=27.0% (21.9-32.4). Compared to IgAN, MN (HR=2.6, 1.7-3.9) and FSGS (HR=3.7, 2.6-5.3) had higher risk, but MCD (HR=1.3, 0.8-2.4) did not. Results were similar when comparing CV events occurring after ESKD. CV risk in GN patients was 2.5-fold higher than the general population (SIR 2.5, 2.1-2.8), and was higher in each GN subtype (IgAN=1.4, 1.0-1.8; MCD=1.8, 1.0-2.8; MN=3.0, 2.2-4.0; FSGS=4.0, 3.2-4.9).

Conclusions: Patients with GN are at high risk of CV disease, both before and after ESKD onset. The CV risk for all GN subtypes was higher than the general population, including MCD and IgAN. This suggests CV preventive strategies should be considered in all patients with GN.
SA-OR37
Prediction of Atrial Fibrillation Using Clinical and Cardiac Biomarker Data: The CRIC Study
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Background: Clinically available biomarkers of myocardial injury (high sensitivity troponin T, hsTnT) and hemodynamic stress (N-terminal brain natriuretic peptide, NT-proBNP) are strongly associated with atrial fibrillation (AF) in chronic kidney disease (CKD), and have been included in AF prediction models in community-based populations. We investigated the incremental prognostic value of NT-proBNP and hsTnT for AF prediction compared to standard clinical variables in CKD patients enrolled in the Chronic Renal Insufficiency Cohort (CRIC) using machine learning methods.

Methods: Among 2690 CRIC participants without prior AF with complete cardiac biomarker data, cardiac biomarkers NT-proBNP and hsTnT were added to a previously developed AF prediction model using machine learning techniques. Calibration of the AF prediction model was assessed using 10-fold cross-validation; calibration was evaluated graphically.

Results: Mean (SD) age of participants was 57 (11) years, 55% men, 38% black, and 74% with stage 3 chronic kidney disease (CKD). Mean (SD) eGFR 45 (15) mL/min/1.73m2; 251 incident AF events occurred during 7.3 (2.8) years of follow-up. CHARGE-AF prediction equations using original and re-estimated coefficients to predict AF. Discriminatory ability of each model was assessed using 10-fold cross-validation; calibration was evaluated graphically.

Conclusions: Cardiac biomarkers NT-proBNP and hsTnT can improve AF prediction in CKD, particularly when paired with machine learning algorithms.

Funding: NIDDK Support

SA-OR38
Renal Hyperfiltration and the Effect of Intensive vs. Standard Blood Pressure Lowering on Cardiovascular Outcomes
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Background: Using the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial and Systolic Blood Pressure Intervention Trial (SPRINT), we examined whether the effect of intensive versus standard blood pressure (BP) lowering on cardiovascular outcomes varies by the presence of renal hyperfiltration.

Methods: We pooled data on adults in ACCORD and SPRINT without chronic kidney disease (eGFR>60 and urine albumin-to-creatinine ratio <30 mg/g). RHF was defined as an eGFR above the 95th percentile for healthy adults in the National Health and Nutrition Examination Survey. Outcomes of interest were major adverse cardiovascular events (MACE, as defined in the ACCORD primary outcome): a composite of cardiovascular (CV) mortality, acute myocardial infarction (AMI) and stroke. Secondary outcomes were all-cause mortality, CV mortality and CV events. We used fixed effect cox regression.

Results: There were 17,824 and 17,912 adults with RHF and without RHF, respectively. Intensive BP lowering modified the effect of intensive versus standard BP lowering on MACE (p-interaction=0.002) but not all-cause mortality (p-interaction=0.059). For adults with RHF, intensive BP lowering reduced incidence of MACE compared with standard BP lowering (HR: 0.82, 95%-CI: 0.73-0.92). The risk reduction was smaller in adults with normal filtration (HR: 0.84, 95%-CI: 0.71-0.98). Intensive BP lowering was also associated with a larger reduction in the incidence of CV mortality and stroke among adults with RHF (Figure, p-interaction=0.001) but not MACE or heart failure (p-interaction=0.41). Separate analyses of ACCORD and SPRINT were similar.

Conclusions: RHF modified the effect of intensive versus standard BP lowering on cardiovascular outcomes.

Intensive Versus Standard Blood Pressure Lowering and Cardiovascular Outcomes in Adults With and Without Renal Hyperfiltration (Pooled Analysis)

SA-OR39
Pooled Analyses of the Phase 3 Roxadustat Studies: Congestive Heart Failure Hospitalization Rates in Dialysis and Non-Dialysis Patients with Anemia Treated with Roxadustat vs. Comparators
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Background: Roxadustat is an orally bioavailable hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Phase 3 roxadustat studies were performed to treat anemia of chronic kidney disease (CKD). Congestive heart failure (CHF), a common comorbidity in CKD, is associated with a poor prognosis in CKD patients, with a prevalence that increases with CKD severity; approximately 20% in mild CKD (eGFR ≥65) to 40% in patients on hemodialysis.

Methods: Safety data were pooled from pivotal phase 3 studies comparing roxadustat to placebo in Stage 3-5 non-dialysis-dependent (NDD) CKD patients, and to epoetin alfa in the overall dialysis-dependent (DD) CKD patients, and to epoetin alfa in the overall dialysis-dependent (DD) CKD patients, and to epoetin alfa in the overall dialysis-dependent (DD) CKD patients, and to epoetin alfa in the overall dialysis-dependent (DD) CKD patients. Patients with baseline (BL) moderate to severe CHF were not enrolled. CHF hospitalization events were a component of the MACE-plus endpoints in CKD, was also analyzed. CHF is associated with a poorer prognosis in CKD patients, with a prevalence that increases with CKD severity; approximately 20% in mild CKD (eGFR ≥65) to 40% in patients on hemodialysis.

Results: In the pooled NDD studies, 4270 patients were analyzed (2386 roxadustat; 1884 placebo). BL CHF history was comparable between roxadustat (13.0%) and placebo (13.6%) arms. Using ITT long-term follow-up, the HR (95% CI) of hospitalization for CHF among the NDD pooled population was 0.89 (0.72; 1.22) for roxadustat vs placebo. In the pooled DD studies, 3946 patients were analyzed (1940 roxadustat; 1904 epoetin alfa). BL CHF history was comparable between roxadustat (25.7%) and epoetin alfa.
Racial-Ethnic and Socioeconomic Disparities in Healthcare Utilization in Patients with CKD, Diabetes, and Recent Acute Coronary Syndrome: Results from the BETonMACE Trial

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Background: Chronic kidney disease (CKD) in type 2 diabetes mellitus (T2DM) patients (pts) is associated with increased cardiovascular disease (CVD) and heart failure risk. We hypothesized that a maladaptive epigenetic response engaging the bromodomain and extraterminal (BET) protein transcription system contributes to excess CVD risk. Hence, the efficacy of BET inhibition (BETi) treatment with apabetalone (APB) was assessed according to presence of CKD in the phase 3 BETonMACE trial.

Methods: BETonMACE compared APB with placebo in 2425 pts with T2DM and recent acute coronary syndrome. The primary outcome was CV death, non-fatal myocardial infarct or stroke (MACE). Hospitalization for congestive heart failure (CHF) was a secondary endpoint. Both outcomes were evaluated according to the presence of CKD (estimated GFR <60 mL/min/1.73 m2 at baseline).

Results: CKD pts were older (71 vs. 61 years), more likely female (42% vs. 23%) or non-white (18% vs. 12%), had longer duration of diabetes (mean 11.3 vs. 8.2 years) and higher serum alkaline phosphatase (91 vs. 81 U/L), and were less likely to receive metformin (69% vs. 84%) or SGLT2 inhibitors (6% vs. 13%) (P<0.05 for all). Under placebo, risk of endpoints was higher in CKD vs. non-CKD pts (MACE: 35/164 (21.3%) vs. 114/1041 (11.0%), HR=2.40, 95% CI [1.67, 3.44]; HCHF: 14/164 (8.5%) vs. 34/1041 (3.3%), HR=3.19, 95% CI [1.66,6.12]; P=0.001 for both). Under APB treatment, pts with CKD had significant reductions in MACE (HR=0.50, 95% CI [0.26, 0.96]; P=0.034) and HCHF (HR=0.26, 95% CI [0.07,0.94], P=0.028) vs. placebo, see Kaplan-Meier figures.

Conclusions: In patients with CKD, the efficacy of BETi treatment with APB was substantially reduced in CKD compared to non-CKD pts, consistent with a maladaptive epigenetic response engaging the bromodomain and extraterminal (BET) protein transcription system in patients with CKD.

SA-OR42

Prevalence of Left Ventricular Hypertrophy in Pediatric Patients on Maintenance Dialysis and After Kidney Transplantation: A NAPRTCS Study

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Background: Left ventricular hypertrophy (LVH) is recognized as the most common cardiovascular complication in children on maintenance dialysis. There have been small single-center, or cross-sectional multi-center studies but there has been no large multi-center studies looking at prevalence of LVH during long-term maintenance dialysis. Using the NAPRTCS database, we determined the prevalence of LVH at time of initiation of maintenance dialysis and changes during long-term dialysis and post kidney transplantation. We also assessed the risk factors associated with LVH in children initiating maintenance dialysis.

Methods: Echocardiographic data were obtained from the NAPRTCS database which initiated collection of echo data in 2013 with the last data obtained in March 2020. LVH was defined as left ventricular mass index (LVMI, height-indexed)>95th percentile for age and sex. Patients with cardiovascular diagnoses, those younger than 1 year old at the time of echocardiography, LVMI values >200 g/m2.7, and LVMI values based on outputting heights were excluded from analysis. Multivariable logistic regression to assess risk factors for LVH at baseline (within first 3 months after initiation of dialysis) was performed.

Results: The study cohort included 606 patients between 1 and 18 years of age (median 10y (IQR 3.8-15.1), 53% females, 48% whites, 27% African-American, and 25% others/unknown) who had LVH data during time on dialysis. Of 182 patients who had echocardiography within first 3 months after initiation of dialysis (baseline), 67% had LVH. In logistic regression, hypertention (OR 2.9, 95% CI 1.4-6.3), anemia

SA-OR41

Racial-Ethnic and Socioeconomic Disparities in Healthcare Utilization Among Children with Glomerular Disease in the CureGN Project

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Background: Inpatient charges for nephrotic syndrome differ across racial-ethnic groups. This study compares rates of ACU (acute care utilization i.e., hospitalization or ED visit) across racial-ethnic groups in children with glomerular disease (GD) and explores demographic, socioeconomic (SE), and disease-related factors that might explain any observed differences.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
42
SA-OR43 Biomarker Panels for Discriminating Risk of CKD Progression in Children

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Background: We used multivariate survival tree analysis to identify plasma and clinical biomarkers to predict CKD progression in children. Methods: The CKiD study prospectively enrolled children aged 6 months to 16 years old with an eGFR of 30-90 and eGFR was assessed annually. The primary outcome of CKD progression was a composite of 50% decline in eGFR or incident ESKD. We used multivariate survival trees to determine combinations of baseline clinical predictors and plasma biomarkers as well as identify optimal thresholds for predicting the time to the composite event. Results: Of the 651 children included, median age was 11 years [IQR, 8-15], 405(62%) were male, 195(30%) had a glomerular cause of CKD, and baseline eGFR was 53 [IQR, 40-67]. 223(34%) of 651 children reached the primary outcome over a median follow-up time of 5.7 years. The Figure shows the best-sized multivariate survival tree and 4 prognosis groups selected after bootstrapping the sample. Plasma KIM1, TNFR1, TNFR2, and baseline eGFR were used to define branching patterns, while MCP1, YKL40, suPAR and the known risk factors of sex, age, glomerular diagnosis, BMI, hypertension, and proteinuria were not included as they did not reach a level of predictive importance. In the final model, KIM1 was the variable with the highest importance, with a median follow-up time of 5.7 years. The Figure shows the best-sized multivariate survival tree and 4 prognosis groups selected after bootstrapping the sample. Plasma KIM1, TNFR1, TNFR2, and baseline eGFR were used to define branching patterns, while MCP1, YKL40, suPAR and the known risk factors of sex, age, glomerular diagnosis, BMI, hypertension, and proteinuria were not included as they did not reach a level of predictive importance. In the final model, KIM1 was the variable with the highest importance, with a median follow-up time of 5.7 years.

Conclusions: Children who had onset of CKD after pubertal onset were excluded. GFR was estimated annually using the bedside and complete CKD equations. Pubertal onset was defined by three separate definitions: transition to Tanner Stage 2, peak growth velocity, and menarche. A mixed effects model with random intercept and random slope was used to compare the slope of eGFR before and after pubertal onset. The model was adjusted for age, race, glomerular diagnosis, baseline proteinuria, and BMI. Results: 339 girls and 552 boys were included; Median age of pubertal onset for girls was 11.0 years [IQR 9.8, 12.1], 14.1 years [IQR 12.4, 17.0], and 14.4 years [IQR 13.1, 15.7] as defined by Tanner stage 2, peak growth velocity, and menarche, respectively. Median age of pubertal onset for boys was 12.4 years (11.3, 13.3) and 14.6 years (IQR 13.4, 16.6) as defined by Tanner stage 2 and peak growth velocity, respectively. Annual percent change in eGFR declined faster among girls and boys after pubertal onset when defined by all measures, after adjustment. For example, annual percent decrease in eGFR was seen to increase from 2.6% prior to 9.0% after Tanner stage 2 in boys using the complete CKD equation (p=0.001).

Conclusions: Estimated GFR declined faster after the onset of puberty among girls and boys with CKD. Clinicians should be aware that puberty may be an important time of kidney function decline among children with CKD. Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Results: We identified a rare homozygous variant, CLF5I H310Y, that segregates with disease in a consanguineous family with two affected siblings and a cousin. CLF5I encodes claveslin1, a component of clatherin-mediated endocytosis. This variant was not present in a homoygous state in >200,000 chromosomes and is predicted to be pathogenic by in silico analyses. Morpholino knockdown of the orthologous CLF5I gene in zebrafish resulted in edema phenotypes indicative of loss of glomerular filtration barrier (GFB) integrity. This edema phenotype could be rescued with wildtype human CLF5I mRNA but not the H310Y variant. Knockdown of CLF5I in cultured human podocytes as well as overexpression of the H310Y variant in HEK 293 cells decreased endocytosis of fluorescein labeled dextran and increased susceptibility to apoptosis. These aberrant podocyte phenotypes could be rescued in the presence of glucocorticoid, mimicking the sterile responsive phenotype in patients bearing the CLF5I H310Y variant.

Conclusions: We identified a mutation in CLF5I as a new cause of hereditary SSNS. Our data demonstrates the requirement of functional steroid responsive phenotype in patients bearing the SSNS. Our data demonstrates the requirement of functional steroid responsive phenotype in patients bearing the SSNS.

Funding: NIDDK Support, Private Foundation Support

SA-OR46
Cross-Talk Between Neutrophils and Macrophages Dictates the Outcome of Acute Pyelonephritis
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Background: Pediatric urinary tract infections (UTIs) account for 1.5 million clinic visits annually in the United States. Uropathogenic Escherichia coli (UPEC) causes over 80% of UTIs. Up to 50% of infants with a UTI develop a kidney infection (acute pyelonephritis, APN). To study cell-type specification of renal epithelial cells, we conducted trajectory analysis and resolved the developmental pseudotime along cell differentiation from nephron progenitors. We show that early differentiation of podocytes from the nephron progenitor pool is associated with sustained Foxl1 expression. Differentiation of renal tubule cells followed a more complex pattern, where Hnf4a expression is associated with a more proximal fate, while Tip2b is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Eoxra and Ppara for proximal tubules and Ertb and Ppara-ga in loop of Henle.

Methods: Here we conducted single-nucleus ATAC sequencing (snATAC-seq) and single cell RNA-sequencing (scRNA-seq) of kidneys from developing and adult mice. After quality control, we obtained 66,254 scRNA-seq and 28,316 snATAC-seq profiles.

Results: Through clustering analysis, we identified all major cell types in the kidney. By integrating snATAC-seq and scRNA-seq data, we revealed cell type- and developmental stage-specific cis-regulatory elements and inferred promoter-enhancer regulatory units. We defined key cell identity TFs and their gene targets through co-expression patterns. To study cell-type specification of renal epithelial cells, we conducted trajectory analysis and resolved the developmental pseudotime along cell differentiation from nephron progenitors. We show that early differentiation of podocytes from the nephron progenitor pool is associated with sustained Foxl1 expression. Differentiation of renal tubule cells followed a more complex pattern, where Hnf4a expression is associated with a more proximal fate, while Tip2b is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Eoxra and Ppara for proximal tubules and Ertb and Ppara-ga in loop of Henle.

Conclusions: We find that loss of Smad4 participates in the Wnt/b-catenin signaling pathway in renal epithelial cells but not the renal interstitium. Smad4 in interstitial cells was confirmed by single cell genotyping and immunostaining. Our findings point to a novel detrimental function for macrophages during APN, and the potential utility of macrophage targeted therapies to reduce long-term sequelae following APN.

Funding: NIDDK Support, Other NIH Support - NIDCD

SA-OR47
Proliferation Control of Interstitial Cells in the Neonatal Kidney
Leif Oxburg, The Rogozin Institute, New York, NY.

Background: Expansion of interstitial cells in the adult kidney is a hallmark of chronic disease, whereas their proliferation during fetal development is necessary for organ formation. An intriguing difference between adult and neonatal kidneys is that the neonatal kidney has the capacity to control interstitial cell proliferation when the target number has been reached in this study, we determine the consequences of inactivating the TGFβ/Smad response on proliferation control of the renal interstitium in the neonatal mouse.

Methods: Smad4 was inactivated using the FloxIcre mouse strain, which is specifically expressed in interstitial progenitor cells in the developing kidney. Loss of Smad4 in interstitial cells was confirmed by single cell genotyping and immunostaining. Interstitial cell lines with tamoxifen-inducible loss of Smad4 were generated from primary interstitial cell progenitor lines for molecular interaction studies.

Results: We find that loss of Smad4 leads to over-proliferation of interstitial cells regionally in the kidney medulla. Analysis of signaling pathway markers in tissue showed that activation of Smad3 is deficient, whereas activation of Smad1/5 is largely unaffected, indicating an effect specifically on TGFβ signaling. Genetic and molecular interaction studies showed that Smad4 participates in the Wnt/b-catenin signaling pathway in interstitial cells, which is responsible for promoting their proliferation. Specifically, Smad4 is required for the expression of the Wnt feedback inhibitor Apcd1.

Conclusions: Based on these findings, we propose a model for interstitial cell proliferation control in which the Wnt/b-catenin proliferative signal is attenuated by Smad4 in interstitial cells was confirmed by single cell genotyping and immunostaining. Our findings point to a novel detrimental function for macrophages during APN, and the potential utility of macrophage targeted therapies to reduce long-term sequelae following APN.

Funding: NIDDK Support

Model for proliferation control of medullary interstitial cells

SA-OR48
Single-Cell Resolution Regulatory Landscape of the Kidney Highlights Cellular Differentiation Programs and Renal Disease Targets
Zhen Miao, Michael S. Balzer, Ziyuan Ma, Hongbo Liu, Junnan Wu, Katalin Susztak. Susztak Lab University of Pennsylvania, Philadelphia, PA.

Background: The kidney cells undergo complex differentiation during development, among which the nephron progenitors differentiate to more than 10 different epithelial cells. However, the driver pathways, cell type specific transcription factors and regulatory circuits are not fully understood.

Methods: Here we conducted single-nucleus ATAC sequencing (snATAC-seq) and single cell RNA-sequencing (scRNA-seq) of kidneys from developing and adult mice. After quality control, we obtained 66,254 scRNA-seq and 28,316 snATAC-seq profiles.

Results: Through clustering analysis, we identified all major cell types in the kidney. By integrating snATAC-seq and scRNA-seq data, we revealed cell type- and developmental stage-specific cis-regulatory elements and inferred promoter-enhancer regulatory units. We defined key cell identity TFs and their gene targets through co-expression patterns. To study cell-type specification of renal epithelial cells, we conducted trajectory analysis and resolved the developmental pseudotime along cell differentiation from nephron progenitors. We show that early differentiation of podocytes from the nephron progenitor pool is associated with sustained Foxl1 expression. Differentiation of renal tubule cells followed a more complex pattern, where Hnf4a expression is associated with a more proximal fate, while Tip2b is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Eoxra and Ppara for proximal tubules and Ertb and Ppara-ga in loop of Henle.

Conclusions: We find that loss of Smad4 participates in the Wnt/b-catenin signaling pathway in renal epithelial cells but not the renal interstitium. Smad4 in interstitial cells was confirmed by single cell genotyping and immunostaining. Our findings point to a novel detrimental function for macrophages during APN, and the potential utility of macrophage targeted therapies to reduce long-term sequelae following APN.

Funding: NIDDK Support, Government Support - Non-U.S.

SA-OR49
Expansion of Human Induced Pluripotent Stem Cell-Derived Ureteric Bud Organoids with Repeated Branching Potential
Makoto Ryosaka, Shin-ichi Mae, Kenji Osafune. Center for iPSC Cell Research and Application (CiRA), Kyoto University, Kyoto, Japan.

Background: The mammalian adult kidney, metanephros, develops by the reciprocal interaction between two embryonic progenitor tissues, metanephric mesenchyme and ureteric bud (UB). UB has epithelial polarity and tubular lumens, consists of two domains, the tip and trunk, and repeats branching morphogenesis. The tip cells produce both new tip and trunk cells that further differentiate into collecting ducts (CDs). Recently, we reported a stepwise protocol to induce human induced pluripotent stem cells (hiPSCs) and embryonic stem cells (hESCs) into UB-like structures through anterior intermediate mesoderm. However, the generation of hiPSC/ESC-derived UB-like tissues that show tubular lumens or sufficient branching has not been achieved.

Methods: We established a novel method to induce hiPSCs to differentiate into induced UB (iUB) organoids. We evaluated our iUB organoids using immunostaining and single cell RNA-sequencing analysis.

Results: Our iUB organoids showed RET+ tip and CK19+ trunk domains, epithelial polarity, tubular lumens and developmental potential to repeat branching morphogenesis. The isolated tip regions from the iUB organoids showed repeated branching to reconstitute iUB organoids. We also succeeded in establishing in vitro monitoring and expansion methods for tip cells that can efficiently reconstitute iUB organoids and differentiate into UB-like structures through anterior intermediate mesoderm. However, the generation of hiPSC/ESC-derived UB-like tissues that show tubular lumens or sufficient branching has not been achieved.

Conclusions: Our induction method for iUB organoids will help elucidate the developmental mechanisms of UB branching and develop a selective differentiation method for CD cells, contributing to the creation of disease models for congenital renal abnormalities.

Funding: Government Support - Non-U.S.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
SA-OR02
Cyclin G1/CDK5-Mediated Dedifferentiation of Proximal Tubular Cells Drives AKI-to-CKD Transition
Kentsi Taguchi, Bertha C. Elias, Craig R. Brooks. Vanderbilt University Medical Center, Nashville, TN.

Background: Acute kidney injury (AKI) is associated with increased morbidity and mortality in hospitalized patients and predisposes patients to chronic kidney disease (CKD). While kidney cells, particularly proximal tubule cells (PTCs), can undergo dedifferentiation, proliferation, and regeneration to facilitate kidney repair after injury, maladaptive repair resulting in prolonged dedifferentiation of PTCs drives fibrosis. We have found that cyclin G1 (CG1), an atypical cyclin, not only promotes G2/M cell cycle arrest, but also regulates dedifferentiation of PTCs. The aim of the current study is to determine how regulating these processes through manipulating cyclin expression prevents CKD.

Methods: 1; Aristolochic acid nephropathy (AAN) was induced by administration of three doses of AA in 8 to 12-week-old male wild-type (WT) and CG1 globally knockout mice (CG1KO). 2; Unilateral ureteral obstruction (UUO) was performed and kidneys were harvested on day 9. 3; To determine the interaction partners of CG1, immunoprecipitation (IP) was performed in CG1-overexpressing LLC-PK1 cells treated with AA. 4; To examine the pathological role of CGDK5, LLC-PK1 cells or primary PTCs with or without siRNA or pharmacological inhibitors of CDK5 were treated with AA.

Results: CG1 was rapidly upregulated in PTCs in response to kidney injury and remained high in chronic phase following AAN and UUO. Kidney fibrosis and markers of dedifferentiation, such as SOX9, Vimentin, and Snail, were reduced in CG1KO animals following AAN and UUO injuries, compared to WT. IP demonstrated that CG1 binds to p53, mouse double minute 2 homolog (MDM2), and CDK5. Of these, the interaction of CG1 activates CDK5 and translocates the complex into nuclei. Phosphorylation of CDK5 in response to injury was reduced by genetic ablation of CG1. Genetic or pharmacological inhibition of CDK5 preserved E-cadherin in AA-induced cellular injury with reduction of profibrotic markers; however, it showed no additional effect in CG1KO PTCs.

Conclusions: CG1 partnering with CDK5 drives a maladaptive dedifferentiation of PTCs after kidney injury, resulting in increased secretion of profibrotic cytokines and progression of fibrosis. As CG1 is highly expressed in injured PTCs, it represents a potential therapeutic target for prevention of kidney fibrosis.

Funding: Private Foundation Support

SU-OR03
Incorporation of Urine-Derived Stem Cells into Kidney Organoids Derived from Human Induced Pluripotent Stem Cells
Julie Bejoy, Richard C. Welch, Lauren E. Woodard. Woodard Lab Vanderbilt University Medical Center, Nashville, TN.

Background: Donor-derived somatic cells or stem cells can be differentiated into renal cell types for disease modeling, drug screening, or therapeutic studies. Modeling of kidney disease with kidney organoids derived from human induced pluripotent stem cells (hiPSCs) has been termed a “kidney in a dish.” The recent advances in stem cell-based therapies have shown great promise for the treatment of kidney injuries. To evaluate the therapeutic properties, we studied the incorporation of urine-derived stem cells (USCs) into a kidney organoid model of acute kidney injury. USCs are viable cells from urine which can be expanded in vitro for more than ten passages. There is evidence suggesting that USCs are most likely cultured glomerular parietal epithelial cells.

Methods: For this project, we cultured kidney organoids from fibroblast-derived hiPSCs by the established protocol from Takasato and Little, following optimization. Co-culturing of USCs labeled with a membrane dye and Day 25 kidney organoids revealed that USCs are indeed incorporated into the organoids efficiently within two days of the co-culture. For injury models, we established nephrotoxicity in the proximal tubule by adding the nephrotoxic drug Cisplatin (5 μm) at Day 21 of kidney organoid culture.

Results: The kidney organoids derived from iPSCs expressed the kidney cell type markers ECAD (distal tube), GATA3 (collecting duct), LTL (proximal tubule) and NEPHRIN (Glomeruli) at Day 21. The organoids were then treated with 5 x 10⁵ USCs at Day 22 for 48 hours and evaluated for the expression of kidney injury molecule-1 (KIM-1). Immunostaining revealed that KIM-1 expression was significantly reduced in the organoids treated with USCs compared to the organoids without USCs, suggesting a positive therapeutic impact of USCs. We are currently performing RNAseq on three sets of whole kidney organoids (Control, +Cisplatin, +Cisplatin+USC) to provide detailed interrogation of cellular apoptosis and related signaling pathways in these three different sets of organoids.

Conclusions: The ability of USCs to reduce KIM-1 expression in human kidney organoids suggests that further investigation into the therapeutic potential of USC for treatment of acute kidney injury is warranted.

Funding: Private Foundation Support

SU-OR04
Supramolecular Nanofibers Containing Arginine-Glycine-Aspartic Acid (RGD) Boost Therapeutic Efficacy of Extracellular Vesicles in Kidney Repair
Gulshat Zhang,1,2 Jie Wu,1 Lingling Wu,1 Xiangmei Chen,1,2 Chinese PLA General Hospital, Beijing, China; 1Nankai University, Tianjin, China.

Background: Extracellular vesicles (EVs) derived from mesenchymal stem cells (MSC-EVs) have been recognized as a promising cell-free therapy for acute kidney injury (AKI), which avoids safety concerns associated with direct cell engraftment. However,
low stability and retention of MSC-EVs have limited their therapeutic efficacy. RGD peptide binds strongly to integrins, which have been identified on the surface of MSC-EV membranes, yet RGD has not been applied to EV scaffolds to enhance and prolong bioavailability.

Methods: Here, we developed RGD hydrogels, which we hypothesized could augment MSC-EV efficacy against AKI.

Results: In vitro tracking of the EVs revealed that RGD hydrogels increased retention and stability of EVs. Upon intrarenal injection, EV-RGD hydrogels provided superior rescuing effects at functional, histopathological and molecular levels. Further analysis revealed that the presence of microRNA let-7a-5p in MSC-EVs served as a novel mechanism contributing to the reduced cell apoptosis and elevated cell autophagy in AKI.

Conclusions: RGD hydrogels boosted the therapeutic efficacy of let-7a-5p-containing-EVs in AKI repair. This study developed an RGD-scaffold to increase the EV integrin-mediated loading and in-turn improved therapeutic efficacy, therefore this strategy shed light on MSC-EVs application as cell-free treatment for potentiated efficiency.

Conclusions: Our data demonstrate that PANX1 overexpression results in overt renal injury during IRI and that is in part mediated by reduced mitochondrial function and in part by metabolites released via Panx1 channels, which facilitates cell death. These results complement our prior studies demonstrating that Panx1 deficiency protects kidneys from IRI and provide strong rationale for the development of selective strategies to inhibit Panx1 in the prevention or treatment of AKI.

Funding: NIDDK Support, Private Foundation Support

**SU-OR06**

Targeting Angiopoietin-Tie2 Signaling in Kidney Ischemia-Reperfusion Injury

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Background: The endothelial angiopoietin (ANG)-Tie2 signaling pathway is required for vascular development and homeostasis. Dysregulation of ang-Tie2 pathway has been implicated in diseases including venous malformation, glaucoma, diabetic nephropathy, and septic acute kidney injury (AKI). The endothelial-specific phosphatase VE-PTP/PTPRB is a negative regulator of Tie2 phosphorylation. Here we investigate the therapeutic roles of Angiopoietin/Tie2 signaling in kidney ischemia-reperfusion injury (IRI).

Methods: A bispecific doxycycline-inducible system (VE-PTP-NLS, Roa26-EtA1, tetO-Cre ) was used to knockout VE-PTP at postnatal day 0 (VE-PTPko). Adult male VE-PTPko and littermate control mice underwent bilateral IRI or sham surgery. Serum creatinine was measured on day 1, day 3 and day 7 after surgery by HPLC method. Data were analyzed using two-way ANOVA. Tissues were harvested on day 7 for histology, immunohistochemistry and RNA/protein analysis. Bulk RNAseq was performed with RNA extracted from whole kidney 5 hours after IRI. Normalization and differential expression were determined using DESeq2. For pharmacological studies, adult male C57BL/6J mice were used. A new soluble ANGPT1 mimetic (C4BP-ANG1) or vehicle were administered by intraperitoneal injection.

Results: Western blot analysis showed VE-PTP protein levels were increased in kidneys post-IRI and following hypoxia-inducible factor stabilization. Genetic deletion of VE-PTP rescued declined Tie2 phosphorylation in kidney after IRI. While serum Creatinine was elevated 1 day post-IRI in control mice, this increase was minimal in VE-PTP iKO mice (p<0.005). Global gene expression analysis indicated minimal kidney transcriptome change at base line whereas in the setting of IRI, VEPTPIKO mice showed a less activated renal endothelium and downregulation of acute stress responsive gene signature. A corresponding decrease in pre-fibrotic genes was observed in VE-PTPko mice on day 7. In the pharmacological study, systemic administration of C4BP-ANG1 activated Tie2 and its downstream AKT/eNOS/NO pathways in mouse kidney in physiological condition. Ongoing studies are analyzing its protective effect in ischemic AKI.

Conclusions: Our data provide evidence for augmenting Tie2 activation-induced vascular protection as a promising therapeutic strategy for renal protection following IR-AKI.

Funding: NIDDK Support

**SU-OR05**

Panx1n 1 Channel Regulates Mitochondrial Function and Cell Survival During AKI


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Background: Panx1n 1 (Panx1) is a membrane associated non-selective channel that, when activated, serves as a conduit for release of small metabolites that have pro- or anti-inflammatory function. We have previously shown that pharmacological inhibition or genetic deletion of Panx1n 1 in mice prior to injury is protective against renal ischemia-reperfusion injury (IRI). How Panx1n 1 contributes to acute kidney injury (AKI) pathology is unknown. We hypothesized that panx1n 1 induces cell death by mediating both intracellular and extracellular events.

Methods: We subjected a novel human Panx1 overexpressing mouse (APANX1-Tg) to IRI or cisplatin-mediated AKI and assessed plasma creatinine and renal expression of neutrophil gelatin associated lipocalin (Ngal). For in vitro studies, Panx1n1 overexpressing TKPTS cells (OX) were challenged with cisplatin. Cell death was assessed by flow cytometry using Annexin-V/7AAD. Mitochondrial function was assessed by measuring TKPTS cells (OX) were challenged with cisplatin. Cell death was assessed by flow cytometry using Annexin-V/7AAD. Mitochondrial function was assessed by measuring respiration at baseline, a greater reduction in mitochondrial function and a higher increase in mitochondrial ROS production after cisplatin exposure compared to controls.

Results: APANX1-Tg mice had significant rise in plasma creatinine and expression of Ngal in the kidneys in both models of AKI compared to their littermate controls. Cisplatin-induced cell death was greater in OX cells compared to control cells. Moreover, cisplatin induced greater death in OX cells than control cells when cultured together. Among genes involved in the cell death pathway, OX cells had reduced expression of Bcl2 and a greater increase in Ho-1 after cisplatin exposure. Assessment of mitochondria showed that OX cells had reduced mitochondrial DNA, Pgc1a expression, and mitochondrial respiration at baseline, a greater reduction in mitochondrial function and a higher increase in mitochondrial ROS production after cisplatin exposure compared to controls.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

**SU-OR07**

Exosome-Based Delivery of Super-Repressor IfxαA Ameliorates Kidney Injury After Ischemia-Reperfusion Injury

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Background: Ischemia-reperfusion (IR) injury (IRI) is a major cause of acute kidney injury (AKI). Recent studies on the pathophysiology of IR-induced AKI showed that immunologic responses significantly affect renal IRI and repair. Nuclear factor (NF)-κB signaling, which controls cytokine production and cell survival, is significantly involved in IR-induced AKI; its inhibition can ameliorate ischemic AKI. We assessed whether the systemic delivery of NF-κB inhibitor using exosomes could ameliorate the course of ischemic AKI.

Methods: Using EXPLOR, a novel, optogenetically engineered exosome technology, we successfully delivered the exosomal super-repressor inhibitor of NF-κB (Exo-srIxB) into B6 wildtype mice before after kidney IRI surgery, and compared outcomes with those of the control exosome (Exo-Naïve)-injected group. To better understand the protective mechanism of Exo-srIxB in renal IRI, the expression of pro-inflammatory cytokines/chemokines and adhesion molecules and the level of apoptosis were measured using quantitative real-time PCR (qRT-PCR), enzyme-linked immunosorbent assay, western blot, and immunohistochemical/immunofluorescent (IF) staining. Immune cell populations of post-ischemic kidneys and spleens were analyzed using flow cytometry and IF staining.

Results: Exo-srIxB treatment resulted in lower levels of serum blood urea nitrogen (BUN), creatinine, and neutrophil gelatinase-associated lipocalin (NGAL) in post-ischemic kidneys than in the Exo-Naïve treatment group (24h/48h BUN, creatinine, and NGAL, p < 0.001). Systemic delivery of Exo-srIxB decreased NF-κB activity in post-ischemic kidneys, leading to reduced apoptosis levels. Post-ischemic kidneys showed decreased gene expression of pro-inflammatory cytokines and adhesion molecules with
Exo-srKt treatment as compared with the control. Exo-srKt treatment also significantly affected post-ischemic renal immune cell populations, lowering neutrophil, monocyte/macrophage, and T cell frequencies than those in the control.

Conclusions: Thus, the modulation of NF-κB signaling through exosomal delivery can be used as a novel therapeutic method for IR-induced AKI.

Funding: Other U.S. Government Support, Commercial Support - ILIAs Biologies Inc., Daejeon, South Korea

SU-OR08 Enhancer and Super-Enhancer Dynamics in Repair After Ischemic AKI Julia Wilhelmsen,1,2 Michaela Willi,2 Hye Kyung Lee,2 Hannes Olsson,1 Jakub Jankowski,3 Takaharu Ichimura,4 Reinhold Erben,4 M. Todd Valerius,5 Lothar Hennighausen,5 Joseph V. Bonventre,1,2 Brigham and Women’s Hospital, Renal Division, Harvard Medical School, Boston, MA; 2Laboratory of Genetics and Physiology, National Institute of Diabetes, Digestive and Kidney Diseases, US National Institutes of Health, Bethesda, MD; 3Division of Renal Medicine, Department of Clinical Sciences, Intervention and Technology, Stockholm, Sweden; 4University of Veterinary Medicine, Department of Physiology, Pathophysiology and Endocrinology, Vienna, Austria.

Background: The endogenous repair process of the mammalian kidney allows rapid recovery after acute kidney injury (AKI) through robust proliferation of tubular epithelial cells. There is currently limited understanding of which transcriptional regulators activate these repair programs. Here we investigate the existence of enhancer and transcription factor dynamics in the regenerating mouse kidney.

Methods: We performed genome-wide ChIP-seq and RNA-seq on kidneys harvested from mice with sham or ischemia/reperfusion injury 2 days after ischemia/reperfusion injury (IRI) to identify activated genes, transcription factor binding, enhancer and super-enhancers associated with kidney repair.

Results: We identified the role of enhancer sets in kidney repair through pharmacological BET inhibition using the small molecule JQ1 in AKI models in vivo.

Response: To injury leads to genome-wide alteration in enhancer repertoire in vivo. We identified 16,781 enhancer and 380 super-enhancer sites (H3K27ac and BRD4 positive) with dynamic binding in SHAM and IRI samples; 5,151 enhancer, 168 super-enhancer lost and 9,774 enhancer, 214 super-enhancer gained after IRI. The lost and gained enhancer sites can be annotated to 62% and 63% of down- and up-regulated transcripts after AKI, respectively. ChIP-seq profiles of predicted transcription factors show specific binding at corresponding enhancer sites with dynamic binding of HNF4a, GR and STAT3. HNF4a and GR show a reduced binding at enhancer and super-enhancer sites after injury, whereas STAT3 binding can be observed at injury gained enhancer and super-enhancer sites. BET (BRD4) inhibition before IRI leads to suppression of 40% of injury-induced transcripts associated with cell cycle regulation, genome-wide Pol II pausing and significantly increased mortality after AKI.

Conclusions: This is the first demonstration of enhancer and super-enhancer and transcription factor binding dynamics in the repairing kidney. In addition, our data call for the need to develop novel therapeutic strategies for AKI.

Funding: NIDDK Support, Private Foundation Support

SU-OR09 Developmental Reprogramming of Kidney Resident Macrophages During Human AKI and Its Implications to CKD Abolfazl Zarjou,1,2 Michaela Willi,2 Frida Rosenblum,1,3 Michaela Mrug,1 Hye Kyung Lee,2 Hannes Olsson,1 Jakub Jankowski,3 Takaharu Ichimura,4 Reinhold Erben,4 M. Todd Valerius,5 Lothar Hennighausen,5 Joseph V. Bonventre,1,2 Brigham and Women’s Hospital, Renal Division, Harvard Medical School, Boston, MA; 2Laboratory of Genetics and Physiology, National Institute of Diabetes, Digestive and Kidney Diseases, US National Institutes of Health, Bethesda, MD; 3Division of Renal Medicine, Department of Clinical Sciences, Intervention and Technology, Stockholm, Sweden; 4University of Veterinary Medicine, Department of Physiology, Pathophysiology and Endocrinology, Vienna, Austria.

Background: Kidney tissue-resident macrophages (KRM) promote naturally occurring and AKI-induced cystic renal disease in mice. AKI also reprograms KRM into the role of kidney repair programs. Here we investigate the existence of enhancer and transcription factor binding dynamics in the regenerating mouse kidney.

Methods: We performed genome-wide ChIP-seq and RNA-seq on kidneys harvested from mice with sham or ischemia/reperfusion injury 2 days after ischemia/reperfusion injury (IRI) to identify activated genes, transcription factor binding, enhancer and super-enhancers associated with kidney repair.

Results: We identified the role of enhancer sets in kidney repair through pharmacological BET inhibition using the small molecule JQ1 in AKI models in vivo.

Response: To injury leads to genome-wide alteration in enhancer repertoire in vivo. We identified 16,781 enhancer and 380 super-enhancer sites (H3K27ac and BRD4 positive) with dynamic binding in SHAM and IRI samples; 5,151 enhancer, 168 super-enhancer lost and 9,774 enhancer, 214 super-enhancer gained after IRI. The lost and gained enhancer sites can be annotated to 62% and 63% of down- and up-regulated transcripts after AKI, respectively. ChIP-seq profiles of predicted transcription factors show specific binding at corresponding enhancer sites with dynamic binding of HNF4a, GR and STAT3. HNF4a and GR show a reduced binding at enhancer and super-enhancer sites after injury, whereas STAT3 binding can be observed at injury gained enhancer and super-enhancer sites. BET (BRD4) inhibition before IRI leads to suppression of 40% of injury-induced transcripts associated with cell cycle regulation, genome-wide Pol II pausing and significantly increased mortality after AKI.

Conclusions: This is the first demonstration of enhancer and super-enhancer and transcription factor binding dynamics in the repairing kidney. In addition, our data call for the need to develop novel therapeutic strategies for AKI.

Funding: NIDDK Support, Private Foundation Support

SU-OR10 Endothelial-Derived mir-17~92 Promotes Angiogenesis to Protect Against Renal Ischemia-Reperfusion Injury Takuto Chiba, Jacqueline Ho, Sunder Simms-Lucas, University of Pittsburgh Medical Center, Pittsburgh, PA.

Background: Acute kidney injury (AKI), resulting from renal ischemia reperfusion injury (IRI) among others, is an independent predictor of morbidity and mortality, and is identified in as many as 50% of ICU patients. Damage to the renal microvasculature is a hallmark of renal IRI. mir-17~92 encodes 6 polycystic microRNAs that show potent pro-angiogenic capacity by targeting anti-angiogenic factors. The function of mir-17~92 in renal microvasculature after renal IRI remains unknown.

Methods: Antibodies bound to magnetic beads were utilized to selectively enrich for renal endothelial cells from mice. Endothelial-specific mir-17~92 knockout (mir-17~92–/-) mice were generated and a renal IRI model was performed. Mice were monitored for the development of AKI using serum chemistries and tissue analysis, and for renal blood flow using a magnetic resonance imaging (MRI). Mice were treated with miRNA mimics during renal IRI to test its therapeutic efficacies.

Results: We demonstrate that miRs-17, -18a, -20a, and -19b are up-regulated in renal endothelial cells after renal IRI in mice. mir-17~92–/-/– mice were generated and a renal IRI model was performed. Mice were monitored for the development of AKI using serum chemistries and tissue analysis, and for renal blood flow using a magnetic resonance imaging (MRI). Mice were treated with miRNA mimics during renal IRI to test its therapeutic efficacies.

Conclusions: These data suggest that endothelial-derived mir-17~92 stimulates a reparative response in damaged renal vasculature during ischemic AKI by regulating angiogenic pathways.

Funding: NIDDK Support, Private Foundation Support

SU-OR11 Inhibition of Cadherin 11 Improves Outcomes in Murine Models of CKD Tessa Huffman,1,2 Michael A. Raddatz,3 Leslie S. Gewin,2 W. David Merriman,3 1Vanderbilt University, Nashville, TN; 2Vanderbilt University Medical Center, Nashville, TN.

Background: Chronic kidney disease (CKD) represents a massive unmet clinical need, as there are virtually no pharmaceutical options for treatment of renal injury. A recent study identified cadherin-11 (CDH11) as a potential biomarker for CKD, as it is expressed in kidney biopsies of patients with samples of CKD patients and its expression is increased in CKD mouse models. We have investigated the role of CDH11 as both a mediator and therapeutic target of CKD.

Methods: In the current study, we used three mouse models of CKD to evaluate the role of CDH11: cadherin-11 (CDH11) as a potential biomarker for CKD, as it is expressed in kidney biopsies of patients with samples of CKD patients and its expression is increased in CKD mouse models. We have investigated the role of CDH11 as both a mediator and therapeutic target of CKD.

Results: Although CDH11 has been found on immune cells and fibroblasts in other fibrotic diseases, we found that in the kidney CDH11 is exclusively expressed in injured proximal tubules (PTs). PTs play a significant role in CKD, as they are both a target and mediator of chronic injury. In our models of CKD, we found that both genetic and pharmacologic CDH11 inhibition improves renal function (BUN and ACR), diminishes cytokine production (TGFβ and IL-6 expression), and reduces tubular injury (expression of KIM-1 and histological analysis). Using primary PT cells, we found that genetic ablation of CDH11 improves cell survival in vitro. Although the specific mechanisms by which CDH11 mitigates PT injury is still under investigation, preliminary data shows that inhibition of CDH11 increases Wnt1-β-catenin activity in the kidneys of injured mice. Wnt1-β-catenin signaling promotes cell survival, which in this context could result in reduced tubular atrophy, cytokine production, and fibrosis. Such pro-survival signaling could be driving the reduction in renal injury we see when CDH11 is inhibited, as PT death strongly correlates with outcomes in CKD.

Conclusions: These results clearly identify CDH11 inhibition as a novel means of improving outcomes in murine CKD models. The mechanism by which CDH11 inhibition protects against renal injury is likely through CDH11 interactions with the Wnt/β-catenin signaling pathway to enhance PT survival. These results could prove an important step towards developing new therapeutic strategies for the treatment of CKD.

Funding: Other NIH Support - NHLBI R35 (HL135790)
SU-OR12
METTL10: A Kidney Disease Risk Gene by Altering Protein Methylation
Hailong Hu, Katalin Susztak. Renal Electrolyte and Hypertension Division, Department of Medicine and Genetics, University of Pennsylvania, Philadelphia, PA.

Background: Genome-wide association studies (GWAS) have identified more than 300 loci where genetic variants are associated with kidney function, however, the causal variants, genes, cell types and the disease mechanism remain mostly unknown.

Methods: We have generated expression of quantitative trait (eQTL) data from microdissected human kidney tubules and glomeruli. We used Bayesian colocalization of eQTL and GWAS to identify likely causal genes for kidney function. We used single cell RNA and ATACseq data to identify causal cell types. Finally, we generated mice with genetic deletion to study kidney disease mechanism.

Results: Kidney disease associated genetic variants showed a strong association with METTL10 expression. Methytransferase-like protein 10 (METTL10), is a non-histone lysine methyltransferase. Patients with CKD variants showed lower level of METTL10 in their kidneys. METTL10 was relatively broadly expressed in kidney tubule cells by single cell expression analysis. Its expression was markedly reduced in mice and patients with kidney disease. We found that Mettl10 controls methylation and the activity of the eukaryotic translation elongation factor 1 alpha (eEF1A). eEF1A is the alpha subunit of the eukaryotic elongation complex, controlling RNA translation. Methylation of eEF1A was markedly reduced in kidneys of Mettl10 KO mice. The reduction in eEF1A activity lead to lower protein translation and tubule cell proliferation. Mettl10 KO mice was more susceptible to injury, it showed more structural damage and collagen expression in the folic acid induced kidney injury model.

Conclusions: Taken together, GWAS and eQTL studies identified Mettl10 a kidney disease risk gene. METTL10 controls the methylation of eEF1A, downstream RNA translation, cell proliferation altering kidney disease risk, defining a novel mechanism for kidney disease development.

Funding: NIDDK Support

SU-OR13
Renal Proximal Tubule Cell Differentiation and Metabolism Are Coupled by Nuclear Receptors
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Background: Kidney proximal tubule (PT) cells have high mitochondrial density to perform their high energy demanding function to secrete and reabsorb metabolites and electrolytes. Chronic kidney disease is characterized by tubule epithelial atrophy and dedifferentiation, resulting in a decline in kidney function. In this study, we aimed to define upstream regulators that control PT differentiation.

Methods: We performed scRNA and snATACseq analysis on kidneys of developing and adult mice, kidney organoids, and kidneys from control and folic acid-induced kidney injury model. Bioinformatic methods included dimension reduction, differential expression, cell fraction and cell trajectory analysis. Functional studies included mice and cultured tubule cells with genetic deletion of ESRRAs.

Results: Single cell expression analysis identified PT cells as the key vulnerable cell type in kidney fibrosis. Cell trajectory analysis showed a sequential differentiation path from precursor to differentiated PT cell state in development and in healthy adult and diseased kidneys. But this differentiation path showed more complexity in fibrosis, as such enhanced cell differentiation and a blockade of terminal differentiation. Pathway analysis indicated fatty acid oxidation (FAO) and oxidative phosphorylation (OXPHOS) were key variable genes along the PT cell differentiation path in the adult, and developing mouse PT cells and organoids. Single cell epigenetics data identified the critical role of nuclear receptors, HNF4A, HNF1B, PPARA, and ESRRAs driving the PT cell differentiation program. These transcription factors did not only directly control FAO and OXPHOS but also the expression of PT differentiation genes.

Conclusions: The coupling of cell state and metabolism is established by nuclear receptors such as PPARA and ESRRAs that not only control cellular metabolism but also the expression of PT-specific genes in mice and patient samples.

Funding: NIDDK Support

SU-OR14
COX17-Mediated Abnormal Mitochondrial Copper Metabolism Promotes Renal Fibrosis
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Background: Copper is a trace element essential for almost all living organisms. Previously, we found that elevated intracellular copper contributes a unique role to kidney fibrosis. Furthermore, copper ions in cells were mainly accumulated in mitochondria, which damage the structure and function of mitochondria. However, the mechanisms of the interaction of copper metabolism and how a disturbed copper balance induces mitochondrial dysfunction remain to be identified. Copper chaperone COX17, a protein required for cytochrome c oxidase (COX) assembly, was previously hypothesized to shuttle copper between the cytosol and mitochondria based on its dual localization. We found that in the fibrosis model COX17 was highly expressed and COX activity decreased. Therefore, we speculated that COX17 might be involved in mitochondrial copper overload and renal fibrosis.

Methods: Expression level and pattern of COX17 were examined in ischemia- reperfusion injury (IRI) and recruited rat kidneys. The regulatory mechanisms of COX17 in IRI were investigated in renal tubule epithelium cell line (NRK-52E) and rat fibroblasts(NRK-49F) by treating with copper or copper chelator tetrathiomolydate (copper-chelating agent). ICP-MS, mitoSOX, electron microscopy, realtime-qPCR and western blot analysis were applied in the current study.

Results: Firstly, the expressions of COX 17, Col1 in the kidney of IRI group were extremely upregulated compared with the sham group. Unexpected, we found dysfunction of mitochondria in IRI kidneys evidenced by it’s appearing swollen and ruptured. Secondly, stimulated by TGF-β1, COX activity was declined, and mitochondrial content was increased in IRI kidneys. TGF-β1/smad3 were significantly upregulated. More importantly, mitochondrial copper content and col1, fibronectin expression were reduced and mitochondrial function was improved after transfecting with COX17 shRNA. Meanwhile, treatment with copper chelator tetrathiomolydate also alleviated renal fibrosis both in vivo and in vitro.

Conclusions: COX17 was significantly increased in renal fibrosis and transported excessive intracellular copper ions into the mitochondria. Copper overload inhibits the activity of COX and impairs mitochondria, subsequently leading to renal fibrosis.

SU-OR15
Protective Effect of Prostacyclin in Renal Fibrosis
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Background: Inadequate repairing process to injury has been reported to play a fundamental role in renal fibrosis. Mounting evidence suggests that prostaglandins are important for the response to physiological changes or pathophysiologic insults to tissues including the kidney. Importantly, under certain conditions such as aging and hypertension, prostacyclin (PGI2), an active production of COX/PGI synthase (PGIS), is reduced. The present study provides data showing that low levels of PGI2 are associated with enhanced renal fibrosis.

Methods: Unilateral ureteral obstruction (UUO) was used as a renal fibrosis model. At days 10 after UUO, the mice were sacrificed. Ischemia-reperfusion (IR) model was induced by clamping the left renal pedicle for 35 minutes on D0. After 4 weeks, the right kidney was removed. The mice were treated with beraprost sodium (300ug/kg body weight per day by twice daily gavage) or vehicle from D32 to D55, and were sacrificed on D56.

Results: The PGIS heterozygous (PGIS+/-) mice had normal body weight, blood pressure and blood urea nitrogen (BUN) level. Lossing one allele of PGIS significantly attenuated the increase of PGIS expression after UUO and aggravates UUO - induced renal fibrosis. 1R model was performed on wild-type mice. Treatment with beraprost sodium (BPS), a analog of PGI2, inhibited the expression of fibronectin, collagen 1 and α-SMA in the kidney and ameliorated extracellular matrix deposition in the kidney tissue. Furthermore, the level of phosphorylated P6KA substrates in the normal obstructed kidney of deficient mice was significantly reduced, suggesting the role of IP receptor. IP agonist treatment reduced the expression of fibronectin, collagen I and α-SMA in rat renal fibroblasts (NRK-49F), which were induced by TGF-β.

Conclusions: PGIS/PGL2 plays an important role in protecting the kidney from fibrosis. Lack of PGIS enhances renal fibrosis, and supplementation with PGI2, analog ameliorates renal fibrosis. PGIS/PGL2, is a potential target for CKD.

SU-OR16
Proteomic Risk Assessment of CKD Progression in the Chronic Renal Insufficiency Cohort
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Background: Quantification of thousands of plasma proteins simultaneously is now feasible in large cohorts using the SomaScan aptamer assay. In this study, we applied large-scale proteomics to patients with chronic kidney disease (CKD) to discover new biomarkers and risk models of CKD progression.

Methods: We measured 4638 unique plasma proteins among 3249 participants in the Chronic Renal Insufficiency Cohort (CRIC), with follow-up to 13 years. Mean age was 59 years; women 54%, non-Hispanic/Latino 94%, estimated glomerular filtration rate (eGFR) was 24 mL/min/1.73m2, and 50% were diabetic. The study outcome was 10-year risk of 50% decline in eGFR, end-stage renal disease or renal transplant (n=1171 events). Associations of individual proteins with the composite outcome were analyzed in Cox survival models adjusted for demographics, comorbidities, eGFR and proteinuria. Protein-only risk models were constructed using elastic net regression and compared to the 4-variable Kidney Failure Risk Equation (K/FRE) model.
Molecular Mechanisms Underlying Sex-Specific Association of Circulating Transforming Growth Factor β1 with the Risk of Accelerated Kidney Disease in Women

Background: Sex differences in kidney function decline and risk of chronic kidney disease (CKD) have been suggested but remain unexplained. We recently showed a sex-specific association between high circulating TGF-β1 in women and a higher risk of accelerated age-related loss of glomerular filtration rate (GFR) in women. Our aim is to investigate the interaction of TGF-β1 with sex on intrarenal TGF-β1 expression, histopathology and kidney function decline in a sex-specific manner.

Methods: Circulating TGF-β1 was measured in plasma samples from 1,738 participants from the Helsingfors Helsespansk Kapitalstudie. They were followed up for 25 years or until diagnosis of CKD. We used logistic regression to test for interaction of sex with circulating TGF-β1 in association with kidney function decline and kidney function at baseline and follow up. Histopathological data from kidney biopsies were examined.

Results: Significant interaction of sex with circulating TGF-β1 was observed in association with kidney function decline (p<0.001). The risk estimates were 1.79 (1.65-1.94) for men and 2.99 (2.74-3.26) for women. Circulating TGF-β1 was associated with higher risk of accelerated age-related decline in GFR in women (OR = 1.79; p <0.001) and histopathologic changes in women (OR = 1.79; p <0.001). Among women, TGF-β1 was associated with the presence of glomerulosclerosis, tubular atrophy, interstitial fibrosis, and tubulointerstitial fibrosis.

Conclusions: Circulating TGF-β1 is associated with accelerated loss of GFR and histopathologic changes in women, but not in men. These findings suggest that TGF-β1 may play a different role in kidney disease progression in women compared to men.
Methods: A deep learning-based method for direct kidney parenchymal volume (KPV) segmentation was developed and validated (Accuracy: Dice 0.956, R² = 0.95) and applied to UKB MRI. Absolute and relative change with age and associations to body weight, BSA and fat free mass from bioimpedance analysis (BIA-FFM) and lean tissue volume from MRI (MRI-LT) were studied using linear regression. Rate changes were compared between and above group mean ages. MRI-LT values (n=8,524) were inferred for 30,308 additional subjects by MRI-based deep learning regression with validated R² = 0.96 (arXiv:2002.06862).

Results: Results KPV from 37,468 subjects (47.6% males) and age changes are shown in Fig1a and Table 1. Correlations between total KPV and BSA and MRI-LT over age are shown in Fig1b. The associated overall correlations were (males / females): Body weight: 0.568/0.460, BSA: 0.574/0.496, BIA-FFM: 0.597/0.536, MRI-LT: 0.636/0.600.

Conclusions: Both sexes show continuous volume decline in the studied age interval. Males show an increasing rate of decline with age. MRI-LT showed strongest correlations to KPV.

Funding: Other NIH Support - The Swedish Heart-Lung Foundation, Swedish Research Council (2016-01040, 2019-04756), Research conducted using the UK Biobank resource (application 14237), Government Support - Non-U.S.

Table 1

<table>
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<th>Age Range (years)</th>
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A) Scatter plot of total KPV and age for males and females including regression lines for subjects below and above respective mean age. An increasing rate of decline is found in males (p<10⁻¹⁵) but not in females. B) Correlation between total KPV and BSA and MRI-LT for males and females over age.

SU-OR21

Variation in Peritoneal Dialysis-Related Peritonitis Outcomes and Treatment Practices: Results from the Peritoneal Dialysis Outcomes and Practice Patterns Study

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Background: Peritoneal dialysis (PD)-associated peritonitis is a leading cause of technique failure and transition to hemodialysis. In the Optimizing Peritonitis Prevention in The United States (OPPUS) study, we explored the impact of various patient, facility and treatment factors on the likelihood of cure following a peritonitis episode.

Methods: Using Peritoneal Dialysis Outcomes and Practice Patterns Study phase 1 (2014-2017) data from Australia and New Zealand, Canada, Japan, Thailand, the UK, and the US, we defined as the absence of a peritonitis relapse or recurrence, PD catheter removal, transition to hemodialysis or death during the 30 days following a peritonitis episode. Multivariable logistic regression was used to test associations between cure and patient, facility, and treatment characteristics.

Results: We identified 1677 peritonitis episodes in 1190 patients across 126 facilities. Overall, 63% of episodes resulted in a cure. Cure was associated with APD (OR v. CAPD=1.35, 95% CI 1.02-1.80), higher serum albumin (OR=1.04 per 0.1 g/dl, 95% CI=1.01, 1.06), facility icodextrin use (OR=1.06 per 10% greater icodextrin use, 95% CI – 1.01-1.12), and aminoglycoside use for Gram-negative peritonitis (OR v. ceftazidime=3.10, 95% CI=1.02, 9.36). Prior peritonitis (OR v. no prior peritonitis episodes during follow-up=0.84, 95% CI=0.74, 0.97) and concomitant exit-site infection (OR=0.42, 95% CI=0.28, 0.63) were associated with lower cure odds. Higher odds of peritonitis relapse were seen among patients with greater residual urine volume (OR=1.14 per 200 ml, 95% CI=1.07, 1.22).

Conclusions: Different characteristics and management practices can impact the likelihood of cure following a peritonitis episode. Our findings can inform future guidelines in addressing the effect of different modifiable patient, facility, and treatment factors on reducing morbidity associated with PD peritonitis.

Funding: Other NIH Support - Agency for Healthcare Research and Quality (AHRO)

SU-OR22

Rate of Decline in Residual Kidney Function Before and After Peritoneal Dialysis Initiation: A Post Hoc Analysis of the IDEAL Study

Isabelle Ethier,1,2 Yeoung Jee Cho,3,5 Carmel Hawley,2,5 Elaine Pascoo,2 Andrea K. Vivecelli,3,2 Scott B. Campbell,2,5 Carolyn L. Van Eps,2,5 Nicole Isbel,2,5 Bruce A. Cooper,4 David Harris,4,6,9 Carol A. Pollock,6,9 Mu H. Geot Wong,6,9,12 David W. Johnson.1,2 Centre Hospitalier de L’Universite de Montreal, Montreal, QC, Canada; 2Princess Alexandra Hospital, Woolloongabba, QLD, Australia; 3The University of Queensland Faculty of Medicine, Herston, QLD, Australia; 4Westmead Institute for Medical Research, Westmead, NSW, Australia; 5The University of Sydney School of Medicine, Sydney, NSW, Australia; 6Royal North Shore Hospital, St Leonards, NSW, Australia; 7George Institute for Global Health, Camperdown, NSW, Australia.

Background: Residual kidney function (RFK) is associated with improved survival and quality of life in dialysis patients. Previous studies have suggested that commencement of peritoneal dialysis (PD) may slow RFK decline compared to the pre-dialysis period. We sought to evaluate the association between PD initiation and RFK decline in the Initiating Dialysis Early And Late (IDEAL) trial.

Methods: In this post hoc analysis of the IDEAL randomized controlled trial, PD participants were included if results from 24-hour urine collections had been recorded within 30 days of dialysis initiation (-30 to +30 days from start), and at least one value pre- and one value post-dialysis commencement were available. The primary outcome was slope of RFK decline, calculated as mean of urinary creatinine and urea clearances. Secondary outcomes included slope of urine volume decline and time from PD initiation to anuria.

Results: The study included 151 participants (79 early-start group, 72 late-start group). The slope of RFK decline was slower after PD commencement (-2.69±0.18 mL/min/1.73m² per year) compared to before PD commencement (-4.09±0.33 mL/min/1.73m² per year) change in slope =±1.19 mL/min/1.73m² per year, 95% CI 0.48±1.90, p<0.001). In contrast, urine volume decline was faster after PD commencement (-0.74±0.05 L/yr) compared to beforehand (-0.57±0.06 L/yr, change in slope =±0.18 L/yr, 95% CI=0.34—0.01, p<0.04). No differences were observed between the early- and late-start groups with respect to RFK decline, urine volume decline or time to anuria.

Conclusions: Commencement of PD was associated with a slower decline of RFK compared to the pre-dialysis period.

Funding: Government Support - Non-U.S.
SU-OR23
Steady Concentration Peritoneal Dialysis Increases Ultrafiltration and Sodium Removal Compared with Continuous Ambulatory Peritoneal Dialysis (CAPD)
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Background: Fluid and sodium removal (NaR) may be a challenge during glucose-based PD, leading to increased use of high glucose solutions to maintain sufficient fluid removal. This may lead to increased sodium sieving, resulting in reduced NaR. Carry Life® UF uses steady concentration PD (SCPD), where the intraperitoneal (IP) glucose concentration is maintained by infusion of glucose to provide a continuous ultrafiltration (UF) throughout the dwell. The present study investigated the effect of Carry Life® UF on CAPD regarding UF, NaR and glucose absorption.

Methods: Eight stable PD patients were included in the study. Subjects were treated with 5-hour Carry Life® UF treatments using three different glucose doses (11, 14, 20 g/h). An initial fill with 1.5 l, 1.36% glucose PD solution was used. A small volume of dialysate was drained hourly to avoid overfill. A 4-hour peritoneal equilibration test (PET) (2.01, 2.27% glucose) served as control. Data expressed as mean±SD, statistical analysis using ANOVA.

Results: UF volumes were significantly increased during Carry Life® UF treatments (64±256, 739±312, 863±380 ml for 11, 14, 20 g/h) vs. PET (162±242 ml, p<0.01). NaR increased significantly during Carry Life® UF treatments (86±27, 92±33, 110±37 mmol/dwell for 11, 14, 20 g glucose/h) compared to PET (22±33 mmol/dwell, p<0.001).

Conclusions: SCPD performed with Carry Life® UF maintained a stable IP glucose concentration during the treatment (figure a) which generated significantly higher UF volumes compared to PET. During the Carry Life UF treatments glucose was used more efficiently, particularly for the two lowest doses, in comparison to PET (figure b). In summary, SCPD using Carry Life® UF increases the efficiency of PD compared to standard, glucose-based CAPD with respect to UF and NaR.

Funding: Commercial Support - Triomed AB

SU-OR24
Efficacy and Safety of Roxadustat in Patients with Dialysis-Dependent CKD and Anemia on Peritoneal Dialysis
Tak Mao D. Chau,1 Lynda Szeczec,2 Jayant Kumar,2 Anjay Rastogi,3 Carol A. Pollock,1 Gopal Saha,1 Tyson T. Lee,1 MakSYM Pola,1 Kin-Hung P. Yu,5 University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China; Renal Medicine Associates, Albuquerque, NM; University of California Los Angeles, Los Angeles, CA; The University of Sydney, Sydney, NSW, Australia; FibroGen Inc, San Francisco, CA; AstraZeneca, Warsaw, Poland.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Dialysis modality in patients with dialysis-dependent (DD) CKD on peritoneal dialysis (PD) is of clinical importance. The population of patients with kidney failure in the United States utilizing home dialysis modalities is growing rapidly. Unlike for in-center hemodialysis, there are no patient-reported experience measures for assessment of the patient experience of care for peritoneal dialysis or home hemodialysis. We sought to develop and establish content validity of a patient-reported experience measure for patients undergoing home dialysis using a mixed-methods multiple stakeholder approach.

Methods: We conducted a systematic literature review, followed by concept elicitation focus groups and interviews among 65 participants, including 21 home dialysis patients, 33 home dialysis nurses, 3 patient care partners, and 8 nephrologists. We generated a list of candidate items for possible measure inclusion, and conducted a national aspects of care prioritization exercise among 91 home dialysis patients and 39 providers using a web-based platform. We drafted the Home Dialysis Care Experience (Home-DCE) instrument and conducted 3 rounds of cognitive debriefing interviews to evaluate item comprehensibility, order, and structure. We iteratively refined the measure based on interview findings.

Results: The literature review and concept elicitation phases supported 15 domains of home dialysis care experience in 6 general areas: communication and education of patients; concern and helpfulness of the care team; proficiency of the care team; patient-centered care; care coordination; and amenities and environment. Focus groups results showed that domains of highest importance for measurement were home dialysis staff education and patient-centered communication, care coordination, and personalization of care (Figure). Aspects of care prioritization exercise results confirmed focus group findings. Cognitive debriefing indicated that the final measure was easily understood and supported content validity.

Conclusions: The Home-DCE instrument is a 26-item patient-reported experience measure for use in peritoneal dialysis and home hemodialysis. Qualitative focus group and prioritization survey data support measure content validity. To our knowledge, the Home-DCE instrument represents the first rigorously developed and content valid English language survey instrument for assessment of patient-reported experience of care in home dialysis.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Cardiovascular Thromboembolic Outcomes by Dialysis Modality Following Primary Total Knee Arthroplasty

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Background: There is a paucity in the literature evaluating the impact of dialysis modalities on cardiovascular thromboembolic outcomes following primary total knee arthroplasty (TKA). Therefore, the purpose of this study was to investigate whether patients treated with hemodialysis (HD) or peritoneal dialysis (PD) have higher rates of 1) medical complications, 2) readmission, and 3) cost of care.

Methods: Patients undergoing primary TKA while receiving HD served as the study group (n = 82,518) and matched 1:1 to a control group of PD patients (n = 82,518) by distribution, age, sex, and Elixhauser-Comorbidity Index (ECI). Outcomes analyzed included rates of 90-day medical complications, readmission rates, and cost of care. Logistic regression analysis was used to calculate odds-ratios (OR) for medical complications and readmission rates. Welch’s t-test was used to test for significance on cost of care and ECI between cohorts. P-value less than 0.05 was considered statistically significant.

Results: Patients undergoing HD prior to primary TKA were found to have a significantly lower incidence and odds of cerebrovascular accidents (PD vs. HD: 0.19 vs. 0.13%; OR: 1.44, p=0.003) and venous thromboemboli (0.15 vs. 0.10%; OR: 1.52, p<0.001), specifically deep vein thromboses (0.13 vs 0.10%; OR 1.75, p<0.001). HD patients did however incur significantly higher 90-day cost of care ($104,341.89 vs. $209,611.67; p<0.001). No statistically significant differences were noted in myocardial infarction, pulmonary embolism, or 90-day readmission rates between the two groups.

Conclusions: While incurring a lower 90-day cost of care, patients treated with PD prior to primary TKA may have a greater odds of developing a cerebrovascular accident or deep vein thrombosis when compared to HD.

Outcome comparisons by dialysis modality following TKA.

Peritoneal Dialysis and Vascular Access: Research Abstracts

SU-OR27

Prognostic Roles of Peritoneal Dialysis Effluent Mitochondrial DNA Level

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Background: circulating mitochondrial DNA (mtDNA) level is associated with the systemic inflammatory state and prognosis of peritoneal dialysis (PD) patients. We explore the relation between mtDNA level in PD effluent and peritoneal transport characteristics and outcomes of PD patients.

Methods: We measured PD effluent mtDNA levels by quantitative polymerase chain reaction and the result is expressed as copy per 1000 copies of the housekeeping gene. Both PD effluent sediment and cell-free supernatant mtDNA levels were measured. Peritoneal transport was determined by the peritoneal equilibration test and represented as mass transfer area coefficient (MTAC) of creatinine. All patients were followed for technique and overall survival.

Results: 168 PD patients were followed for 41.3 (IQR: 19.3-52.0) months. Their mean age was 60.4±11.8 years; 99 (58.9%) were men. Median PD effluent (PDE) supernatant mtDNA was 255.4 unit (IQR: 157.5-451.3); median PDE sediment mtDNA was 201.6 unit (IQR: 147.8-267.3). PDE supernatant mtDNA level had a modest but significant correlation with MTAC creatinine (r = -0.364, p<0.001) and the number of previous peritonitis episode (r = -0.235, p=0.002). After adjusting for age, gender, Charlson’s Comorbidity Score, total weekly Kt/V, and residual renal function, PDE sediment mtDNA was a significant predictor of technique survival (adjusted hazards ratio [AHR] 1.002, 95%CI 1.000-1.003, p=0.001). In contrast, PDE sediment mtDNA level did not correlate with technique or patient survival.

Conclusions: PDE supernatant mtDNA level had a significant correlation with peritoneal transport. PDE sediment mtDNA level was a significant predictor of technique survival for PD patients. The mechanism of the differential implications between PDE sediment and supernatant mtDNA levels deserves further investigations.

SU-OR28

Hemodynamics and Geometry of Rat Arteriovenous Fistulas: Effect of Sildenafil Treatment

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Background: Arteriovenous fistula (AVF) maturation is dependent on hemodynamics and remodeling of the vessel wall to increase the AVF flow rate and lumen area for dialysis. Sildenafil is a phosphodiesterase 5 inhibitor that promotes vasodilation and is used clinically to treat erectile dysfunction and pulmonary hypertension. Here we investigate the effect of sildenafil on lumen geometry and hemodynamics in rat AVFs.

Methods: Femoral AVFs were created in 12-16 week-old male Sprague-Dawley rats. Sildenafil was administered at 90 mg/kg in drinking water starting 14 days prior to AVF creation surgery (n=4). 21 days post creation, animals were subject to non-contrast MRI scans, and the MR images were used for reconstruction of the AVF lumen and computational fluid dynamic simulations of the AVF blood flow. Hemodynamic parameters (flow rate, wall shear stress (WSS), vorticity, and oscillatory shear index (OSI)) and geometrical analysis (cross sectional lumen area, anastomosis angle (AA), tortuosity, and nonplanarity angle (NA)) were calculated.

Results: Sildenafil significantly increased the lumen area and flow rate of both the venous and arterial limbs of the AVFs when compared to no-treatment controls (p<0.0001) (Fig. 1). WSS, vorticity, and OSI of treated rats were also significantly higher than controls (p<0.0001). AA, tortuosity, and OSI were significantly higher in treated rats compared to control, which may be due to the increased flow rate. Sildenafil may have therapeutic potential to enhance AVF maturation by affecting the hemodynamics.

Funding: NIDDK Support, Other NIH Support - NHLBI, Veterans Affairs Support

SU-OR29

Single-Center Real-World Experience with Endovascular Arteriovenous Fistulas

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Background: Endovascular arteriovenous fistulas (EndoAVFs) are created percutaneously via an anastomosis between the radial artery and the perforator vein (Ellipsys), or between the ulnar artery and vein or radial artery and vein (Wavelink). Flow is directed via the perforator vein to the superficial veins.

Methods: We report partial outcomes for 69 technically successful endoAVF creations for patients on hemodialysis between 5/2019 and 4/2020 using 2 catheter-based devices.

Results: 12/69 endoAVFs failed (17%), all before reaching physiologic usability (ok to use) except for 1 which failed due to failure to cannulate at the dialysis center. The most common reason for failure was thrombosis of the perforator vein. In 49 endoAVFs that reached physiologic usability at time of data review, mean duration from creation to physiologic usability was 92 days and mean number of procedures between endoAVF creation and physiologic usability was 1. At time of data review, 9 endoAVFs were pending physiologic usability. 14/49 (29%) of endoAVFs that reached physiologic usability did so with 0 secondary procedures. Mean postoperative brachial artery flow in this subset was 718 ml/min (range 400-1100 ml/min). Mean flow at 4-6 weeks was 843 ml/min. 35/49 (71%) needed at least 1 procedure. Mean postoperative flow in this subset was 545 ml/min. Mean flow at 4-6 weeks was 721 ml/min. In 44 endoAVFs that had been cannulated at time of data review, mean duration from physiologic usability to cannulation was 9 days. In 33 patients whose dialysis catheters had been removed at time of data review, mean duration from first cannulation to dialysis catheter removal was 57 days.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Conclusions: Successfully created endoAVFs have shorter maturation time than surgical AVFs and require less maturation procedures. Immediate postoperative brachial artery flow is an important predictor of endoAVF behavior/outcome. All endoAVFs that reached physiologic usability with 0 secondary procedures had a postoperative flow above 400 ml/min, and mean postoperative flow was higher than those that needed at least 1 procedure. Time from first cannulation to dialysis catheter removal represents a pragmatic measure for endoAVFs. Cannulation injuries sometimes obligate a period of endoAVF rest. Removal of the dialysis catheter not only indicates functional usability of the endoAVF but also proficiency of the dialysis units in cannulating them.

SU-OR30

Association Between Antimicrobial Barrier Cap Use and Outcomes Among Hemodialysis Patients Using a Central Venous Catheter Scott Sibbel,1 Abigail Hunt,1 David B. Van Wyck,2 Lyssa Jordan,1 Francesca Tentori,1 Allen R. Nissenson,3 Steven M. Brunelli.3 Davita Clinical Research, Minneapolis, MN; 2Davita Inc, Denver, CO.

Background: Bloodstream infections (BSIs) are a common complication of central venous catheter (CVC) use and contribute to hospitalization, mortality, and high costs of care in patients on hemodialysis (HD). In a prior randomized clinical trial, patients using CVCs with antimicrobial barrier caps (AmBC; ClearGuard® HD, Pursuit Vascular Inc, Maple Grove, MN, USA) had significantly lower catheter-related BSI rates compared to patients using CVCs with the historical standard of care. Based on these findings, AmBCs were introduced in May 2019 as standard of care for CVC patients across a large dialysis organization (LDO). This study assessed changes in clinical outcomes in a real-world HD population following implementation of AmBC use.

Methods: Study data were derived from LDO electronic medical records over two 3-month periods: Pre (Jul-Oct 2018) and Post (Jul-Oct 2019) AmBC adoption. Included patients were adults receiving in-center HD treatment 3x/week using a CVC. Crude outcome rates were calculated for individual calendar months and for the pre- and post-periods overall; formal comparisons were made using generalized linear models.

Results: A total of 37,642 patients in the pre-period and 40,498 patients in the post-period met eligibility criteria. Overall BSI rate fell from 0.54/100 CVC days in the pre-periods overall; formal comparisons were made using generalized linear models. The contribution of underlying temporal changes (eg, background year-over-year change) could not be quantified.

Conclusions: Adoption of AmBCs for use in HD patients using a CVC for vascular access was associated with an early 34% reduction in infections assessed on the basis of change (difference in [95% CI]) and a 15% reduction in infections assessed on the basis of baseline versus the pre-period overall and within each calendar period met eligibility criteria. Overall BSI rate fell from 0.54/100 CVC days in the pre-periods overall; formal comparisons were made using generalized linear models. The contribution of underlying temporal changes (eg, background year-over-year change) could not be quantified.

SU-OR31

Two-Year Results from a Randomized, Controlled Study of Obinutuzumab for Pro liferative Lupus Nephritis Brad H. Rovin,1 Gustavo Aroca Martinez,2 Analia Alvarez,2 Hilda E. Fragosio loy,2 Adolfin A. Zuta,2 Richard Furie,2 Paul G. Brunetta,3 Thomas Schindler,4 Innan Hassan,5 Matthew Cascino,5 Jay P. Garg, Ana Malvar,6 Ohio State University, Columbus, OH; 2Simon Bolivar University and Clinica de la Costa, Barraquilla, Colombia; 3CEMIC, Buenos Aires, Argentina; 4Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico; 5Instituto de Ginecologia y Reproduccion, Lima, Peru; 6Northwell Health, Great Neck, NY; 7Genentech, Inc, South San Francisco, CA; 8F Hoffmann-La Roche AG, Basel, Switzerland; 9F Hoffmann-La Roche Ltd, Mississauga, ON, Canada; 10Organizacion Maedica de Investigacion, Buenos Aires, Argentina.

Background: NOBILITY demonstrated a sustained benefit of OBI through week 104, approximately 18 months after the final OBI infusion. There were no unexpected safety findings. OBI use in LN will be further evaluated in the Phase 3 REGISTRY trial.

Table. Week 104 Results

Conclusions: NOBILITY demonstrated a sustained benefit of OBI through week 104, approximately 18 months after the final OBI infusion. There were no unexpected safety findings. OBI use in LN will be further evaluated in the Phase 3 REGISTRY trial.

SU-OR32

Complement C5a Receptor Inhibitor Avacopan Improves Renal Function in ANCA Vasculitis David R. Jayne,1,2 Peter A. Merkel,1 Huibin Yue,3 Catherine L. Kelleher,2 Thomas J. Schall,2 Pirow Bekker.2 1Addenbrooke’s Hospital, Cambridge, United Kingdom; 2ChemoCentryx Inc, Mountain View, CA; 3University of Pennsylvania, Philadelphia, PA.

Background: Renal impairment is common in anti-neutrophil cytoplasmic autoantibody-associated vasculitis. The resulting chronic kidney disease and exacerbation of the toxicity risks of high dose or prolonged glucocorticoid use, a mainstay of ANCA treatment, are major consequences. Avacopan was tested for efficacy and effects on renal endpoints compared to standard prednisone therapy in a randomized double-blind Phase 3 trial in ANCA vasculitis.

Methods: Subjects randomized 1:1 received either prednisone (60 mg tapered to 0 over 20 weeks) or avacopan (30 mg twice daily for 52 weeks), combined with either cyclophosphamide (CYP) or rituximab (RTX). Primary endpoints: Disease remission at week 26 and sustained remission at week 52. Changes in urinary albumin to creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) were also assessed.

Results: 330 subjects were treated: 166 to avacopan and 164 to prednisone treatment groups. Avacopan remission at week 26 was 72.3% vs. 70.1%, for prednisone (P=0.0001 for non-inferiority); avacopan was superior to prednisone for sustained remission (week 52, 65.7%, avacopan vs. 54.9%, prednisone, P=0.0066). 81% percent of subjects had renal disease. UACR decreased more rapidly with avacopan than prednisone: week 4 avacopan was 40% below baseline vs. no change for prednisone (P=0.0001). Baseline to week 52 eGFR (mL/min/1.73 m²) improvement: avacopan eGFR +7.3 vs. prednisone +4.1 (P=0.029). In subjects with baseline eGFR <30: mean eGFR improved 67% more with avacopan than prednisone to week 52: avacopan eGFR +13.7 vs. prednisone +8.2 (P=0.011).

Conclusions: Treatment with avacopan for ANCA vasculitis compared with standard glucocorticoid therapy (both combined with either CYP or RTX) as is effective for remission induction at 26 weeks, and superior to prednisone for sustained remission after 52 weeks. Avacopan led to faster falls in UACR and greater recovery in eGFR when compared to standard prednisone therapy. These findings have important implications for the long term health of AA V patients through better overall disease control, reduced prednisone exposure and reduced severity of chronic kidney disease.

Funding: Commercial Support - ChemoCentryx, Clinical Revenue Support

SU-OR33

Prognostic Value of Persistent Proteinuria and Hematuria After Induction Therapy in ANCA-Associated Vasculitis Charles, M.,1,2,3, April, B.,1,2 Benjamin Lonergan,2,3, Thomas F. Houton,2,3 Rachel B. Jones,4 David R. Jayne,4 Alexandre, S.,1,2 HEGP, Hospital Européen Georges Pompidou, Paris, France; 1Université de Paris, Paris, France; 2Cambridge Clinical Trials Unit, Cambridge, United Kingdom; 3Addenbrooke’s Hospital, Cambridge, United Kingdom; 4Institut Mutualiste Montsouris, Paris, France; 5Hôpital Cochin, Paris, France.

Background: In ANCA-associated vasculitides (AAV), hematuria and proteinuria are biomarkers reflecting renal involvement at diagnosis. Yet, the prognostic value of their persistence after immuno suppressive induction therapy, which may reflect renal damage or persistent disease, remains uncertain.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
SU-OR34
Belimumab (BEL) Improves Renal Outcomes in Active Lupus Nephritis (LN): A Phase 3 Randomized, Placebo (PBO)-Controlled Trial
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Background: BEL is approved for patients (pts) with systemic lupus erythematosus (SLE) treatment-resistant active lupus nephritis (LN). Methods: This 104-week trial (GSK Study BEL114054; NCT01639339) randomized adults with active LN (class III, IV, and/or V) 1:1 to monthly BEL 10 mg/kg IV or PBO, plus standard therapy (ST) with high-dose corticosteroids + either cyclophosphamide (CYC) or mycophenolate mofetil (MMF) for induction at the investigator’s discretion. CYC was followed by azathioprine (AZA), and MMF by MMF maintenance. The primary endpoint was Primary Efficacy Renal Response (PERR = urine protein:creatinine ratio [UPCR] ≤0.7, estimated glomerular filtration rate [eGFR] no more than 20% below pre-flare value or ≥60 ml/min/1.73 m²; no rescue therapy) at Week 104. Other endpoints were Complete Renal Response (CRR = UPCR ≤0.5; eGFR no more than 10% below pre-flare value or ≥90 ml/min/1.73 m²; no rescue therapy) at Week 104; time to renal event (end-stage kidney disease, doubling of serum creatinine, increased proteinuria and/or impaired renal function, renal disease-related treatment failure) or death. Endpoints were analyzed using the Kaplan-Meier method. Results: 224 pts were randomized to each arm. At Week 104, there were significantly more PERR and CRR responders on BEL vs PBO (43.0% vs 32.3%, OR [95% CI] 1.7 [1.1-2.7]; p = 0.012), respectively. Risk of renal event or death was lower in BEL pts relative to PBO (HR [95% CI] 0.5 [0.3, 0.8]; p = 0.001). Week 104 PERR response rates in pts on CyCAZA were 33.9% with BEL and 27.1% with PBO, and 46.3% vs 34.1% with PBO in those on MMF. BEL significantly reduced risk of renal event or death on background of CyCAZA (HR [95% CI] 0.5 [0.2-1.0]) and MMF (HR [95% CI] 0.5 [0.3, 0.8]) relative to PBO. Adverse events (AEs; ≥1) occurred in 95.5% of BEL and 94.2% of PBO pts, and 25.9% of BEL and 29.9% of PBO pts had ≥1 serious AE. Conclusions: The addition of BEL to commonly used ST for the treatment of LN significantly improved renal responses with no unexpected safety signals. Funding: Commercial Support - GSK

SU-OR35
24-Week Interim Analysis of a Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Atacicept in Patients with IgA Nephropathy and Persistent Proteinuria
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Background: IgA nephropathy (IgAN) is the most common primary glomerulonephritis and currently has no approved therapy. Its central pathogenic feature is circulating immune complexes of poorly O-galactosylated polyclonal IgA1 (Gd-IgA1) that often deposit in the kidneys (causing inflammation and scarring) and trigger formation of IgA1 aggregates that deposit in glomeruli. This Phase II study (NCT02808429) examines atacicept safety and efficacy in reducing Gd-IgA1 and renal activity in IgAN.

Methods: Patients with Gd-IgA1 (≥0.5 g/l) or 0.75 mg/m² for 24 hr urine protein:creatinine-ratio (UPCR) despite maximal standard of care (ACE inhibitor and/or ARB) were enrolled. Patients were randomized to subcutaneous placebo, atacicept 25mg or 75mg weekly. Primary endpoint: change in proteinuria at Week 48; secondary endpoints: changes in eGFR, serum IgA, IgG, and IgM. Results: This interim analysis showed that, at Week 24, IgAN patients (placebo=5; atacicept 25mg=6; 75mg=5) had a consistent, dose-dependent reduction in IgA, IgG and IgM, and in Gd-IgA1 (Fig 1A), and a higher median % reduction from baseline in UPCR with atacicept than with placebo (Fig 1B); eGFR remained stable. TEAEs were reported in ≤81% of patients (mild/moderate, none severe), with no serious events related, severe hypogammaglobulinemia, or fatal outcomes.

Conclusions: These results provide proof of concept for the potential treatment of patients with IgA nephropathy with atacicept. Funding: Commercial Support - EMD Serono Research & Development Institute Inc. (a business of Merck KGaA, Darmstadt, Germany).

Figure 1. Median changes from baseline to Week 24 in a) serum Gd-IgA1 and b) 24-hour UPCR

SU-OR36
Grading System Utilizing Total Score of Oxford Classification for Predicting Renal Prognosis in IgA Nephropathy
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Background: The Oxford classification of IgA nephropathy (IgAN) can evaluate each MEST-C score comprehensively. Therefore, we aimed to analyze the usefulness of a new grading system that utilized the total score of each MEST-C score in predicting renal prognosis.

Methods: A total of 871 IgAN patients were classified into three groups using the Oxford classification system (O-grade) that utilized the total score of each MEST-C score (O-grade 1-3; II: 2-4, and III: ≥5 points) according to the renal survival rate (>10%, 10%-30%, >30%, respectively). The 20-year renal prognosis was analyzed, and the O-grade combined with the Japanese clinical classification (C-grade) was also evaluated.

Results: The clinical findings became significantly severer with increasing O-grades, and the renal survival rate by the Kaplan-Meier method was 78.5%, 74.9%, and 42.2% for O-grades I, II, and III, respectively (p=0.001). The hazard ratios (HRs) for O-grades I, II, and III with reference to O-grade I were 1.0 (95% CI 1.0-2.9; p=0.363) and 4.7 (95% CI, 2.6-8.4; P<0.001), respectively. In the multivariate analysis,
mean blood pressure and renal function, proteinuria, and O-grade (HR, 1.35; 95% CI, 1.02-1.90; P=0.036) were the independent factors predicting the renal prognosis of this disease. 

**SU-OR38**

Development of a Deep Learning Model to Predict ESKD in Patients with Immunoglobulin A Nephropathy (iAN) at Kidney Biopsy Time 

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**Background:** Many prediction models to support clinical decision making have been developed for decades but they are based on traditional statistical linear methods. Another approach is the application of artificial intelligence (AI) that is based on machine learning or deep learning algorithms. We developed an artificial neural network (ANN) tool to predict ESKD in patients at kidney biopsy time.

**Methods:** The classifier model to predict ESKD was composed of 4 hidden layers with 100 neurons in each layer. The regression model to predict the time-to-event endpoint consisted of 3 layers containing 125 neurons each.

**Results:** Our tool, based on these two models, was developed in a cohort of 948 iAN patients of the VALIGA and Greek cohort. Then, the tool was validated in an independent cohort of 167 iAN patients from 6 nephrology units. After Cox’s regression analysis 7 variables (age, sex, blood pressure values, serum creatinine, daily proteinuria, MEST classification for the kidney biopsy and therapy at baseline) were chosen to develop the ANN model. The AUC of the ANN model in the study cohort was 0.80. The performance was 0.82 (precision 0.83, accuracy 0.80) for ESKD prediction at 5 years of follow-up and 0.89 (precision 0.81; accuracy 0.83) for patients with 10 years of follow-up. Stable renal function and ESKD were correctly predicted in 91% of iAN patients in the test cohort.

**Conclusions:** (i) Our ANN is a promising alternative to the mathematical models in solving non-linear and multidimensional problems. (ii) We have developed a new clinical decision support system that provides additional information to identify iAN patients at high risk of ESKD (iii) This tool may straitly patients in the context of a personalized therapy. (iv) This tool will be validated in a clinical prospective study.

**Funding:** Government Support - Non-U.S.

**SU-OR39**

Complete Remission of Proteinuria in Patients with Focal Segmental Glomerulosclerosis Treated with Sparsentan, a Dual Endothelin and Angiotensin Receptor Antagonist, in the DUET Trial 

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**Background:** In FSGS, partial remission (FSGS partial remission endpoint [FPRP]: 40% reduction in proteinuria) and complete remission (FPRP<1.5 g/day) were more likely in patients who reached CR (proteinuria) of strong predictors of kidney survival. In the DUET trial, sparsentan (SPAR) resulted in greater reductions in proteinuria and higher rate of FPRP vs ibersartan (IRB) over the 8-week double-blind (DB) period. This antiproteinuric effect of SPAR was sustained during the open-label extension (OLE) period of DUET. Here we analyze patients who achieved CR (UP/C <0.3 g/g) during OLE period of DUET. Here we analyze patients who achieved CR (UP/C <0.3 g/g) during OLE period of DUET.

**Methods:** DUET randomized patients age 8-75 years with biopsy-proven FSGS, UP/C >1 g/day, and eGFR<30 mL/min to SPAR or IRB for 8 weeks, followed by OLE with all patients treated with SPAR. Baseline and other proteinuria parameters were measured every 12 weeks during OLE. This post-hoc analysis included all patients on SPAR treatment regardless of original randomization.

**Results:** Median follow-up on SPAR was 42.5 months. Of 108 subjects dosed with SPAR, 39% of patients reached CR (68% of CR patients). CR was achieved by 28 patients within the 1st year on SPAR (Kaplan-Meier estimate: 29%). A history of, or nephrotic syndrome at baseline, was documented in 8 (18%) of CR patients. Of subjects with CR, 14%, 41%, and 45% were originally assigned to 200, 400, and 800 mg/day of SPAR dose cohorts, respectively. No patient achieved CR while on IRB during the DB period. Compared to the overall DUET population, CR patients had similar age, sex, and baseline eGFR, but lower baseline mean UP/C (1.67 g/g vs 2.65 g/g), and higher proportion of baseline immunosuppression (45% vs 35%), in particular with mycophenolate mofetil (18% vs 12%). Achieving CR was associated with better preservation of kidney function compared to not achieving CR. In 6 patients (14%), occurrence of CR followed the initiation of new steroid treatment.

**Conclusions:** In the DUET trial, a high proportion of patients achieved CR on at least one occasion. These observational data support the long-term nephroprotective potential of sparsentan.

**Funding:** Commercial Support - Retrophin, Inc.

**SU-OR40**

Characteristics and Outcomes of Pregnancy-Triggered Atypical Hemolytic-Uremic Syndrome (aHUS): Global aHUS Registry Analysis

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**Background:** Pregnancy-triggered aHUS (P-aHUS) accounts for 10–20% of aHUS diagnoses. Complement-mediated thrombotic microangiopathy (CM-TMA) may be associated with high maternal and fetal morbidity and mortality such as ESRD. The clinical characteristics of P-aHUS and survival probability in patients treated with the complement C5 inhibitor eculizumab are described, using the largest collection of P-aHUS data available in a single study.

**Methods:** Patients with a clinical diagnosis of aHUS were included in the global aHUS registry (NCT01522183). Patients with P-aHUS were selected as those first TMA manifestations during pregnancy or within 60 days postpartum. Patients with other triggers of aHUS were excluded. Survival, based on time to ESRD, was calculated by the Kaplan-Meier method.

**Results:** In the registry, 51/1029 female patients were selected with P-aHUS and 27 received eculizumab. Mean ± SD age at pregnancy onset was 30.7 ± 5.9 years. P-aHUS occurred during pregnancy in 28 (54.9%) patients, with the remainder occurring within 60 days of pregnancy. A diagnosis of pre-eclampsia or HELLP (hemolysis elevated liver enzymes low platelet count) syndrome was reported in 28 (54.9%) and 17 (33.3%) patients, respectively. A complement pathogenic variant was identified in 23 (45.1%) patients, of whom 3 (8.3%) also tested positive for anti-complement factor H antibodies. Mean ± SD eculizumab treatment duration was 1.8 ± 1.1 years. Survival probability was higher in eculizumab-treated patients compared with patients not receiving eculizumab (Figure).

**Conclusions:** Survival probability was higher in patients who received eculizumab compared with patients who did not receive eculizumab. Successful treatment with eculizumab, in addition to a complement pathogenic variant, confirms the appropriate classification of P-aHUS as a CM-TMA.

**Funding:** Commercial Support - Alexion Pharmaceuticals Inc.
SU-OR41
Differences in Kidney Failure Risk by Race/Ethnicity at the Time of GFR-Based Transplant Eligibility
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Background: Glomerular filtration rate (GFR) less than 20 ml/min/m² is a criterion for kidney transplant listing, but variation in underlying end-stage kidney disease (ESKD) risk distributions by race/ethnicity has the potential to produce systematic racial disparities due to under recognition of the higher progression risk when a singular eGFR threshold is used as a decision point.

Methods: We compared predicted kidney failure risk by race/ethnicity for patients at the time their eGFR fell below 20 ml/min/m² using the OptumLabs® Data Warehouse (OLDW), a longitudinal, real-world data asset with de-identified administrative claims and electronic health record (EHR) data. We identified patients 18-70 years old from 1/1/2014-6/30/2019 who had at least one eGFR ≥20 ml/min/m², and at least two later eGFR values ≥20 ml/min/m² that were a 90 days separated, who also had a urine albumin/creatinine ratio (UACR) measured within 90 days of the first eGFR ≥20 ml/min/m². We calculated 2-year risk of ESKD for each patient using the 4-variable Kidney Failure Risk Equation and compared the distributions by race/ethnicity.

Results: Of 2926 patients, 2024 were non-Hispanic white (NHW), 649 non-Hispanic black (NHB), and 253 Hispanic. At the time of incident eGFR ≥20 ml/min/m², NHWs were older than NHB or Hispanic patients (mean age 59.2 versus 56.2 or 54.3 years, respectively) and had lower median UACR (0.67 versus 1.36 or 1.72 g/g, respectively). Compared to ESKD risk among NHWs (median predicted risk 38.7%), the risk distribution was skewed toward higher risk for NHB and Hispanic patients, who had median predicted risks of 49.4% and 55.8% respectively (Figure).

Conclusions: At the time of incident eGFR ≥20 ml/min/m², NHB and Hispanic populations had greater risk of ESKD. A racial/ethnic disparity in time from GFR-based transplant eligibility to ESKD may exist even with elimination of disparities in timing of transplant referral and waitlisting. Consideration of kidney failure risk might be given greater attention in access to transplantation.

Funding: NIDDK Support

SU-OR43
Do Social Determinants of Health Predict Patient-Reported Outcomes in Transplant-Eligible ESRD Patients?
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Background: Measuring and understanding patient reported outcomes [PRO, e.g., health related quality of life (HRQoL) and satisfaction with transplant clinic service] is a critical consideration for the care of kidney transplant (KT) eligible patients with end-stage renal disease (ESRD), because research has demonstrated that pre-transplant HRQol predicts both the receipt of a KT as well as post-KT mortality. Although research demonstrated the importance of social determinates of health (e.g., cultural factors, psychosocial characteristics, transplant knowledge) on clinical outcomes, less is known about how they predict PRO in KT-eligible ESRD patients.

Methods: We examined whether social determinants of health (Time 1, assessed shortly after initiating KT evaluation) are risk or protective factors for PRO (Time 2, assessed after notification of KT evaluation outcome – accepted or not), controlling for evaluation outcome, in a prospective cohort study. Of the initial 1152 adults referred for KT evaluation (2010-2012), 955 completed a Time 2 interview, most within 1 year of completing KT evaluation [n=46 months=70% (669), n=6 months<12 months=9% (76), n=12 months>22% (210)]. We used the Physical Composite Score (PCS), Mental Health Composite Score (MCS), and Kidney Summary Score (KSS), from the Kidney Disease Quality of Life Short Form (KDQoL-SF) to measure HRQol, and the Client Satisfaction Questionnaire to measure satisfaction with KT clinic service.

Results: Participants completed KT evaluation in an average of 11.7 months (range=0-43 months). In adjusted multivariable regression models, a stronger sense of mastery predicted higher PCS (β=4.5, p <0.001), MCS (β=5.4, p=0.001), and KSS (β=5.6, p=0.001). Depression predicted lower MCS (β=4.2, p<0.001), and lower KSS (β=5.1, p=0.002). More medical mistrust predicted lower odds of higher patient satisfaction scores (OR=0.6, 95% CI=0.4, 0.8, p=0.002).

Conclusions: Transplant teams should consider identifying and targeting patients with a low sense of mastery, greater depressive symptoms, or an increased sense of medical mistrust, with additional psychosocial support to improve PRO during the KT evaluation process.

Funding: NIDDK Support, Private Foundation Support
SU-OR44

Genetic vs. Self-Reported African Ancestry and Kidney Allograft Outcome: Analysis of Two Large Multietnic Urban Transplant Cohorts

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Background: African-American (AA) kidney transplant recipients have higher risk of allograft rejection and failure. However, it is unknown to what extent the inferior outcomes in self-reported AA are due to genetic versus environmental effects. Herein, we compared the effects of self-reported race versus genetic African admixture on graft outcomes.

Methods: A discovery multicentric cohort of 1,083 kidney transplant recipients from Columbia University and a replication cohort of 761 kidney transplant recipients from University of Pennsylvania were genotyped with high resolution SNP arrays. African admixture proportions, a genetically-derived quantitative measure of African ancestry, was estimated with ADMIXTURE software. Multivariable Cox models were used to investigate associations between African ancestry measures and time to rejection and time to death-censored graft failure, with adjustments for relevant covariates. Akaike information criterion (AIC) was used to compare the models.

Results: 206 and 346 self-identified AA were included in the discovery and replication cohorts, respectively. Over a median follow-up time of 78 months, 432 patients had rejection and 193 had graft failure in the discovery cohort. Self-reported AA ancestry and African admixture were associated with acute rejection (self-report: HR 1.47, 95% CI: 1.18-1.83, AIC: 5540.1; admixture: HR 1.64, 95% CI: 1.22-2.19, AIC: 5548.1, p=0.0001), and graft failure (self-report: HR 1.42, 95% CI: 1.02-1.97, AIC: 2228.9; admixture: HR 1.48, 95% CI: 0.96-2.29, AIC: 2228.9). In the replication cohort, during a median follow-up time of 49 months, 113 patients had rejection and 121 had failure. Self-reported AA ancestry and African admixture measures confirmed to be associated with both acute rejection (self-report: HR 1.36, 95% CI: 1.96-4.78, AIC: 1289.5; admixture: HR 1.36 95% CI: 2.21-6.16, AIC: 1288.9) and failure (self-report: HR 2.16, 95% CI: 1.43-3.27, AIC: 1113.8; admixture: HR 2.46, 95% CI: 1.54-3.94, AIC: 1113.1). In this cohort, the models including African admixture proportion had a better fit when compared to self-report.

Conclusions: In conclusion, self-reported AA race and a genetically-derived continuous measure of African ancestry predict the risk of allograft rejection and failure in multietnic and genetically diverse cohorts.

Funding: NIDDK Support

SU-OR45

Deceased Donor Families and Authorization for Research: Differences Among Ethnic Groups

Mariella O. Goggins,1,2 Giselle Guerra,1,2 Miami Transplant Institute 1University of Miami School of Medicine, Miami, FL; 2Miami Transplant Institute, Miami, FL.

Background: Research in transplantation requires next of kin (NOK) to authorize for participation in research. Aim was to determine the rate of research authorization by the NOK within different ethnic groups: African American (AA), White (W) or Hispanic (H).

Methods: Single center study of all deceased donor kidney transplants referred to our institution during 3/1/2019-10/31/2019 from multiple organ procurement organizations (OPO) across the United States. We looked at the authorization for donation form in DonorNet. We searched for the NOK research authorization agreement at the time of organ donation. Donors were grouped by self-identified ethnic groups as W, AA or H.

Results: We had a total of 297 donors, yielding 401 kidney offers. 71% were from OPOs. Donors were from: 46% of W, 29% of AA and 25% of H. In 13% of the donors, no authorization was found. In 57% of cases, the family did not authorize donation.

Conclusions: In conclusion, family authorization rate was lower in AA donors compared to W donors (43% vs 62%, p=0.0001) and H donors (35%, p=0.0002). Multivariable analysis showed that donors from AA were more likely to decline research authorization, yielding multivariable p=0.0001 for AA donor and p=0.002 for younger donor age. Multivariable percentages who were more likely to decline research authorization, yielding multivariable p=0.0001 for AA donor and p=0.002 for younger donor age. Multivariable percentages who were more likely to decline research authorization, yielding multivariable p=0.0001 for AA donor and p=0.002 for younger donor age.

Funding: Miami Transplant Institute.

SU-OR46

Minimum Diagnostic Criteria for Thrombotic Microangiopathy in Renal Allograft: The Banff TMA Working Group Phase I Results

Marian Afrozian, Banff TMA Working Group University of Texas Medical Branch at Galveston, Galveston, TX.

Background: Thrombotic Microangiopathy (TMA) is a serious complication of renal transplantation, usually with poor outcome. The Banff TMA Working Group (TMA-WG) was formed to study renal transplant TMA (t-TMA) aiming to: 1- Survey current practices used in the diagnosis of t-TMA; 2- Define minimum diagnostic criteria (MDC); and 3- Develop recommendations for adequate diagnosis integrating morphological, clinical, laboratory and molecular findings, where applicable. The project started with Phase I (pathology phase) and is continuing in Phase II (Nephrology phase).

Methods: Using the Delphi methodology during phase I, 23 nephrologists who had >3 years of experience with t-TMA were asked to list their MDC for t-TMA in the following categories: 1- Light, 2- immunofluorescence, and 3- electron microscopy, 4- clinical history, 5- laboratory findings, 6- genetic testing and 7- raised differential diagnoses. Nine rounds (R) of surveys were designed. At the end of each R, MDC were narrowed down following Delphi rules. R6 and R7 were designated as the validation Rs in which the narrowed criteria were validated on 37 renal biopsies (25 TMA and 12 non-TMA cases) using Aperio Imagescope and whole slide digital images scanned @ X400. For each biopsy, pertinent pathology/history/laboratory/genetic information were provided. Descriptive statistical analysis was performed using SPSS program.

Results: Starting with 338 criteria in R1 and following analysis of total 8,677 data entries, MDC were narrowed down to 35, by the end of R9. The graph illustrates the evolution of the criteria over 9 R. A complete list of 35 MDC will be presented at the meeting.

Conclusions: Applying the Delphi methodology to a cohort of t-TMA biopsies in Phase I of the project, nephropathologists from 4 continents generated histopathologic, clinical and laboratory MDC for renal t-TMA. Phase II (Nephrology consensus) and Phase III (consensus of the consensus groups- Combined Phases I & II) will follow Phase I to generate final MDC for t-TMA.

Funding: Commercial Support - Alexion Pharmaceuticals

SU-OR47

Does Screening for Coronary Artery Disease Predict Cardiac Outcomes Following Renal Transplantation?

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Background: Screening for asymptomatic coronary artery disease (CAD) prior to transplantation aims to reduce perioperative cardiac events. There is conflicting evidence as to whether this is achieved.

Methods: Individuals recruited to the Access to Transplant and Transplant Outcome Measures (ATTOM) study in England who received a renal transplant between 2011-2017 were studied. Patient demographics and details of screening investigations from ATTOM were linked to outcome data from the Hospital Episode Statistics dataset. Major Adverse Cardiac Events (MACE) comprised unstable angina, myocardial infarction, coronary bypass graft, coronary angioplasty or cardiac death. The effect of screening on MACE was analysed in propensity score-matched groups, using Cox survival analyses, up to 5 years post-transplant.

Results: 2572 individuals received a renal transplant; 51% underwent CAD screening (Figure 1). Age, ethnicity, ischaemic heart disease and diabetes were independently associated with screening. The incidence of MACE at 90 days, 1 and 5 years was 0.9%, 2.1% and 9.4%. After propensity score matching, 1854 individuals were examined. There was no association between screening and MACE at 90 days (HR 0.68, 95% CI 0.28-1.64), 1 year (HR 1.24, 95% CI 0.60-2.54) or 5 years (HR 1.31, 95% CI 0.95-1.79) (Figure 2).

Conclusions: Screening for CAD did not influence the rate of ischaemic cardiac events up to 5 years post-transplant. Units should review protocols with lengthy cardiac workup processes.
SU-OR48
Albuminuria in Kidney Transplantation Patients Predicts Cardiovascular Morbidity After Two Years
Dana Bielopolski,1,2 Ruth Rahaminov,1 Boris Zingerman,1 Avry Chagnac,1 Limor Azulay gitter,1 Benaya Rozen-zvi.1 1The Rockefeller University, New York, NY; 2Rabin Medical Center, Petah Tikva, Israel.

Background: Moderately Increased Albuminuria (MIA) is a well characterized marker of kidney malfunction, both in diabetic and non-diabetic populations, and is used as a prognostic marker for cardiovascular morbidity and mortality. A few studies implied that it has the same value in kidney transplanted patients, but the information relies on spot or dipstick urine protein evaluations, rather than the gold standard of timed urine collection.

Methods: We revisited a cohort of 286 kidney transplanted patients, several years after completing a meticulously timed urine collection and assessed the prevalence of major cardiovascular adverse events (MACE) in relation to albuminuria.

Results: During a median follow up of 8.3 years (IQR 6.4-9.1) 144 outcome events occurred in 101 patients. By Kaplan-Meier analysis MIA was associated with increased rate of CV outcome or death (p=0.03), and this was still significant after stratification according to propensity score quartiles (p=0.048). Time dependent Cox proportional hazard analysis showed independent association between MIA and CV outcomes over 5 years. Cox regression analysis revealed male gender [HR 2.14], pre-emptive renal transplantation [HR 6.57] and HLA mismatch >4 [5.60] as significant risk factors for renal graft failure in SKHT recipients as compared to DDKT recipients at 4 years. Predominant cause of graft failure in SKHT recipients was primary failure (36%) and in DDKT recipients was acute rejection (26%).

Conclusions: This is the largest analysis of the UNOS database till date to describe risk factors associated with renal allograft loss in SKHT recipients. We also showed that 38% of grafts that fail in SKHT recipients, failed in the first year following transplant and primary failure was the predominant cause. Our analysis provides much needed data to policy makers for future combined organ allocation policies.

SU-OR50
Recurrence of IgA Nephropathy After Kidney Transplantation: TANGO Multicenter Study
Audrey Uffing,1,2 Paolo Cravedi,1 Leonardo V. Riella.1 TANGO-project 1Brigham and Women’s Hospital, Boston, MA; 2Universitair Medisch Centrum Groningen, Groningen, Netherlands; 3Icahn School of Medicine at Mount Sinai, New York, NY.

Background: In patients who received a kidney transplantation for end-stage renal disease (ESRD) due to IgA nephropathy, IgA deposits can recur in the transplanted kidney. The incidence, impact and predictors of these recurrent deposits is unclear.

Methods: As part of The Post-Transplant Glomerular Disease (TANGO) project, we performed a multicenter, international, retrospective study to determine the incidence, predictors and treatment response of recurrent IgA deposits after kidney transplantation. Patients with biopsy-proven IgA nephropathy, transplanted in the period 2005-2015 were selected in 16 TANGO centers in Europe, United States and Brazil.

Results: In a total of 504 patients, recurrent IgA deposits were identified by kidney biopsy in 82 patients (16%; 95%CI: 13-19), with a median time to recurrence of 3.4 years (IQR 1.4-5.7 years). Kaplan-Meier analysis showed similar graft survival between patients with and without recurrence in the first years after kidney transplant, though after 8 years, graft failure rates were higher in patients with recurrence (10 year death-censored graft survival 76% and 89%, respectively). Multivariable Cox-regression revealed a higher risk for IgA recurrence.
in patients with a pre-emptive kidney transplant (HR 2.56, 95%CI: 1.59-4.17), patients with DSA at time of transplant (HR 2.74, 95%CI: 1.22-6.14) and patients with shorter time from diagnosis to ESRD (HR 0.84 per month, 95%CI: 0.74-0.96). The presence of systemic autoimmune diseases associated with IgA nephropathy did not affect recurrence rates, nor did early steroid withdrawal. In multivariate analysis of post-transplant complications, de novo DSA was associated with recurrence of IgA deposits (HR 1.91, 95%CI: 1.04-3.51).

**Conclusions:** In our international cohort, IgA deposits reappeared in 16% of patients and was associated with worse graft outcomes after 8 years of transplant compared to patients without recurrence. A pre-emptive transplant, shorter time from native diagnosis to ESRD, DSA at time of transplant and de novo DSA after kidney transplantation were associated with recurrence of IgA deposits.

**PO2614**

**Renin Does Not Associate with Mortality or AKI in Acute Respiratory Distress Syndrome**

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**Background:** Renin may be a marker of severity of illness and mortality in critically ill patients. Angiotensin II infusions in patients with lower renin levels may increase the rate of renal recovery from dialysis-requiring AKI. Given that most ACE is found in the lungs and an ACE defect would lead to higher renin levels, we tested associations between renin and clinical outcomes in patients with acute respiratory distress syndrome (ARDS).

**Methods:** We studied 63 patients with plasma renin measurements enrolled in a phase 2/3 trial of bone marrow-derived human MSCs for moderate-severe ARDS. We estimated associations between renin levels (as a continuous variable) and ARDS severity (assessed by PaO2/FiO2), mean arterial pressure (MAP), and serum creatinine at randomization. We then examined if renin was associated with subsequent AKI (defined as ≥ 2x SCR or new dialysis) or in-hospital mortality.

**Results:** The median renin was 72 pg/mL (25%-75% percentile 33-181 pg/mL). At randomization, there was no cross-sectional correlation between renin level and PaO2/FiO2 (R = 0.03, 95% CI 0.00-0.14, p = 0.21), between renin level and MAP (R = 0.01, 95% CI 0.00-0.12, p = 0.32), or between renin level and serum creatinine (R2 = 0.003, 95% CI 0.00-0.08, p = 0.68). In longitudinal unadjusted analysis, renin did not significantly associate with AKI (OR 1.006 per 10 pg/mL increase, 95% CI 0.992-1.021, p = 0.41) or 28-day mortality (OR 1.00 per 10 pg/mL, 95% CI 0.987-1.014, p = 0.97). Results were similar in a nested analysis of serum creatinine at randomization was associated with AKI (OR 3.27 per mg/dL, 95% CI 1.47-7.30, p = 0.004).

**Conclusions:** We did not find that renin level is a risk factor for mortality or AKI in moderate-severe ARDS.

**Funding:** NIDDK Support

**ARDS Patient Characteristics**

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<th>Variables</th>
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<tr>
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<td>Renin (pg/mL)</td>
<td>72 (33-181)</td>
<td>82 (40-158)</td>
<td>68 (25-127)</td>
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</tbody>
</table>

Continuous values given as mean (SD). AKI and AKI-D percentages are reported from among the 55 patients not on dialysis at the time of randomization.

**PO2615**

**Renal Denervation Alleviates Renal Ischemic-Reperfusion Injury-Induced Acute and Chronic Kidney Injury Partly by Modulating miRNAs in Rats**

Xiangyu Zou, Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China.

**Background:** Renal denervation (RDN) has been used as a potential medium for kidney injury repair and miRNAs involved in the pathophysiology of renal injury. However, the change of miRNAs after RDN and its proper protective mechanisms has yet to be determined.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline:** represents presenting author.
PO2618
Male, but Not Female, Spontaneously Hypertensive Rats (SHR) Have Sustained Renal Injury Following a Single Ischemic Insult Progressing to CKD
Riyaz Mohamed, Jennifer C. Sullivan. Augusta University, Augusta, GA.

Background: Renal ischemia-reperfusion (IR) injury is a major cause of acute kidney injury (AKI), which is an independent risk factor for the development of CKD and all-cause mortality. The goal of the current study was to test the hypothesis that hypertensive males will have greater IR injury than hypertensive females resulting in the development of CKD.

Methods: 13-week old male and female SHR were subjected to sham or 30-minute warm bilateral ischemia followed by reperfusion (n=5-6). Systolic blood pressure (BP) measured weekly by tail-cuff.

Results: Plasma creatinine (Pcr) and urine protein creatinine ratio (UPCR) remained elevated at 1-week post IR in male SHR compared to sham (Pir<0.005); Per and UPCR returned to baseline in SHR females. Histological examination of SHR kidneys 7 days post-IR showed greater increases in vascular congestion (P<0.002) and tubular damage (P<0.001) in males. However, glomerular filtration rate (GFR) and systolic BP were not altered in both male and female SHR at 1-week post IR. To determine if this was sustained dysfunction or simply delayed recovery, additional 13-week old male and female SHR were subjected to sham or 30-minute warm bilateral ischemia followed by 20 weeks of reperfusion (n=4-5). Male SHR showed progressive increases in UPCR (P<0.05) and systolic BP up to 20 weeks post-IR compared to respective sham (P<0.001). Whereas in female SHR, UPCR remained at baseline up to 16-week post IR compared to respective sham. However, at 20 weeks of post IR, both male and female SHR exhibit an increase in UPCR compared to respective sham control; although the increase in UPCR was greater in males (P<0.01; Pir<0.09). Male SHR also exhibited greater decreases in glomerular filtration rate (GFR; P<0.0025; Pir<0.12) and increases in systolic BP (P<0.0001; Pir<0.27) compared to females.

Conclusions: Our data demonstrated that impaired renal recovery following IR in SHR males results in exaggerated progression towards CKD.

Funding: Other NIH Support - NHLBI

PO2619
High Serum Strontium May Predict AKI After Cardiac Surgery with Cardiopulmonary Bypass
Natsumi Tomita,1 Yuji Hotta,1 Karin Matsuoka,2 Hidekazu Ito,1 Yoko Yamamoto,4 Kazuki Ohashi,2 Masahiro Kondo,2 Tomoaki Hayakawa,2 Tomoyo Kataoka,1,3 Kazuya Sobue,1 Kazunori Kimura.1,2 1Department of Hospital Pharmacy, Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, Japan; 2Department of Pharmacology, Nagoya City University Hospital, Nagoya, Japan; 3Department of Clinical Pharmaceutics, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan; 4Aichi-ken Eisei Kenkyujo, Nagoya, Japan; 5Department of Anesthesiology and Intensive Care Medicine, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan.

Background: The prevalence of acute kidney injury after cardiac surgery under cardiopulmonary bypass (AKI-CPB) is high and it worsens patient prognosis, which renders it a major concern during intensive care. Therefore, a predictable marker of AKI-CPB is required. Because some trace metals have been found to affect renal injury, we investigated their association with AKI-CPB.

Methods: Study 1. We enrolled 30 patients from the Nagoya City University Hospital. Serum concentrations of 19 trace metals were measured before surgery and immediately after CPB withdrawal. We defined AKI according to the KDIGO criteria. Factors associated with AKI-CPB were identified by univariate and multivariate analyses. Study 2. We treated male Wistar-ST rats with 1 mg/kg/day of strontium (Sr) or vehicle orally for 3 days, followed by the application of 30 min of ischemia and reperfusion to cause renal injury. Serum creatinine (Scr) and blood urea nitrogen (BUN) levels were evaluated 24 h later. We also incubated human kidney (HK)-2 cells with Sr (0.25 μM, high-Sr or 0.19 μM, normal-Sr) or PBS for 24 h in vitro. These Sr concentrations were determined according to the average serum Sr concentrations in patients with and without AKI. The cells were incubated under normoxia (20% O2) or hypoxia (1% O2) conditions; then, cell viability and mRNA expression were assessed.

Results: Study 1. The incidence of AKI-CPB was 30% (n = 9). Serum Cr levels before surgery were high in the AKI group. Intraoperative factors did not differ between patients with and without AKI. Univariate analysis revealed significantly higher levels of Sr and arsenic before surgery, and higher Sr, arsenic, and zinc levels after CPB in the AKI group (p < 0.05). Multivariate analysis showed that only Sr levels after CPB withdrawal correlated independently with AKI. Study 2. The Scr and BUN levels were higher in Sr treated rats than vehicle treated rats. Incubating HK-2 cells with Sr did not affect their viability under normoxia and hypoxia conditions. However, NF-kB mRNA levels increased only under hypoxia conditions following exposure to high Sr levels.

Conclusions: High Sr levels before CPB may be a useful predictor of AKI-CPB. This study suggested that high Sr levels enhance ischemia-induced inflammation following CPB.

PO2620
BAM15 and Mitochondrial DNA Form a Drug-Companion Biomarker Pair Working Through Reactive Oxygen Species in Septic AKI

Background: Sepsis is multifactorial, so drug-biomarker co-development is likely necessary for developing effective therapeutics. Administration of BAM15, a mitochondrial uncoupler, improved sepsis AKI mortality, kidney function, and mitochondrial function in kidney tubules (ASN, 2019). We now evaluate if BAM15 and mtDNA form a drug companion biomarker pair and are linked mechanistically.

Methods: Mice with sepsis AKI [cecum ligation/puncture (CLP) in CD-1 mice] were treated with BAM15 (5mg/kg IV) at 0h (early) or 6h (delayed) after surgery. Serial plasma and urinary mtDNA was measured by qPCR. This was mimicked in vitro by incubating mouse primary cultured proximal tubular cells (PTCs) with serum from CLP mice. Mitochondrial superoxide generation was measured by live cell imaging with MitoSox-Red. Mitophagy detected in Mt-Keima mice [transgenic for pH-sensitive ratiometric fluorescent protein] by measuring mitochondrial pH.

Results: Plasma and urinary mtDNA were increased in CLP mice starting at 3 hr after CLP. Delayed treatment with BAM15 (6 hr) decreased mtDNA at 12 hrs (Fig 1).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
CLP serum stimulated superoxide production and release of mtDNA into cultured PCT media, both were proportionately inhibited by BAM15 (Fig 2A-C). Released mtDNA correlated with superoxide production. BAM15 recovered mitochondrial biogenesis through activation of PGC1α pathway and, inhibited CLP reduction of mitophagy.

**Conclusions:** Sepsis increased kidney mtROS and released mtDNA from PT cells. BAM15 attenuated generation of mtROS and inhibited mtDNA release into urine and also circulating mtDNA even delayed BAM15 treatment. In sepsis AKI, BAM15 changed the trajectory of mitochondrial fate. Our results suggest that BAM15 and mtDNA are mechanistically linked via ROS, and form a drug-companion biomarker pair.

**Funding:** NIDDK Support

**PO0001**

**AKI Identification: Use of Electronic AKI Alerts vs. Electronic Health Records in Hospital Episode Statistics**

**Manuela Saving,1 Anna Casula,1 Esther H. Wong,1 Nitin V. Kolhe,2 James Medical Center,2 Dorothea Nitsch,1 UK Renal Registry, Bristol, United Kingdom; 3 Royal Derby Hospital, Derby; United Kingdom; 4 London School of Hygiene & Tropical Medicine, London, United Kingdom; 5 Leicester General Hospital, Leicester, United Kingdom.

**Background:** Acute Kidney Injury (AKI) refers to an abrupt decline in the glomerular filtration rate (GFR) potentially associated with significant morbidity and mortality. Since April 2015, an automated real-time electronic (e)-alert system for AKI was introduced and progressively implemented in England, with alert data being sent to the UK Renal Registry (UKRR) for collection into a master patient index (MPI). Historically, the only way to routinely measure AKI incidence in hospital was to analyse the Hospital Episode Statistics (HES). This project aims to determine whether episodes of AKI identified in the UKRR MPI correspond to coded diagnoses on the discharge record held in HES.

**Methods:** The UKRR MPI of all AKI e-alerts (stages 1, 2 and 3) identified in AKI (stage 1) and stage 3 (mean 83.3% SD 7.3) (figures 1). Younger adults with AKI e-alerts were less often coded in HES for all three AKI stages (33% people aged 18-29 years versus 64% people aged 85 years).

**Conclusions:** In 2017, earlier stages of AKI e-alerts were poorly coded in HES. There was also high degree of inter-hospital variability, particularly for AKI stage 1, reflecting potentially poor clinical recognition and documentation in medical records and subsequent clinical coding. AKI e-alerts were poorly captured in HES for younger adults in comparison to those of older age. Use of HES to identify cases of AKI is likely to underestimate the incidence of AKI, especially for AKI stage 1, though a high proportion of the most severe cases will be captured.

**Funding:** Private Foundation Support

**PO0002**

**Assessment of a Modified Renal Angina Index for the Prediction of AKI in Hospitalized Adult Patients**

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**Background:** Risk-stratification tools of incident AKI in hospitalized patients are needed. The renal angina index (RAI) was developed and validated in the pediatric population. The purpose of this study was to evaluate the performance of a modified RAI (mRAI) for the prediction of AKI in hospitalized patients.

**Methods:** We analyzed data from 55 hospitalized patients admitted to our center. Inclusion criteria consisted of age ≥ 18, hospital stay ≥ 3 days, at least 2 serum creatinine (Scr) measures in the first 2 days of hospital stay and one measure at 3-7 days of stay. Exclusion criteria consisted of ESKD, kidney transplant or baseline eGFR <15. At admission, mRAI was calculated using the following formula: **risk level criteria 1** (ICU admission), 2 (mechanical ventilation or vasoactive drug support, and 3) diabetes. **X injury level criteria** of Scr increments of ≥ 0.1 mg/dL, ≥ 0.1 mg/dL, and ≥ 0.4 mg/dL. AKI was defined as an increase of serum creatinine level ≥ 0.3 mg/dL or a 1.5 times within 48 hours or ≥ 1.5 times in contrast to baseline creatinine level. We assessed the performance of the mRAI to predict the subsequent development of AKI using KDIGO Scr criteria.

**Results:** Mean (SD) age was 67.9 (13.3), 47.3% were women and 100% Hispanic. The incidence of AKI at 3-7 days of hospital or ICU stay was 52.7%. Most patients developed AKI stage 1 (61.3%) and 38.7% developed severe AKI (KDIGO-Scr stage 2) at 3-7 days. Performance metrics are reported in Table. The RAI exhibited a good, AUC of 0.87 (95% confidential interval [CI]: 0.77-0.96; p <0.0001) in ROC analysis, with a cutoff of 8.

**Conclusions:** The mRAI have robust predictive capacity to identify hospitalized adults patients at high risk of developing AKI. Incorporation of AKI biomarkers into the RAI may potentially improve prediction. The preliminary data of our ongoing study warrants future studies to validate these findings.

**Funding:** Private Foundation Support
Early Prediction of Hospital-Acquired AKI from Electronic Health Records Using Machine Learning

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1Geisinger Medical Center, Danville, PA; 2Sanofi Genzyme, Cambridge, MA.

Background: Hospital-acquired acute kidney injury (HA-AKI) leads to increased morbidity and mortality. Early prediction of HA-AKI using Electronic Health Records (EHR) may enable clinicians to modify treatment to minimize risk and AKI severity.

Methods: Inpatient admissions from 7/13/2012 – 7/11/2018 who had serum creatinine measured were included. Patients with end-stage renal disease, length of stay <48 hours and AKI at admission were excluded. A validated algorithm was used to determine baseline renal function. AKI was defined according to KDIGO guidelines. Machine learning algorithms were implemented to predict development of HA-AKI beyond the initial 24-hours of admission. 50 input variables to machine learning algorithms (random forest, XGBoost, regression) included demographics, initial laboratory values taken within the first 24-hours of admission, active medications at time of admission, and prevalent comorbidities. Multiple imputation by chained equations (MICE) was used for missing variables. Univariate Feature Selection was utilized where variables were ranked by evaluating contribution to classification outcome. Randomized search was performed to obtain the optimal hyperparameter set for each algorithm. Models were evaluated using a mean area under the receiver operating characteristic curve (AUC) over 5-fold cross-validation.

Results: Among 209,300 inpatient admissions, 26,410 (12.6%) developed HA-AKI. Using AKI prediction, the AUC of the full model was 0.88 for both random forest and XGBoost, and 0.86 for logistic regression. To balance the tradeoff between model simplicity and performance, 23 variables from univariate feature selection evaluated using random forest were selected in predicting HA-AKI (AUC = 0.67). The probability cutoff-off point of AKI prediction outcome was determined using Youden’s Index based on the balance between false positives and false negatives. A probability cutoff of > 0.23 provided sensitivity and specificity of 78% and 81%, respectively.

Conclusions: Our machine learning algorithm applied at 24 hours of admission identified patients at risk for HA-AKI with excellent accuracy. Significant variables included in this algorithm should be monitored in real-time to allow early identification and preventive interventions in patients at risk for HA-AKI.

Funding: Clinical Revenue Support

A Meta-Analysis of Clinical Predictors for Renal Recovery and Mortality in AKI Requiring Continuous Renal Replacement Therapy

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Background: Acute kidney injury (AKI) is a common complication in critically ill patients and can result in a broad spectrum of severity. It is well-established that severe AKI requiring continuous renal replacement therapy (CRRT) carries a significant risk for increased mortality compared to non-dialysis AKI. However, there are no consensus guidelines describing the discontinuation criteria from CRRT. Thus, we performed this meta-analysis to determine the clinical predictors for CRRT discontinuation and overall mortality in patients with AKI.

Methods: Ovid MEDLINE, EMBASE, and Cochrane Library were searched without language restrictions up to January 2020. Our inclusion criteria included patients ≥ 18 years of age, AKI stage 2+. The area under the curve (AUC) was 0.76 (95% bootstrap confidence interval 0.66-0.84). A probability cutoff of > 0.7 predicted renal recovery with 88% sensitivity and 80% specificity. To balance the tradeoff between model simplicity and performance, 23 variables from univariate feature selection evaluated using random forest were selected in predicting HA-AKI (AUC = 0.67). The probability cutoff-off point of AKI prediction outcome was determined using Youden’s Index based on the balance between false positives and false negatives. A probability cutoff of > 0.23 provided sensitivity and specificity of 78% and 81%, respectively.

Conclusions: Our machine learning algorithm applied at 24 hours of admission identified patients at risk for HA-AKI with excellent accuracy. Significant variables included in this algorithm should be monitored in real-time to allow early identification and preventive interventions in patients at risk for HA-AKI.

Funding: Clinical Revenue Support

Regional Variation in Recovery of Kidney Function in Patients Requiring Maintenance Hemodialysis with Acute Tubular Necrosis

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Background: Geographic variations in the likelihood of recovery of kidney function in ESKD attributed to acute tubular necrosis (ATN) has not been well established.

Methods: Using data from United States Renal Data System, we performed a retrospective cohort study of incident maintenance hemodialysis (HD) patients between 1/1/1996-12/31/2015 with ESKD attributed to ATN followed up to 1 year. Recovery of kidney function was defined as discontinuation of HD for at least 90 days and alive without the need for kidney transplantation during this period. We used Fine-Gray models to determine unadjusted and adjusted hazard of recovery while accounting for the competing risk of death.

Results: In 48,771 patients included for analysis, 30% recovered kidney function within 1 year. Most patients received HD within a 10-mile radius of their home. Recovery rates at 1 year were lowest in the northeast and highest in the south; lower in metropolitan compared to micropolitan/rural areas. Recovery of kidney function was less likely to occur with distance between patient and dialysis facilities in adjusted analysis.

Conclusions: Patients living in rural/micropolitan locations and receiving dialysis close to home had higher recovery rates. Studies examining regional differences in practice patterns are warranted.

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AKI Epidemiology, Risk Factors, and Prevention: Clinical Research

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Adequacy of Kidney Follow-Up Among AKI Survivors After Hospital Discharge


Background: Acute kidney injury (AKI) affects 20% of hospitalized patients and results in long-term adverse outcomes. To limit its complications, post-discharge follow-up is advised. The objective of the study was to evaluate the frequency of appropriate follow-up after discharge among AKI survivors.

Methods: This was a population-based cohort study of adult Olmsted County residents hospitalized at their local hospital (Mayo Clinic in Rochester, MN) with an episode of stage II or III AKI between 2006 and 2014. Those dismissed from the hospital on dialysis or who died within 30 days after discharge were excluded. The cumulative incidence of adequate kidney follow-up defined by a serum creatinine (SCr) level and/or an in-person healthcare visit within 30 days, 90-days, or 1-year after discharge was described.

Results: There were 563 survivors of AKI studied (Stage II: N=360 (64%); Stage III: N=203 (36%)). The 30-day cumulative incidence of follow-up with SCr was 78% (95% confidence interval (CI): 74%, 81%), by provider visit was 80% (95% CI: 77%, 83%), by both SCr assessment and provider visit was 70% (95% CI: 65%, 73%). Within 90-days and 1-year, the cumulative incidences of both SCr assessment and provider visit rose to 81% and 91%, respectively. Within 30-days after discharge, only 13% (95% CI: 10%, 16%) of these stage II or III AKI survivors saw a nephrologist. The statistically significant predictors of receiving both a SCr assessment and provider visit within 30-days included higher body mass index, worse baseline and discharge kidney function, higher comorbidity burden, greater maximum AKI severity, and longer duration of AKI during the hospitalization. Age, sex, race/ethnicity, education status, and socioeconomic status did not predict kidney follow-up.

Conclusions: These data demonstrated that 30% of patients with moderate to severe AKI received insufficient kidney follow-up in the 30-day post-discharge interval. Medical risk factors rather than social/demographic characteristics were the primary determinants of kidney follow-up.

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Predicting Intra-ICU Mortality Using Machine Learning Algorithms in Patients Who Require Acute Renal Replacement Therapy in a Critical Care Unit

Hsin-Hsiung Hsin, Kianoush Kianoush, Hsin-Hsiung Adequacy of Kidney Follow-Up Among AKI Survivors After Hospital Discharge

Background: Acute kidney injury (AKI) occurs in over 20% of hospitalized patients and is associated with both long-term morbidity and mortality. The purpose of this study is to identify risk factors for readmission for renal cause and mortality following a hospitalization with AKI in US Veterans.

Methods: AKI was defined as a creatinine increase of ≥0.3 mg/dL or at or after admission in ≥1 VA hospital between 2013 and 2018. The primary outcomes were death and hospital readmission for a renal indication. Proportional hazards frailty model was applied. Variables evaluated included demographics, comorbidities, and laboratory data. The final model was chosen based on clinical relevance and parsimony.

Results: From a cohort of 624,822 Veterans with AKI, 218,839 (35%) met inclusion criteria. Reasons for exclusion were <1 year of prior patient data (35%), missing serum creatinine values (14%), palliative status or metastatic cancer (13%), or death during the hospitalization (4%). AKI was present on admission in 71% of patients and developed after admission in 29%. Overall, 48,202 (22%) died within one year. Between 2013 and 2018, 101,170 (46%) died and 21,116 (9%) experienced a renal readmission. The patient characteristics associated with increased hazard of death included age (HR=1.53 per 10 years, CI 1.52-1.54, p<0.001), male sex (HR=1.27, CI 1.22-1.32, p<0.001), heart failure (HR=1.55, CI 1.53-1.57, p<0.001), prior myocardial infarction (HR=1.14, CI 1.11-1.17, p<0.001), lower eGFR, lower systolic blood pressure, lower serum albumin, and higher serum creatinine. The intra-ICU mortality AUC of machine learning algorithms was calculated using the area under the receiver operating characteristic curve (AUC). The intra-ICU mortality AUC of the Sequential Organ Failure Assessment (SOFA) score using data collected one day prior to RRT initiation was 0.683 (95% CI 0.636-0.729) in MICU and 0.685 (95% CI 0.630-0.729) in IMICU. The intra-ICU mortality AUC of machine learning models using logistic regression (LR), XGBoost, random forest (RF) and multilayer perceptron (MLP) trained in eICU were 0.858 (95% CI 0.850-0.867), 0.858 (95% CI 0.850-0.866), 0.859 (95% CI 0.848-0.870), 0.864 (95% CI 0.851-0.876) and validated in MIMIC were 0.799 (95% CI 0.770-0.824), 0.809 (95% CI 0.780-0.833), 0.814 (95% CI 0.791-0.837), 0.800 (95% CI 0.776-0.825), respectively. When training the models using MIMIC dataset, the intra-ICU mortality AUC of LR, XGBoost, RF and MLP were 0.818 95% CI (0.786-0.852), 0.821 (95% CI 0.787-0.856) 0.822 (95% CI 0.791-0.854), 0.827 (95% CI 0.795-0.858), respectively. Validating these models using eICU dataset, the AUC of LR, XGBoost, RF and MLP were 0.846 95% CI 0.828-0.864, 0.847 95% CI 0.829-0.865, 0.853 (95% CI 0.835-0.870), 0.846 (95% CI 0.828-0.865), respectively.

Conclusions: In this study, we designed machine learning models to make intra-ICU mortality prediction for patients who required RRT. Our models correlated better that those used in the prior mortality prediction of patients requiring RRT in ICU. All of the models almost had excellent performance in both databases.
PO0011

Region-wide Implementation of Best Practice in AKI

Anirudh Rao, Kottarathil A. Abraham. On behalf of the Cheshire & Merseyside Acute Kidney Injury Network (CHAMKIN) Liverpool University Hospitals NHS Foundation Trust, Liverpool, United Kingdom.

Background: The Cheshire & Merseyside Acute Kidney Injury Network, United Kingdom, rolled out best practice guidelines of 13 interventions for Acute Kidney Injury (AKI) in October 2014. The aim was to assess the impact of the guidelines.

Methods: Setting & Population: Hospitals in Cheshire & Merseyside. Predictor: Time period before & after introduction, allowing six-month bedding in period. Outcome: Percentage AKI: Number of AKI per month, divided by total number of admissions/month expressed as %. Percentage AKI deaths: Number of AKI related deaths per month divided by total deaths/month expressed as %. Data analysis: Descriptive & Piecewise Linear Regression.

Results: The region saw a notable increase in the number of admissions/month (31.173 vs 38.443) and AKI episodes (4,871 vs 44,493) in the 8 hospitals in pre and post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post implementation data (1). The outcomes in the 2 periods are detailed in the Table. The introduction of E-alert saw an increase in AKI detection across the hospitals. The figure shows longitudinal piecewise regression curves. The most significant reduction was noted in hospital A.

Conclusions: The rollout of interventions caused an increased and sustained recognition of AKI, across the hospitals. The % AKI deaths stayed the same except in hospital A. We theorise that the onsite nephrology team in Hospital A aided implementation of the guidelines and training of wider healthcare staff which made the impact. This study highlights the hurdles faced in implementing AKI improvement strategies across various healthcare settings.

PO0013

Incidence and Impact of AKI on Patients with Implantable Left Ventricular Assist Devices: A Meta-Analysis

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Background: This systematic review and meta-analysis was performed to evaluate the acute kidney injury (AKI) incidence and its associated risk of mortality in patients with implantable left ventricular assist devices (LVAD).

Methods: A systematic literature search in MEDLINE, EMBASE, and Cochrane Databases was conducted through January 2020 to identify studies that provided data on the AKI incidence, and AKI-associated mortality risk in adult patients with implantable LVADs. Pooled effect estimates were examined using random-effects, generic inverse variance method of DerSimonian-Laird.

Results: 56 cohort studies with 63,663 LVAD patients were enrolled in this meta-analysis of AKI incidence. The pooled incidence of reported AKI was 24.9% (95%CI: 20.1%-30.4%), but rose to 36.9% (95%CI: 31.1%-43.1%) when applying the standard definition of AKI per RIFLE, AKIN, and KDIGO criteria. The pooled incidence of severe AKI requiring renal replacement therapy (RRT) was 12.6% (95%CI: 10.5%-15.0%). AKI incidence did not differ significantly between types of LVAD (p = 0.35) or indication for LVAD use (p = 0.62). While meta-regression analysis did not demonstrate a significant association between study size and overall AKI incidence (P=0.55), the study year was negatively correlated with incidence of severe AKI requiring RRT (slope = -0.068, p <0.001). The pooled odds ratios (ORs) of mortality at 30 days and 1 year in AKI patients were 3.66 (95% CI, 2.00-6.70) and 2.22 (95% CI, 1.62-3.04), respectively. The pooled ORs of mortality at 30 day and 1 year in severe AKI patients requiring RRT were 7.52 (95% CI, 4.58-12.33) and 5.41 (95% CI, 3.63-8.06), respectively.

Conclusions: 37% of LVAD patients developed AKI based on standard definitions and 13% developed severe AKI requiring RRT. There has been potential improvement in the incidence of severe AKI requiring RRT for LVAD patients. AKI in LVAD patients was associated with increased 30-day and 1-year mortality.

PO0014

AKI in the Emergency Department: A Prospective Case-Control Study

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Background: Acute kidney injury (AKI) is an abrupt decline in kidney function that occurs in hours or days. AKI has been thoroughly studied in the hospital setting, however data on community-acquired AKI are scarce. The aim of this study was to investigate the incidence, causes and prognosis of patients presenting with AKI to the emergency department (ED).

Methods: This was a prospective case-control study in which serum creatinine (SCr) measurements of all patients presenting to the ED of Landspitali–The National University Hospital in Reykjavik were examined for the presence of AKI. The study started on January 1, 2020, and we present data until March 3, 2020. All patients who met the criteria for AKI were invited to participate. Randomly selected control cases (1:2) were paired according to age, sex and time of ED admission. Participants signed informed consent and were questioned about their medical history, habits and use of medications, including over-the-counter (OTC) medications and supplements, in the week prior to admission. Medical records were also reviewed with regard to prior diseases and medical prescriptions.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
PO0015
Prehospital Systolic Blood Pressure and Lactate Are Early Predictors of AKI After Trauma: A Prospective Validation Study
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Background: We have already reported that prehospital systolic blood pressure and lactate can be predictive factors for acute kidney injury (AKI) after trauma. This study is a prospective validation study to determine whether these risk factors are helpful.

Methods: We evaluated all trauma patients who were admitted from January 2019 to December 2019. Patients who were <10 years of age, patients with burns, and patients with chronic kidney disease were excluded from the present study. AKI was defined according to the risk, injury, failure, loss of the kidney function, and end-stage kidney disease (RIFLE) classification from serum creatinine alone.

Results: Four hundred and three patients were included in the analysis. The prevalence of AKI in the overall population was 14.7% including 11.7% of patients with stage R, 2.0% of patients with stage I and 1.0% with stage F. The incidence of stage I and F AKI in the high-risk group (5 of 38 patients, with the positive predictive value of 13.2%) was significantly higher (P=0.001) than that in the low-risk group (7 of 358 patients, with the negative predictive value of 98.1%).

Conclusions: The prehospital systolic blood pressure and early hospital arterial lactate showed good performance in the early prediction of AKI after trauma. These parameters are associated with the early onset of AKI after trauma and may be an early predictor of the effects of treatment to prevent AKI.

PO0016
Association of Race and Risk of Future Scleroderma Renal Crisis at Systemic Sclerosis Diagnosis
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Background: Scleroderma renal crisis (SRC) is a rare and severe manifestation of systemic sclerosis (SSc). Although it is well documented that Blacks with SSc have worse morbidity and mortality than non-Blacks, racial predilection for SRC is underreported. We examine the association of race and future development of SRC in an SSc cohort.

Methods: Using the electronic medical record of the U.S. Military Health System Databank for Cardiovascular Disease (DDCD) who underwent PCI at Duke between January 1, 2003 and December 31, 2013. AKI was defined as a 1.5-fold increase in serum creatinine from outpatient reference value before PCI to the peak value within 7 days post-PCI or a 0.3 mg/dl increase from the reference value within 48 hours. We used logistic regression adjusted for demographics, comorbidities, predispensing medications (NSAIDS, RAAS inhibitors, diuretics), PCI indication (presenting with vs without acute coronary syndrome), peri-procedural prophylaxis with IV fluids and n-acetylcysteine, urgency of PCI and BP at time of PCI.

Results: Of 9422 patients (median age 63y [IQR 54 to 72]; 33% female; 75% white, 20% black, 5% other race), 9% developed AKI: 14% of blacks, 8% of whites, 10% in other race groups. After adjustment, black race was associated with greater likelihood of AKI: odds ratio (OR) 1.80 in black (vs white) patients (95% confidence interval (CI) 1.49 to 2.18. Compared to white, other race was not associated with AKI: OR 1.31, 95% CI 0.91 to 1.87. Low baseline eGFR was associated with graded, higher likelihood of AKI for trend <0.001. There was no interaction between race and baseline eGFR.

Conclusions: Black patients had nearly twice the likelihood for AKI following PCI than whites despite adjustment for baseline kidney function, prophylaxis and procedural characteristics. Future investigations should identify other factors that predispose black individuals to disparate AKI risk following PCI.

Funding: Private Foundation Support

PO0017
Racial Differences in AKI Following Percutaneous Coronary Intervention
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Background: Percutaneous coronary intervention (PCI) is a risk factor for AKI, but few studies have quantified racial differences in AKI incidence following PCI. Methods: We examined the association of self-reported race – black, white, and other – and baseline eGFR with AKI incidence among patients captured in the Duke Databank for Cardiovascular Disease (DDCD) who underwent PCI at Duke between January 1, 2003 and December 31, 2013. AKI was defined as a 1.5-fold increase in serum creatinine from outpatient reference value before PCI to the peak value within 7 days post-PCI or a 0.3 mg/dl increase from the reference value within 48 hours. We used logistic regression adjusted for demographics, comorbidities, predispensing medications (NSAIDS, RAAS inhibitors, diuretics), PCI indication (presenting with vs without acute coronary syndrome), peri-procedural prophylaxis with IV fluids and n-acetylcysteine, urgency of PCI and BP at time of PCI.

Results: Of 9422 patients (median age 63y [IQR 54 to 72]; 33% female; 75% white, 20% black, 5% other race), 9% developed AKI: 14% of blacks, 8% of whites, 10% in other race groups. After adjustment, black race was associated with greater likelihood of AKI: odds ratio (OR) 1.80 in black (vs white) patients (95% confidence interval (CI) 1.49 to 2.18. Compared to white, other race was not associated with AKI: OR 1.31, 95% CI 0.91 to 1.87. Low baseline eGFR was associated with graded, higher likelihood of AKI for trend <0.001. There was no interaction between race and baseline eGFR.

Conclusions: Black patients had nearly twice the likelihood for AKI following PCI than whites despite adjustment for baseline kidney function, prophylaxis and procedural characteristics. Future investigations should identify other factors that predispose black individuals to disparate AKI risk following PCI.

Funding: Private Foundation Support

PO0018
The Spectrum of Biopsy-Proven Kidney Diseases in 2027 Patients with AKI
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Background: Acute kidney injury (AKI) is a group of highly heterogeneous, complicated clinical syndrome. The kidney biopsy plays an irreplaceable role in the evaluation of patients with unexplained AKI and may offer fresh insights into disease heterogeneity. Hence, in this study we aim to analyze the pathological disease spectrum, etiology, and renal recovery of biopsy-proven AKI patients.

Methods: We retrospectively analyzed the clinical and pathological data of AKI patients who went to a kidney biopsy during the hospitalization at our center from January 2013 to December 2018. We classified included patients into pure AKI and ACKD two groups.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

Higher Ambient Level of Nitrogen Dioxide Is Associated with an Increased Risk of AKI
Xin Xu, Yanli Li, Lincou Zhang, Fan Fan Hou. Xin Xu Nantang Hospital, Southern Medical University, Guangzhou, China.

Background: Previous studies have suggested that long-term exposure to air pollution increased the risk of chronic kidney disease and its progression. However, the effect of air pollution on the risk of acute kidney injury (AKI) has not been studied.

Methods: We selected from the Epidemiology of AKI in Chinese Hospitalized Patients (EACH2 study) AKI cases of which the onset date could be unambiguously determined. We obtained city-specific daily averages of the ambient level of PM2.5, CO, NO2, SO2 and O3 from the Ministry of Environmental Protection of China. We used the time-stratified case crossover approach to examine the association between the ambient level of air pollutants and the risk of AKI in the selected cases.

Results: A total of 11,923 AKI cases that met the inclusion and exclusion criteria were selected, of which, 3175 (28.1%) were severe AKI (stage 2 or 3). In unvariable analysis, the ambient levels of NO2 and SO2 were significantly associated with the risk of AKI. In the multivariable analysis that incorporated all six pollutants in the same model, NO2 was the sole pollutant whose level remained to be associated with the risk of AKI (p<0.001). The relationship between level of NO2 and the risk of AKI appeared to be linear, with an estimated odds ratio of 1.072 (95% CI: 1.033, 1.113) for each increment of one standard deviation in the exposure. The association was consistent across the subgroups stratified by age, gender, baseline eGFR, AKI severity, need for intensive care, and season.

Conclusions: Higher ambient level of NO2 was associated with an increased risk of AKI in hospitalized adults in China.
PO0023
Decreased Urinary Uromodulin Is Potentially Associated with AKI: A Systemic Review and Meta-Analysis
You Ruilian, Hua Zheng, Limeng Chen. Peking Union Medical College Hospital, Beijing, China.
Background: Conventional diagnostic criteria based on the serum creatinine isn’t sensitive enough to detect Acute Kidney Injury (AKI) timely. Urinary uromodulin (uUMOD) is one of the novel biomarkers being studied for the value of predicting AKI. However, currently available publications showed inconsistent outcomes. This meta-analysis aimed to evaluate the potential association between uUMOD and AKI.
Methods: We searched research articles in Pubmed-Medline, Web of Science, Cochrane library, Embase, China National Knowledge Infrastructure, and Weipu Database(up to 2020.3). Random-effects models were used to estimate the standardised mean difference (SMD) between AKI and Non-AKI. The sensitivity analysis was conducted using the leave-one-out method. Random-effects meta-regression was performed to evaluate the impact of potential confounders on age and surgery.
Results: The meta-analysis was comprising 2678 subjects of 8 studies, which showed that the uUMOD in the patients with AKI was significantly lower than the Non-AKI patients (SMD = -0.77, P = 0.001, 95% confidence interval -1.07, -0.47). Subgroup analysis indicated a significant difference in different ages and surgery group (Figure1-2). Sensitivity analysis displayed the synthetic outcome always in the 95% CI of the pool SMD suggesting a robust result.
Conclusions: The study suggests a potential negative association between uUMOD and AKI. Further studies are needed to investigate the promising diagnostic values and mechanisms in protecting AKI.

PO0025
Relationship of Loop Diuretic with Hospital-Acquired AKI: A Multicenter, Propensity Score-Matching Analysis
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Background: Loop diuretics have been widely used to prevent and treat acute kidney injury (AKI). However, there is no clear consensus on the role of loop diuretics in AKI. Methods: The Epidemiology of AKI in Chinese Hospitalized patients is a multicenter retrospective cohort included 3,044,024 hospitalized patients from 25 tertiary hospitals across China during 2013-2015. Patient data were obtained from the electronic hospitalization information system. We selected 575,895 adult patients who had at least two serum creatinine tests within any 7-day window during their first 30 days of hospitalization and excluded those with end-stage renal disease, community-acquired AKI and without prescription data. AKI was defined using the SCr data by the Kidney Disease Improving Global Outcomes criteria. Exposure to Loop diuretics as any filled prescription within 14 days prior to the detection date of AKI in patients with HA-AKI and within 14 days prior to the last SCr testing date in those without AKI. Propensity scores (PS) were calculated using a logistic regression model with age, gender, hospital, division, baseline SCr, SCr testing times, comorbidities, operation procedures, need for intensive care and exposure to other nephrotoxic drugs. Moreover, the inverse probability of the treatment weighting (IPTW) method and standardized mortality ratio weighting method was also used.
Results: Of 575,895 adult analysed, 20,599 (35.8%) used diuretics, 17,077 (29.7%) used loop diuretics, and 6277 (10.9%) had HA-AKI events during hospitalization. 8,274 pairs matched after nearest-neighbor matching without replacement and within caliper width (0.2*SD of the logit of PS). By IPTW, use of loop diuretics was associated with a significantly increased risk of HA-AKI compared with non-users (OR, 1.39; 95% CI, 1.28-1.52). The associations were consistent across multiple regression models. Conclusions: Loop diuretics were widely used and associated with an increased risk of HA-AKI in hospitalized adult in China.
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AKI and Bleeding Risks Associated with Vitamin K Antagonists and Antiplatelet Agents in Patients with CKD

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Background: Anticoagulation in patients with chronic kidney disease (CKD) is challenging because of altered pharmacodynamics/pharmacokinetics. Patients prescribed vitamin K antagonists (VKA) are at high risk of bleeding, and possibly also acute kidney injury (AKI). We assessed bleeding and AKI risks associated with VKA and/or antiplatelet agents (AP) prescription in patients with moderate or advanced CKD.

Methods: We studied a cohort of 3022 nephrology outpatients with CKD stages 2-5 in 25 academic medical centers. Drug prescriptions and their duration were collected prospectively. We used cause-specific Cox proportional hazard models to estimate hazard ratios (HR) of bleeding (identified through hospitalizations) and AKI (as defined according to KDIGO 2012) associated with VKA only, AP only, or VKA + AP prescriptions treated as a time-dependent variable and adjusted for baseline comorbidities, laboratory data, and medications.

Results: At baseline, 65% of the patients were men, median age was 69 (interquartile range (IQR), 60-76), median eGFR was 32 mL/min/1.73m² (IQR, 23-41), 328 (10%) patients were prescribed VKA only, and 1196 (40%) AP only, and 100 (3%) both VKA and AP. Over a median follow-up of 3.0 years (IQR, 2.6-3.1), 71 (2%) patients were newly prescribed VKA and 187 (6%) AP; 152 patients experienced a bleeding event requiring hospital visit/stay (crude incidence rate (IR): 1.9% person-years [95%CI, 1.6-2.2]) and 414 patients developed AKI (crude IR: 1.3% person-years [95%CI, 1.1-1.5]). Adjusted HRs for bleeding associated with prescriptions of AP only, VKA only and AP+VKA were 0.77 [95% CI, 0.48-1.22], 2.29 [95%CI, 1.41-3.73] and 3.77 [95% CI, 2.06-6.83], respectively. Prescription of VKA was associated with increased AKI risk, adjusted HR, 1.79 [95% CI, 1.39-2.32] but not that of AP, 1.19 [95% CI, 0.94-1.49].

Conclusions: This study confirms the high risk of AKI associated with VKA prescription in CKD patients. It also highlights the potential aggravating effect of combining VKA and AP on the risk of bleeding in this population.

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Use of Ibuprofen and the risk of Hospital-Acquired AKI in Children

Liong Su, Yangin Li, Xin Xu. Nanfang Hospital, Southern Medical University, Guangzhou, China.

Background: Ibuprofen is widely used in children worldwide, especially in children with cancer, fever or trauma. However, large and high-quality studies on the association between ibuprofen and acute kidney injury (AKI) in children have been lacking.

Methods: The Epidemiology of AKI in Chinese Hospitalized patients (EACH2 study) is a multicenter, retrospective study of 3,044,023 patients admitted from 1st July 2015 to 30th December 2017 from the largest tertiary hospital and a major public primary care institution in Singapore. Laboratory, hospitalization and medication data from 6 months before until 30 days after enrollment were collected. Individuals prescribed ibuprofen within 30 days of hospitalization were identified as the “ibuprofen group” and the controls were matched to the “ibuprofen group” based on age, gender, and hospital and division. Laboratory, other nephrotoxic drugs use and stratification by hospital and division. We compared the effect sizes of ibuprofen among subgroups stratified by age, gender, chronic kidney disease, need for intensive care and exposure to other nephrotoxic drugs.

Results: Among 50,420 children who met the inclusion and exclusion criteria, 5,526 (11.0%) were ibuprofen users, and 3,476 (6.9%) had AKI during hospitalization. Ibuprofen use was associated with significantly increased risk of AKI (hazard ratios, 1.52 [95% CI, 1.11-2.04]) after adjusting for age, sex, and baseline eGFR. The greatest nephrotoxic potential of ibuprofen was observed in children who had chronic kidney disease, required intensive care, or were of elder age.

Conclusions: Ibuprofen was widely used and associated with an increased risk of HA-AKI in hospitalized children in China.

Nonsteroidal Anti-Inflammatory Drugs and Risk of Acute Adverse Renal Outcomes in Hospitalized Children

Cynthia C. Lim,1 Hanis B. Abdul Kadir,1 Jason Choo Chun Jun,1 Teck W. Ang,2 Yong Mong Bee,2 Nguei chuan Tan,2 Singapore General Hospital, Singapore, SG, Singapore, Singapore; (3) Singapore Health Polyclinics, Singapore, Singapore.

Background: Individuals with diabetes mellitus (DM) may be susceptible to non-steroidal anti-inflammatory drug (NSAID)–induced acute kidney injury (AKI). However, information on their risk of NSAID-related adverse renal events is sparse. We aimed to estimate the risk and factors for acute kidney injury and/or hyperkalemia after NSAID prescription to individuals with DM.

Methods: Retrospective cohort study of individuals a21 years with DM who received prescriptions during 1st July 2015 and 30th December 2017 in the largest tertiary hospital and a major public primary care institution in Singapore. Laboratory, hospitalization and medication data from 6 months before until 30 days after first prescription were collected from electronic medical records. Individuals prescribed ibuprofen >14 days before index date were excluded from the “NSAID group”. We included those with systemic NSAID in the preceding 6 months, missing laboratory values, or had baseline estimated glomerular filtration rate (eGFR) <15 ml/min/1.73 m². The outcome was the incidence of AKI (serum creatinine increased >50%) and/or hyperkalemia (serum potassium >5.5 mmol/L) within 30 days after prescription.

Results: We studied 3896 individuals (mean age 65.4 ± 13.3 years) with incident prescriptions: 138 in the NSAID group and 3758 in the non-NSAID group. 30-day AKI and/or hyperkalemia occurred in 525 individuals (13.5%). After adjusting for age, gender, diabetes, renal baseline eGFR, serum potassium, NSAID, RAAS blocker and diuretic, baseline eGFR (adjusted OR 1.41, 95% CI 1.02-1.93, p=0.03) and RAAS blocker (adjusted OR 1.42, 95% CI 1.15-1.75, p<0.001) were independent predictors for the outcome. NSAID prescription for ≥4 days was associated with a higher risk of AKI (adjusted OR 1.62, 95% CI 1.09-2.65, p=0.05). However, the risk of AKI and/or hyperkalemia was markedly increased if NSAID was prescribed concurrently with RAAS blocker (adjusted OR 4.17, 95% CI 1.74-9.98, p<0.001) or diuretic (adjusted OR 3.31, 95% CI 1.90-9.08, p=0.04). More importantly, ≥4-day NSAID prescription was associated with higher 30-day risk of AKI and/or hyperkalemia, especially with concurrent RAAS blocker or diuretic.

Funding: Private Foundation Support

A Retrospective Cohort Study of Chemotherapy-Related AKI

Xin Kang, Li Yang. Renal Division, Peking University First Hospital, Peking University, Beijing, China.

Background: Chemotherapy-related acute kidney injury (CR-AKI) is increasing with the growing number of cancer patients and the development of chemotherapeutic agent. The systemic inflammatory status in AKI is still underestimation.

Methods: This is a multicenter retrospective cohort study of cancer patients with CR-AKI screened from a cohort of hospital-acquired adult AKI patients based on a nationwide AKI survey in China. The enrolled CR-AKI patients were divided into three groups according to peak AKI stages (1 to 3) during hospitalization. The primary outcome was all-cause death in hospital, and the secondary outcome was AKI recovery.

Results: Of 3,468 adult inpatients with hospital-acquired AKI identified basing on the China nationwide AKI survey, 258 patients with CR-AKI were enrolled in our study, of which 20.1% (52/258) were ≥70 years old. A total of 413 person-time chemotherapeutic agents were related to AKI, of which platinum compounds (24.5%, 101/413) were the most common ones, followed by fluoropyrimidines (13.1%, 54/413), and anthracyclines (9.2%, 38/413). Among the 258 CR-AKI patients, 61 (23.0%) reached AKI stage 3, and 144 (55.7%) received RRT in the hospital mortality (17.9, 48/264). Of 907 surviving patients with a reliable serum creatinine value at discharge, 48.3% (100/207) failed to renal recovery. AKI stage 3 remained the independent risk factor for in-hospital death (OR 2.930, 95% CI 1.156-7.427) after adjustment for age, gender, comorbidities, and medications. It is surprising to note that, although patients of AKI stage 1 had lower levels of SCr both at peak and at discharge compared to patients of AKI stage 2 or 3, there was a higher proportion of patients of AKI stage 1 not achieving renal function significantly improved at discharge (failure to recover) compared to those of AKI stage 2 or 3 (57.1% vs. 41.4% vs. 36.4%, P = 0.032). More importantly, a lot more AKI episodes were not recognized or diagnosed by physicians in charge in patients of AKI stage 1 compared to the other two groups (82.8% vs. 60.0% vs. 36.1%, P < 0.001).

Conclusions: CR-AKI accounted for a considerable proportion of hospital-acquired AKI. Severe CR-AKI increases in-hospital mortality. Mild CR-AKI that overlooked by physicians sustained kidney injury was common in these patients. Recognizing CR-AKI at an early stage and making personalized treatment should be emphasized when offering chemotherapy to patients.
PO0030

Characterizing AKI from Vancomycin-Associated Nephrotoxicity in Adult Non-ICU Patients at an Inner City Hospital: Incidence and Predictors

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Background: Vancomycin is a widely used antibiotic in the in-patient setting. Concerns of vancomycin-associated nephrotoxicity (VAN) were raised due to impurities associated with the first released parenteral formulations in the 1950s. Nephrotoxicity is reported to have markedly declined with a wide variability in the incidence. There is a dearth of information on the current incidence of VAN as a cause of acute kidney injury (AKI) in adult non-ICU populations. The purpose of this study was to estimate the incidence of VAN AKI and identify risk factors of VAN for this population.

Methods: A cohort of patients admitted between January 2015 and December 2017 with the diagnosis of AKI and who received at least 3 days of parenteral vancomycin were identified through a retrospective chart review. Exclusions were ESRD or CKD history. Our primary outcome was the occurrence of VAN AKI, defined as an increase in serum creatinine by 0.3 mg/dl or 50% above baseline after vancomycin exposure. The incidence of VAN AKI was estimated and we estimated risk factors associated with VAN in a logistic regression model.

Results: 587 adult patients received at least 72 hours of parenteral vancomycin for the treatment of sepsis during the period. Demographics were: male 350 (59.6%), female 237 (40.4%) and mean age of 62.3 years. Distribution by ethnicity: non-Hispanic Blacks 71.2%, Hispanics 12.6%, non-Hispanic white 3.4% and 12.4% were other ethnicities. The incidence of VAN AKI was 15.24%. These patients had a longer hospital stay (26.8 versus 21.3 days for no VAN AKI), higher mean vancomycin trough levels, longer duration of exposure to vancomycin and a higher Charlston Comorbidity Index (3.5 versus 2.6). Independent predictors for VAN were: mean vancomycin trough level, hypertension, COPD, congestive heart failure, liver disease, severe obesity and dementia (all p values <0.05). Previous ICU admission and hypotension status did not predict VAN AKI.

Conclusions: We report an incidence of VAN AKI of 15.24% in non-ICU adult patients with no history of ESRD or CKD. Risk factors associated with the development of VAN include mean vancomycin trough level, hypertension, congestive heart failure, COPD, liver disease, severe obesity and dementia.

PO0031

Baseline Urinary Protein Biomarkers as Predictors of eGFR Decline in Cancer Patients Receiving Cisplatin

Melanie S. Joy,1 Blessey George,1 Yichun Hu,2 Susan L. Hogan,3 Xia Wen,3 Lauren Afekousov.1 1University of Colorado, Skaggs School of Pharmacy, Cancer Center, and Division of Renal Diseases and Hypertension, Denver; CO; 2University of North Carolina, Kidney Center, Chapel Hill, NC; 3Rutgers University, Ernest Mario School of Pharmacy, Piscataway, NJ.

Background: Previous data from our group reported significant changes in urinary biomarkers of sub-clinical kidney injury over 10 days after receiving i.v. cisplatin. The current study evaluated the performance of single and a combination of two urinary biomarkers at the time of cisplatin initiation in predicting a reduction in eGFR.

Methods: Patients (n=57) with solid tumors receiving i.v. cisplatin (25 mg/m²) were enrolled in a study to characterize concentrations of 9 urinary proteins (Table). For the outcome of eGFR decline, the eGFR (MDRD equation) after the first dose and one measure at 5-7 days of stay. Exclusion criteria consisted of ESKD, kidney transplant or baseline eGFR <15 ml/min/1.73m². AKI was defined as an increase of serum creatinine level ≥0.3 mg/dl or 1.5 times in contrast to baseline, or the development of renal tubular abnormalities within 48 hours. We evaluated if the microscopic examination of the urine sediment (score ≥2) could be use as a non-invasive detector of renal damage.

Results: Mean (SD) age was 65.1 (17.2), 38.4% were women and 100% Hispanic. The incidence of AKI at 3-7 days of hospital or ICU stay was 34.9%. From the 30 patients that developed AKI, 20 were on stage 1 (66.6%), 8 were on stage 2 (26.6%) and 2 were on stage 3 (6.6%). Performance metrics of the urinary score used are reported in Table. A urine sediment score ≥2 exhibited a fair, but not good, AUC of 0.681 (95% confidence interval [CI]: 0.554–0.808) in ROC analysis.

Conclusions: Urinary protein biomarkers are emerging as tools to identify overt and sub-clinical kidney injury. However, single and double combinations of urinary proteins are insufficient to reliably predict reductions in eGFR as an ideal model outcome. Future studies must determine an improved outcome benchmark for evaluating urinary protein biomarkers.

Funding: NIDDK Support

Table: Performance of the urinary sediment score for the prediction of AKI in hospitalized patients

PO0032

Urinary Sediment Score Is a Useful Predictor of AKI in Hospitalized Patients

Pablo J. Heredia-Murillo,1 Rolando Claire-Del Granado,2,3 Universidad Mayor de San Simon Facultad de Medicina, Cochabamba, Bolivia, Plurinational State of; 2Clínica Los Olivos, Cochabamba, Bolivia, Plurinational State of.

Background: Risk-stratification tools of incident AKI in hospitalized patients are needed. Early documentation of impaired kidney function through a simple examination like the urinary sediment may provide risk reduction in such patients. The present study aims to explore an association between urinary sediment score described by Perazella et al. and hospital-acquired AKI.

Methods: This study included 86 patients who underwent urinalysis, including scoring the urinary sediment during the first 24 hour of admission. Inclusion criteria consisted of age ≥18, hospital stay ≥3 days, at least 2 serum creatinine (SCr) measures in the first 2 days of hospital stay and one measure at 5-7 days of stay. Exclusion criteria consisted of ESKD, kidney transplant or baseline eGFR <15 ml/min/1.73m². AKI was defined as an increase of serum creatinine level ≥0.3 mg/dl or 1.5 times in contrast to baseline, or the development of renal tubular abnormalities within 48 hours. We evaluated if the microscopic examination of the urine sediment (score ≥2) could be use as a non-invasive detector of renal damage.

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Conclusions: Cellular casts and granular casts are occasionally observed in hospitalized adult patients with risk factors for AKI. The urinary sediment score proposed by Perazella et al. could be a potentially useful marker for early documentation of hospital-acquired AKI.

Funding: Private Foundation Support
Kidney Biopsy Findings in AKI in the Cohort of Patients of Mexico Tertiary Hospital

Background: The study of the epidemiology of biopsy-confirmed renal disease provides useful information about the prevalence of renal disease and its clinical manifestations. Performing a kidney biopsy is necessary to accurately diagnose diseases such as glomerulonephritis and tubulointerstitial nephritis, among other such conditions. Kidney biopsy in acute kidney injury (AKI) of unknown origin provides irreplaceable information for diagnosis, treatment, and prognosis. In this report, we analyze the frequency and clinicopathologic correlations of renal native biopsied AKI in Mexican cohort during the period 2014 to 2019.

Methods: We analyzed the frequency and clinicopathologic correlations of AKI confirmed by native renal biopsy in Mexico tertiary hospital and the distribution of the different clinicopathologic findings. From 2014-2019 period, totally 515 patients first received renal biopsy. AKI was diagnosed based on the Kidney Disease: Improving Global Outcomes criteria.

Results: Of the 515 patients investigated, 200 (38.8%) showed AKI. Of these, 102 (51%), 47 (23.5%), and 51 (25.5%) presented with AKI classified as stages 1, 2, and 3, respectively. The primary indication for performing biopsy was rapidly progressive glomerulonephritis (RPGN) in 70 (35%) and nephrotic syndrome in 47 (23.5%). Dialysis previous kidney biopsy was necessary in 48 patients (24%). Focal segmental glomerulosclerosis was the most prevalent primary disease in 37 (18.5%) and lupus nephritis was the most prevalent secondary disease in 53 (26.5%). In the early patients, the most prevalent disease was pauci-immune rapidly progressive GN Multivariate analysis of risk factors associated with AKI showed hemoglobin levels (OR 0.90, 95% confidence interval [CI] 0.671–0.941, p=0.01), dialysis previous kidney biopsy (OR 3.970, 95% CI 2.949–4.392, p<0.008), and baseline serum creatinine levels (OR 2.402, 95% CI 1.371–4.758, p=0.001) were significantly associated with AKI.

Conclusions: We observed a high prevalence of AKI in patients who underwent kidney biopsy to investigate their renal disease, particularly glomerulonephritis. The prevalence of vasculitis and crescentic GN is high, especially in elderly patients.
Late Presentations of Secondary Oxalate Nephropathy
Muna Hale, Pranay Kathuria. The University of Oklahoma - Tulsa, Tulsa, OK.

Introduction: Secondary Oxalate nephropathy is an important differential diagnosis for acute kidney injury (AKI) in chronic malabsorptive disease. Mean presentation is typically within 1-2 years. The following three cases are example of late, abrupt presentations of secondary oxalate nephropathy.

Case Description: Our first case includes a 69-year-old female, with gastric bypass surgery 14 years prior, who presented to emergency room (ER) with AKI. Six months prior her creatinine (Cr) was 1.6 mg/dL, but abruptly increased to 5.99 mg/dL. Serologic work up was negative. Renal biopsy was obtained that revealed deposition of oxalate crystals within renal tubules (Figure 1). Our second case showed a 59-year-old male with history of recurrent pancreatitis due to bulimia that presented to the ER for nausea and vomiting. In the ER, patient had a serum Cr of 5.79 mg/dL. Two months prior, Cr was 1.1 mg/dL. Renal biopsy showed widespread oxalate crystals in the interstitium. The last case was a 48-year-old male with chronic pancreatitis who presented with AKI with suspect acute tubular necrosis. He had been diagnosed with chronic pancreatitis for at least 6 years with Cr 0.9 mg/dL. Patient’s Cr remained at 4.00 mg/dL one month later. Renal biopsy revealed interstitial fibrosis and calcium oxalate crystals.

Discussion: Secondary oxalate nephropathy is a side effect of malabsorptive gastrointestinal (GI) disorders. According to prior case series, the mean presentation of oxalate nephropathy is 1-2 years. These cases illustrate that secondary oxalate nephropathy can present at a later course with rapid onset. Patients also likely progress to ESRD after diagnosis. A systemic review of 108 cases, with 13 months follow up, showed 55% of patients required hemodialysis. Currently, there is no treatment and lifestyle changes include a low fat, oxalate diet. Secondary oxalate nephropathy should be considered in the differential of all patients with malabsorptive states presenting with AKI.

PO0037

Presentation and Outcome of Oxalate Nephropathy Without Known Genetic or Gastrointestinal Cause
Erin E. Bolen, Mina Abdelmalek, John C. Lieske, Mira T. Keddis. Mayo Clinic Arizona, Scottsdale, AZ; Mayo Clinic Minnesota, Rochester, MN.

Background: Oxalate nephropathy (ON) is a frequent and often unexpected finding on kidney biopsy. This study aimed to characterize causes and outcomes in biopsy-proven ON not due to known enteric cause or primary hyperoxaluria (PH) in a multisite health system.

Methods: Cases were identified based upon diagnosis of ON on kidney biopsy between 2009 to 2020 without known enteric or primary cause.

Results: Thirty-four cases were identified with a median follow-up of 11.9 months. None had known fat malabsorption. Genetic testing for PH was negative in 11, and there was no clinical suspicion of PH in the rest. Likely causes of ON included documented high dietary oxalate (7, 21%), oral and/or IV vitamin C supplementation (7, 21%), ethylene glycol (3, 9%), and orlistat (1, 3%). No cause could be identified in 16 (47%). Table 1 shows variables across three etiologies: unknown cause, diet-related, and vitamin C. All cases except one had diffuse intratubular calcium oxalate deposition on biopsy. End stage kidney disease (ESKD) was present in 53%. AKI stage III at biopsy was predictive of ESKD at last follow-up (p<0.05). Treatments included low oxalate diet (29, 85%), calcium supplementation (18, 53%), pyridoxine (12, 35%), and prednisone taper (12, 35%). Diet-related ON appeared to have lower rates of AKI stage III at diagnosis (5, 67%), ESKD (3, 43%), and mortality (2, 29%) compared to vitamin C-related ON and ON of unknown etiology.

Conclusions: This is the largest study of ON not due to PH or enteric cause. The most common causes were high-oxalate diet and high-dose vitamin C. In 47% of cases no cause was identified. ESKD was common, and AKI severity at presentation predicted ESKD at last follow up. Cases attributed strictly to dietary excess may have better short and long term outcomes.

Funding: Clinical Revenue Support
acquiring ESBL producing bacteria in urine or blood cultures. ESBL producing bacteria after previous antibiotics exposure (OR 2.102; 95% CI 1.014-4.356) were risk factors for APN occurrence after 2015 (OR 1.170; 95% CI 1.057-1.296) and AKI Epidemiology, Risk Factors, and Prevention: Clinical Research. The rate of ESBL producing bacteria has steadily increased over the years, which is consistent with the findings from early studies [1,2]. However, recent studies have shown that the rate of ESBL producing bacteria is now significantly higher, with Klebsiella spp. (0.9%) and Enterobacter spp. (0.5%) being the most common pathogens followed by Pseudomonas aeruginosa (0.9%) or diagnosis of ESRD or kidney transplant (ICD-10 codes) were excluded. Clinical data collected included; admission demographics and past history; UOP; pre-identified medication, laboratory results and order sets; specific consultations; and discharge diagnoses.

Results: A total of 22980 patient visits were evaluated. Of the 2067 patients who were admitted through the ED with a discharge diagnosis of septic shock, 433 (20.9%) received one dose of IVcV 1500mg and were categorized as the IVcV group; 1634 (79.1%) did not receive IVcV. A chi-square analysis can be seen in Table 1.

Conclusions: This retrospective study EMR observed that IVcV in the treatment of septic shock is associated with an increase in the incidence of AKI.

Funding: Clinical Revenue Support

Table 1. Chi-square Analysis Examining the Relationship between IVcV and the Development of AKI among Inpatients with Septic Shock.

<table>
<thead>
<tr>
<th>Variable</th>
<th>IVcV Group</th>
<th>Non-IVcV Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI</td>
<td>57.9%</td>
<td>63.3%</td>
<td>0.65</td>
</tr>
<tr>
<td>Moderate-severe renal injury</td>
<td>69.4%</td>
<td>70.6%</td>
<td>0.77</td>
</tr>
<tr>
<td>Renal failure</td>
<td>70.4%</td>
<td>71.6%</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Note. A logistic regression revealed that the odds of AKI were 2.57 times higher for IVcV patients compared to non-IVcV patients (95% CI 2.053, 2.37).
Case Description: A 64 year old female with non-small cell lung cancer stage IV with brain metastasis was initiated on pembrolizumab therapy seven months prior to presentation. Three weeks prior to presentation she started omeprazole 20mg daily. At time of presentation the creatinine was found to be 3.07 mg/dL, up from 0.8 mg/dL eleven days prior, improved with cessation of the PPI, however shortly there after the PPI was restored and creatinine again rose and peaked at 7.6 mg/dL. Renal biopsy was performed and confirmed interstitial nephritis. The patient was started on prednisone 1mg/kg/day with rapid improvement in renal function back to baseline.

Discussion: There has been some research linking both pembrolizumab and pembrolizumab in combination with other chemotherapeutic agents to kidney injury. However, in these trials many patients who suffered kidney injury were also receiving proton pump inhibitors, a class of medications known to provoke acute interstitial nephritis. If synergism can be proven, this combination would be avoided, thus preventing this immune related adverse event. Furthermore, reinitiation of check point inhibitors alone after cessation of the PPI and normalization of kidney function in cases such as these, could be trialed.

PO0043
Zolpidem Mega Dose Resulting in Hemodialysis

Introduction: Depression and hypoventilation syndromes are factors that may be overlooked when prescribing Zolpidem. Although hypnotics are not directly associated with rhabdomyolysis, they can lead to severe intoxication and prolonged immobilization. This can lead to compartment/ crush syndromes and depressed respiratory drive and may cause seizures. As consequence of the above renal failure ensued and hemodialysis was required.

Case Description: This case portrays a 36-year-old law student who tried to end his life with the ingestion of 90 Zolpidem pills. As consequence of his metabolic derangement he had seizures, rhabdomyolysis and renal failure that required hemodialysis. Due to pront intervention, hemodynamic stability and full recovery were achieved.

Discussion: A 36-year-old man with hypertension, insomnia and epilepsy was brought to the emergency room by ambulance. Chief complaint was of disorientation and seizures after the ingestion of 90 Zolpidem pills. He was initially combative, disoriented and with incoherent speech. Once consulted, he presented a Glasgow Coma Scale of 3 for which he was intubated. He was diaphoretic with scattered petechiae and associated incoherent speech. Once consulted, he presented a Glasgow Coma Scale of 3 for which he was intubated. He was diaphoretic with scattered petechiae and associated subconjunctival hemorrhage. On lab work he had central bicarbonate at 4.6 mEq/ L. Arterial pH was at 6.5 and PaCO2 at 24, which represented severe metabolic acidosis which he was intubated. He was diaphoretic with scattered petechiae and associated subconjunctival hemorrhage. On lab work he had central bicarbonate at 4.6 mEq/ L. Arterial pH was at 6.5 and PaCO2 at 24, which represented severe metabolic acidosis.

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Calcium oxalate crystals in tubules (PAS stain, polarized light)

P00046

Postrenal AKI due to a Rarely Seen Neoplastic Phenomenon in an Adolescent

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Introduction: AKI is an important cause of morbidity & mortality in adult and pediatric patients. Based on a lit review by Ceto-Yamane, et al., the pediatric incidence & mortality of AKI in the USA in 2013 was 0.39% and 15.3%, respectively. In general, a patient’s presentation may provide clues to the etiology of AKI (i.e. prerenal, intrarenal and postrenal). AKI due to postrenal/obstructive causes is less common in children as compared to adults and is usually associated with congenital abnormalities e.g. posterior urethral valves, or acquired due to stones or tumors. We report the case of a 14 yo previously healthy female with a unique clinical presentation due to lower urinary tract obstruction secondary to a tumor.

Case Description: The patient presented with 3 weeks of back pain, R leg swelling, headaches, urinary frequency, n/v and hematuria. In the ED, her BUN and creatinine were 107 mg/dL and 21.1 mg/dL, respectively. A RUS showed enlarged non-echogenic kidneys with mild bilateral hydrenephrosis & a heterogeneous pelvic mass. Further labs revealed anemia, low PTH, normal complement levels, ASO & ANA titers. A LE Doppler study was negative for venous thrombosis. A non-contrast MRI revealed a pelvic mass & possible metastasis. Peds Oncology was consulted, and biopsies of bone marrow & pelvic tumor revealed a small round blue cell tumor with immunohistochemical stains diagnostic for rhabdomyosarcoma. She developed oliguria, hyperkalemia & hyperuricemia (24mg/dL). A RUS revealed a small round blue cell tumor with immunohistochemical stains diagnostic for rhabdomyosarcoma. She developed oliguria, hyperkalemia & hyperuricemia (24mg/dL). Rasburicase was given & CRRT was initiated. She received emergent chemotherapy with cyclophosphamide, doxorubicin & vincristine. Bilateral percutaneous nephrostomy tubes were placed with improvement in UOP & renal function allowing CRRT to be stopped. Labs showed a downward trend of BUN & creatinine to 14 mg/dL and 0.8 mg/dL, respectively.

Discussion: Our patient’s clinical presentation was atypical in that her initial US findings of mild hydrenephrosis were not consistent with the severity of her renal injury. Her AKI was likely a combination of obstructive uropathy from the large pelvic tumor compressing her lower urinary tract & uric acid nephropathy. Decompensation of the urinary system, management of hyperuricemia & initiation of tumor directed chemotherapy resulted in marked improvement of kidney function. Our case highlights the importance of considering an obstructive etiology in older children presenting with AKI.

P00047

Profiling AKI Trajectories: Early Results from the Million AKI Project

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Background: Clinical guidelines for risk stratification of acute kidney injury (AKI) patients are based on peak increases in serum creatinine (SC). These definitions do not consider other characteristics of change in SC that may provide information on risk of adverse outcomes. Identification of patient groups that display distinct patterns in trajectory of SC and outcome profiles may lead to more nuanced risk-based definitions of AKI.

Methods: Data from the United States Veterans Health Administration were obtained. A latent class growth model identified patient groups based on similar patterns of trajectory in serum creatinine during a hospitalization with an AKI. Regression models examined associations of trajectory groups with risk factors and in-hospital mortality.

Results: We constructed a cohort of 480,575 veterans with an AKI during an inpatient stay (a subset of the Million AKI Project cohort). Of these, 343,471 (71.5%), 63,665 (13.3%), and 73,439 (15.3%) met KDIGO AKI stages 1, 2, and 3 criteria. 9.4% died during their hospitalization. We identified 9 latent trajectories summarized by 4 phenotypes: a mild increase in SC from low baseline (66%), and varying degrees of increase in SC with no (9%), moderate (17%), and near-full recovery (8%). Higher systolic blood pressure (OR=1.02; 95% CI=1.01-1.02 per 1 mmHg), sepsis (2.24; 2.10-2.39), non-use of ACE/ARB (1.54;1.47-1.61), diuretic use (1.16; 1.12-1.20), albuminuria (1.36; 1.31-1.41), and prior history of AKI (1.27; 1.22-1.32) were associated with trajectories with larger increases in SC, while major surgeries (2.48; 2.37-2.60) were associated with trajectories that recovered. Compared to the mild increase group, those with partial or no recovery had a higher odd of in-hospital mortality (1.64; 1.57-1.71) that increased in magnitude with higher baseline SC and a greater increase in SC (2.73; 2.66-2.80). Groups that experienced near-full recovery showed no evidence of a difference in mortality profile (0.97; 0.90-1.05) despite differences in other aspects of the trajectory.

Conclusions: Leveraging the depth and breadth of a high-quality longitudinal electronic health record system, we characterized nearly half a million cases of AKI; our results suggest that profiling of AKI trajectories informs risk stratification and may guide development of post-AKI care.

Funding: Veterans Affairs Support, Private Foundation Support
Preoperative Urine Alpha 1 Microglobulin Levels Are Associated with AKI and Mortality After Cardiac Surgery


Background: Higher urine alpha-1 microglobulin (a1m) levels are a marker of proximal tubule dysfunction and may improve CKD assessment and risk stratification. We hypothesized that a1m levels would be associated with adverse outcomes after cardiac surgery.

Methods: In 1464 adults undergoing cardiac surgery (CABG and/or valve) and prospectively enrolled in the multicenter TRIBE-AKI study, we measured urine a1m pre- and post-operatively. Outcomes were post-operative AKI during index hospitalization (AKIN stage ≥1) and all-cause mortality (median follow-up (IQR) 6.7 (4.0, 7.9) years). Urine a1m was analyzed as a continuous (log2) predictor in multivariable analyses adjusting for demographics, surgery characteristics, comorbidities, baseline eGFR, urine albumin, and urine creatinine. Results: There were 230 AKI events and 459 deaths. Higher pre-operative a1m was independently associated with AKI (aOR=1.36, 95% CI 1.14-1.62) and all-cause mortality (HR=1.19, 95% CI 1.06-1.33) (see table). We observed a significant interaction (p=0.01), whereby a1m had a stronger association with mortality in the subset without CHF (HR=1.29, 95% CI 1.12-1.47) than among those with CHF (HR=1.06, 95% CI 0.85-1.32). However, post-operative changes in a1m were not associated with AKI or mortality risk.

Conclusions: Even after adjusting for baseline kidney function and comorbidities, preoperative a1m was associated with post-operative AKI and all-cause mortality.

Funding: Other NIH Support - NHLBI; study also supported by NIH grant RO1HL085757 (CRP) to fund the TRIBE-AKI Consortium.

Elevated Serum Tenascin C Predicts All-Cause Mortality in Critically Ill Patients with Multiple Organ Dysfunction

Qionghong Xie, Xu Yunu, Chuan-Ming Hao. Huashan Hospital Fudan University, Shanghai, China.

Background: Tenascin-C (TNC) is a matricellular protein that is rarely expressed in most of adult tissues, but re-induced following injury. This study aimed to evaluate serum TNC in critically ill patients with multiple organ dysfunction.

Methods: Adult critical ill patients who met the criteria of at least two organs dysfunction and acute organ injury with an increase of SOFA ≥2 points within 7 days were prospectively enrolled in one derivation cohort (Medical ward) and one external validation cohort (Emergency ward). Serum TNC was measured within the first 24 hours after enrolment and the association between serum TNC and 28-day all-cause mortality was analyzed.

Results: A total of 113 patients with median age 56 (38, 66) years and male of 65.2% in derivation cohort and 66 (53, 73) male and 67% in validation cohort were included. Serum TNC was 210.2 (96.8, 469.6) ng/ml in derivation cohort and 229.4 (141.6, 472.5) ng/ml in validation cohort, both significantly higher than in that healthy controls (median 80.9 ng/ml, n=46, p<0.01 for both). The TNC level >100 ng/ml was associated with the critical illness scores such as SOFA, APACHE II, and SAPS II, as well as 28-day mortality (p=0.01 for all). Compared to the patients with TNC<300ng/ml, patients with TNC≥300ng/ml had a remarkably higher 28-day mortality (38.6% vs. 14.1%, p=0.003 in derivation cohort; 57.8% vs. 13.8% p<0.001 in validation cohort). In multivariable analysis, serum TNC was independently associated with the mortality after adjustment for age, gender and SOFA in both cohorts. The areas under the Receiver Operating Curve of TNC for 28-day mortality was 0.797 in derivation cohort and 0.803 in validation cohort, not inferior to SOFA (0.844 and 0.808), APACHE II (0.86 and 0.762) and SAPS II (0.872 and 0.797).

Conclusions: Serum TNC was significantly increased in critical ill patients with multiple organ dysfunction and was positively associated with the severity of illness and all-cause mortality. It was a useful prognostic tool for predicting all-cause mortality in critical ill patients.

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MBGC-sedi contains unique proteins compared to the supernatant. These proteins can serve as a foundation for the search of an ATN biomarker and surrogate for MBGCs detection by MicrExUrSed in patients with AKI. The predominance of mitochondrial proteins in MBGCs-sedi may explain the characteristic brown pigmentation of MBGCs.

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PO0053

Urinary Waxy Casts Are Associated with Persistence of AKI Requiring Dialysis

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Background: Waxy casts (WxCs) can be identified during microscopic examination of the urinary sediment (MicrExUrSed) and they have been classically linked to chronic kidney disease (CKD). We previously showed that WxCs predict severity of acute kidney injury (AKI). Thus, we hypothesized that WxCs may inform about duration and persistence of AKI and AKI requiring renal replacement therapy (AKI-RRT).

Methods: We conducted a retrospective observational study in patients seen in inpatient nephrology consultation with AKI stage 2 (AKIN) over the 2.5 years. On the day of consult, MicrExUrSed was performed to determine the percentage of low power fields with WxCs. The outcome measures were persistence of need for RRT at the time of hospital discharge (AKI-RRT-Persist) and the serum in creatinine (sCr) from baseline at the time of hospital discharge (AKI-Persist).

Results: Urine specimens from 286 patients [median age 60 (20 – 88), 37% women] were assessed. The etiology of AKI (de novo AKI 67%, AKI on CKD 33%) was ischemic ATII (47%), toxic ATII (9%), ischemic/toxic ATII (11%) or other (33%). WxCs were found in 85 patients (30%), 61 (72%) of which had de novo AKI. Median sCr for those with WxCs was 3.5 (0.9 – 22.0)mg/dL and 3.1 (0.9 – 12.5) mg/dL for those without WxCs (p=0.12). AKI-RRT at any point during the course of AKI was seen in 45% (38/85) of those with WxCs compared to 32% (54/201) of those without WxCs (p=0.043). There was a greater risk for AKI-RRT Persist for those with WxCs [15.3% vs 7.5%, odds ratio (OR): 2.2, CI 1.1 – 4.9, p=0.046]. Presence and abundance of WxCs were also associated with a greater risk for Persist AKI with the percentage of WxCs: >10% WxCs and >50% WxCs, respectively; chi-square for trend p<0.01.

Conclusions: In patients with AKI, the presence and abundance of WxCs are associated with a greater risk for persistent need for RRT and persistent increase in sCr at the time of hospital discharge. These findings suggest that WxCs inform about the severity of AKI and the timeline of significant AKI.

PO0045

Retrospective Analysis of the Efficiency of Caplacizumab in the Treatment of Acquired Thrombotic Thrombocytopenic Purpura: Results from the REACT-2020 Study Group

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Background: Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare but life-threatening disorder, caused by the formation of inhibitory and occasionally non-inhibitory autoantibodies against ADAMTS13. Despite plasma exchange and immunosuppression, long-term mortality and morbidity associated with acute episodes remain high. Here, caplacizumab – a nanobody approved in Germany in 2018 – has developed a non-favorable outcome comprising disease exacerbation or relapse. In some instances, caplacizumab led to a rapid normalization of the platelet count (median 0.5 (0.05-4.8)) and an improvement of the vWF activity.

Methods: We conducted a retrospective observational study in patients seen in inpatient nephrology consultation with aTTP and aTTP-RRT over the 2.5 years. On the day of consult, MicrExUrSed was performed to determine the percentage of low power fields with WxCs. The outcome measures were presence (n=76) and increase (n=48) in sCr from baseline (n=124) at the time of hospital discharge (AKI-Persist).

Results: Among the more than 40,000 patients admitted to Beth Israel Deaconess Medical Center between 2001 and 2012 in the MIMIC-III database, we selected patients with AKI clinical, outcomes, and trials - 1.

Conclusions: Presence and abundance of WxCs were also associated with a greater risk for Persist AKI with the percentage of WxCs: >10% WxCs and >50% WxCs, respectively; chi-square for trend p<0.01.

PO0054

Erythropoiesis-Stimulating Agents in AKI Requiring Dialysis

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Background: Erythropoiesis-stimulating agents (ESAs) are used in patients with CKD to treat anemia. AKI may also be a state of erythropoietin deficiency, although data on this is conflicting. Few studies have examined ESA use in AKI, including the most severe AKI-RRT patients (AKI-D). It is unknown whether and to what extent clinicians prescribe ESAs in AKI-D.

Methods: Among the more than 40,000 patients admitted to Beth Israel Deaconess Medical Centers between 2001 and 2012 in the MIMIC-III database, we selected 591 AKI-D patients and 276 ESKD patients based on ICD-9 diagnostic codes. In a cross-sectional analysis, we determined the frequency of ESA usage and estimated associations between ESA usage and age, sex, surgical (vs medical) ICU admission, ICU length of stay, admission hemoglobin, admission serum creatinine, history of CKD, and ESKD (versus AKI-D) status using multivariable logistic regression. We also examined the relationship between ESA use and the number of bladder catheters, UF NET prescription and practice.

Results: ESA usage (any time during ICU stay) was 13% in AKI-D (vs 21% in ESKD). Among AKI-D patients (Table 1), CKD (adjusted OR 3.59, 95% CI 2.06-6.25, p<0.0001), length of stay (1.06 [1.04-1.08] per day, p<0.0001), sepsis (2.06 [1.08-3.92], p=0.03), and female sex (0.31 [0.13-1.00], p=0.05) were significantly associated with ESA use. Patients treated with ESAs received six more blood transfusions on average than patients who were not treated with ESAs (6.1 more transfusions, 95% CI 2.6-9.7, p=0.0006), but this difference disappeared when adjusted for the variables significantly associated with ESA usage (AUC 0.76). In a multivariable model, AKI-D patients treated with ESAs had a higher risk of persistent need for RRT (50% rise in serum creatinine (sCr) from baseline, AKI-Persist) at discharge. The difference was significant (p=0.03). In patients with AKI-D, the presence and abundance of WxCs were associated with a greater risk for persistent need for RRT at discharge.

Conclusions: Presence and abundance of WxCs were also associated with a greater risk for Persist AKI with the percentage of WxCs: >10% WxCs and >50% WxCs, respectively; chi-square for trend p<0.01.

PO0056

Survey of US Critical Care Practitioners on Perspectives Toward Net Ultrafiltration Prescription and Practice

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Background: Previous studies suggest international practice variation in net ultrafiltration (UF NET) among critically ill patients with acute kidney injury treated with kidney replacement therapy. We examined U.S. critical care practitioner attitudes toward UF NET prescription and practice.

Methods: Secondary analysis of a multinational, cross-sectional, internet-assisted, open survey administered to intensivists, nephrologists, advanced practice providers, ICU and dialysis nurses in the U.S.

Conclusions: Of 1,569 international survey respondents, 465 (29.6%) practitioners were from the U.S. Practitioners were mostly nurses and nurse practitioners (58%) and intensivists (38.2%). Median duration of practice was 8.7 (IQR, 4.2-19.4) years and 63.4% practiced in a university- based hospital. Practitioners reported using continuous kidney replacement therapy (CRRT) as the first modality for UF NET in 60% (ICU 20% vs 40% of their patients with median UF NET rate of 51 mL/h, ICUs 25-100 mL/h) for hemodynamically unstable and a maximal rate of 285 mL/h (ICU 1, 200-341 mL/h) for hemodynamically stable patients. 58.3% (range 28.7%-70.2%) of practitioners assessed net fluid balance hourly. Hemodynamic instability was reported in 25% (ICU 10%-100%) of the patients, and practitioners decreased the rate of fluid removal (71.2%); started or increased dose of a vasopressor (56.8%); completely stopped fluid removal (44.5%); and administered a fluid bolus (28.7%). Most clinicians (79.8%) reported patient intolerance as a major barrier. Other barriers include frequent interruptions (50.1%), under prescription (17.3%), and trained staff (17%), inability to titrate fluid removal (10.1%), and unavailability of dialysis machines (8.6%) and cost (2.4%) (Figure 1). More than 70% of clinicians agreed with early protocelated fluid removal and expressed desire to enroll their patients in a future clinical trial.

Conclusions: This study provides new knowledge on UF NET in practices in the U.S. We also identified barriers and specific targets for quality improvement initiatives. Our data reflect the need for evidence-based practice guidelines for UF NET.

PO0057

A Pilot Trial to Evaluate the Clinical usefulness of Contrast-Enhanced Ultrasound in Predicting Renal Outcomes in Patients with AKI

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Background: Contrast-enhanced ultrasound (CEUS) enables the assessment of real-time renal microcirculation. This study investigated CEUS-driven parameters as biomarker predictors for renal outcomes in patients with acute kidney injury (AKI).

Methods: Forty-eight patients who were diagnosed with AKI were prospectively enrolled and underwent CEUS at the occurrence of AKI. Parameters measured were the wash-in slope (WIS, time to peak intensity, peak intensity (PI), area under the time–intensity curve (AUC), mean transit time (MTT), time for full width at half maximum, and rise time (RT). The predictive performance of the CEUS-driven parameters for Kidney Disease Improving Global Outcomes (KDIGO) AKI stage, initiation of renal replacement therapy (RRT), AKI recovery, and chronic kidney disease (CKD) progression was
assessed. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic performance of CEUS.

**Results:**
Cortical MTT (OR = 1.07) and RT (OR = 1.20) predicted the initiation of RRT. Cortical WIS (OR = 1.00) predicted AKI recovery. Medullary PI (OR = 1.25) and WIS (OR = 76.23) and medullary PI (OR = 1.25) predicted AKI recovery. Medullary PI (OR = 1.25) and WIS (OR = 76.23) and medullary PI (OR = 1.25) predicted AKI recovery. The areas under the ROC curves showed reasonable performance for predicting the initiation of RRT and AKI recovery. The sensitivity and specificity of the quantitative CEUS parameters were 60–83% and 62–77%, respectively, with an area under the curve of 0.69–0.75.

**Conclusions:** CEUS may be a supplemental tool in diagnosing the severity of AKI and predicting renal prognosis in patients with AKI.

**Funding:** Government Support - Non-U.S.

**PO0058**

**A Clinical Score to Predict Recovery in ESKD due to AKI**

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**Background:** Acute kidney injury (AKI) is a major contributor to end-stage kidney disease (ESKD). About one-third of patients with ESKD due to AKI recover kidney function. However, there is lack of clinical models to predict kidney recovery in ESKD due to AKI.

**Methods:** Using data from the United States Renal Data System (2005-2014), we developed a clinical score to predict kidney recovery by 90-days post-dialysis initiation in patients with ESKD due to AKI (N=22,922). We used multivariable logistic regressions to model the effects of patient demographics, comorbidities, and laboratory measures on kidney recovery. The resulting logistic parameter estimates were transformed into integer point totals by doubling and rounding the estimates. The predictive accuracy of the score models was compared to the underlying logistic models by comparing areas under the receiver operating characteristic curves (AUROC) and internal validation was performed.

**Results:** In ESKD due to AKI, kidney recovery within 90-days occurred in 24% of patients. Median recovery time for patients who recovered was 2 months; 72% recovered within 90-days. In the logistic models of recovery at 90-days, older age, lower body mass index, hemoglobin < 12 gm/dl, Black and Native American race, Hispanic ethnicity, congestive heart failure, amputation, poor functional status, and pre-dialysis nephropathy care were associated with a lower likelihood of recovery. Eight patient characteristics were included in the final clinical score- age, body mass index, race, congestive heart failure, amputation, functional status, and prior nephropathy care. Recovery scores ranged from zero to 11, with corresponding recovery rates ranging from 6% to 86%. Three risk categories (score range of 0-5, 6-7, and 8-11) exhibited 90-day recovery rates of 11%, 23%, and 45%. The internal validation assessment showed no overfitting of the models. The AUROC of the score was 0.70, similar to the original AUROC of 0.71.

**Conclusions:** A simple clinical risk score derived from information available at incident dialysis can accurately predict kidney recovery at 90 days in ESKD due to AKI. This predictive tool can be utilized by dialysis providers and policymakers to individualize care, and to improve the quality and processes of care.

**Funding:** Clinical Revenue Support

**PO0059**

**AKI in Hospitalized Patients with Influenza Is Associated with Worse Outcomes: A Study of National Inpatient Sample from 2012 to 2014 in the United States**

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**Background:** Influenza causes significant morbidity and mortality every year. Physiologically, kidneys receive only 25% of the cardiac output in an average weight adult and therefore often develop acute kidney injury (AKI). Our study determines outcomes of AKI in adults hospitalized with influenza between 2012 and 2014 in the US.

**Methods:** We analyzed adult patients with a principal diagnosis of influenza from the 2012 to 2014 National Inpatient Sample. ICD-9-CM was used to identify the diagnosis variables. Patients were divided into two cohorts; with and without AKI. Patient characteristics between both groups were compared. Chi-squared analysis for categorical variables and multivariate regression analysis was done using STATA 16.0 to determine the relationship of outcomes. P <0.05 was used as the level of statistical significance.

**Results:** 120,730 hospitalizations with influenza were sampled. 16,270 (13.5%) of these had AKI (image 1). After adjusting for potential confounders, patients with AKI had higher odds of mortality (adjusted odds ratio (aOR): 3.83; 95% confidence interval (CI) 3.00-4.89, p<0.001), developing severe sepsis (aOR: 2.74; 95% CI 2.46-3.07, p<0.001), and septic shock (aOR: 9.53; 95% CI 6.42-14.16), riboflavinemia (aOR: 3.03; 95% CI 2.39-3.84), requiring intubation (aOR 5.57; 95% CI 4.61-7.74, p<0.001), a longer length of stay (1.8 days; 95% CI 1.52-2.08, p<0.001) and higher costs ($5054.9; 95% CI $3981.8-$6190.1, p<0.001).

**Conclusions:** Influenza complicated with AKI in hospitalized patients is associated with a worse outcome in terms of morbidity and mortality along with increased healthcare costs and a longer length of stay.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

**PO0060**

**Impact of Chloride-Rich Crystalloids on Sepsis-Associated Community-Acquired AKI Recovery in Critically Ill Patients**

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**Background:** The use of chloride-rich crystalloids for resuscitation is associated with developing acute kidney injury (AKI). We aimed to explore the impact of resuscitation with chloride-rich crystalloids compared to balanced crystalloids on the recovery of kidney function in patients presenting with established sepsis-associated community-acquired AKI (SACA-AKI).

**Methods:** This was a single-center, historical cohort study of patients admitted to the intensive care unit (ICU) who presented to the emergency department (ED) with SACA-AKI at Mayo Clinic, Rochester, MN, from January 2011 to April 2018. We divided the cohort into two groups based on the primary type of crystalloids received in the ED and the first 48-hours of ICU. The first group received primarily normal saline with <20% balanced solutions, and the second group received at least ≥20% balanced crystalloids during the initial volume resuscitation.

**Results:** We included 736 patients who were resuscitated with crystalloids after SACA-AKI diagnosis (mean age 64±16, n = 463 (63%) males). There were 286 (39%) females in the second group, found to have higher positive fluid balance during the first 48-hours of admission compared to the first group [median 5.7 (IQR: 3.6; 8) vs. 3.8 (IQR: 2.1; 6.1) L, P<.001]. By multivariable logistic regression, the patients in the second group had a higher rate of kidney function recovery after adjustments for known recovery risk factors (OR 1.4; 95% CI: 1.04-2.1, P = 0.027).

**Conclusions:** The use of balanced crystalloids during the initial resuscitation is associated with higher odds of kidney function recovery in patients with SACA-AKI.

**Funding:** Other NIH Support - National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number K23AI143882 (PI, EFB).

**PO0061**

**The Effect of Care Bundles for AKI: A Systematic Review and Meta-Analysis**

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**Background:** Acute kidney injury (AKI) is common and associated with increased rates of morbidity and mortality. Implementation of a set of evidence-based AKI care bundles may have some benefits to patients’ outcomes by reducing variable standards of care. We aimed to systematically review the literature to quantify the effect of AKI care bundles on patient outcomes.

**Methods:** We searched PubMed (Medline), EMBASE and Cochrane databases for studies that compare the effect of AKI care bundles with usual standard care in patients with or at risk of AKI from database inception to December 31, 2019. The quality of included studies was assessed using the Newcastle-Ottawa Scale. Heterogeneity was
assessed using Cochrane Q test and I² test statistics. Data were analyzed by RevMan 5.3 and Comprehensive meta-analysis (CMA 3.0). The primary outcome was in-hospital or longest follow-up mortality. Secondary outcomes included AKI incidence and AKI severity.

Results: A total of 11 studies (23,491 patients) were included in the meta-analysis. The implementation of AKI care bundles significantly reduced mortality in all patients (odds ratio, 0.87; 95% CI, 0.79–0.94; P < 0.001; I² = 0%; Fig 1). And in patients at high risk for AKI (identified by novel biomarker, risk prediction score or electronic alert), care bundles significantly reduced AKI incidence (odds ratio, 0.62; 95% CI, 0.44–0.86; P = 0.005; F = 70%; I² = 0%; Fig 2) and rates of AKI severity (odds ratio, 0.52; 95% CI, 0.35–0.76; P = 0.001; F = 41%; Fig 3). In addition, there was no evidence of publication bias among the included studies.

Conclusions: The introduction of AKI care bundles can effectively improve outcome in patients with or at risk of AKI, especially when combined with novel biomarker, risk prediction score or electronic alert to manage AKI at early stage. However, the evidence so far is limited and not strong enough to make definite conclusions.

PO062
Block Randomized Implementation of a Decision-Making Algorithm for Renal Replacement Therapy Initiation in AKI Compared with Standard Care on AKI-Related Outcomes
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Background: Acute kidney injury (AKI) requiring renal replacement therapy (RRT) is associated with high mortality and utilization. Clinical decision-making related to AKI-RRT initiation in the intensive care setting is not standardized.

Methods: We conducted a 12 month single center block randomized controlled trial in the intensive care units (ICUs) of a large academic tertiary medical center; alternating use of an AKI Standardized Clinical Assessment and Management Plan (SCAMP), a decision-making algorithm to guide front-line clinicians, with use of a “sham” control form in 4-6 week randomization blocks. The SCAMP provided recommendations about optimal indications for initiating RRT on the basis of various clinical parameters, whereas the sham control form did not provide any recommendations for management of AKI-RRT.

Results: 122 patients were managed with AKI-SCAMP while 102 patients were managed using the sham control form. There was no significant difference in the primary outcome of odds of inpatient, 30-day or 60-day mortality associated with use of the AKI-SCAMP. With respect to secondary outcomes, use of the AKI-SCAMP resulted in a significantly reduced ICU length of stay (relative risk 0.68; 95% CI 0.66–0.69, p < 0.0001; I² = 0%) and hospital length of stay (relative risk 0.75; 95% CI 0.72–0.79, p < 0.0001), as well as a reduced 30-day hospital readmission rate (odds ratio 0.38; 95% CI 0.15–0.99, p = 0.05).

Conclusions: Use of an AKI-SCAMP clinical decision support tool for assessment and management of AKI-RRT led to reduced ICU and hospital length of stay and 30-day hospital readmission rates. We advocate for increased study and use of this clinical decision support tool.

PO063
The Effect in Renal Function and Vascular Decongestion in Type 1 Cardiorenal Syndrome Treated with Two Strategies of Diuretics: A Randomized Clinical Trial
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Background: The main treatment strategy in type 1 cardiorenal syndrome (CRS1) is vascular decongestion, it is probable that sequential blockage of the renal tubule with combined diuretics (CD) will obtain similar benefits when compared with stepped furosemide (SF).

Methods: We conducted a double-blind randomized clinical trial in CRS1 consecutive patients, we randomized in a 1:1 fashion to SF group or CD. The SF group received a continuous infusion of furosemide 100mg during the first day, with daily incremental doses to 200mg, 300mg and 400mg during the second, third and fourth day, respectively. The CD group consist in the combination of diuretics trying to block different tubular segments, including 4 consecutive days of oral chlorothalidone 50mg, spironolactone 50mg and infusion of furosemide 100mg. The objectives were asses renal function recovery, and variables associated with vascular decongestion.

Results: During July 2017 to February 2020, 80 patients were randomized, 40 to the SF and 40 to the CD group, both groups were similar at baseline and had several very high-risk features. Mean age was 59 ± 14.5 years, male gender was 37 (46.2%), the median follow up was 182 days, Primary endpoint occurred in 20% in the SF group and in 15.2% in the DC group (p = 0.49), all secondary and exploratory endpoints were similar between groups with non-significant differences. Adverse events occurred frequently (85%) with no differences between groups (p = 0.53).

Conclusions: In patients with SCR-1 and high risk of resistance to diuretics, the strategy of CD compared to SF, offers the same frequency of renal recovery, diuresis, vascular decongestion and adverse events, so it can be considered as an alternative, especially in cases where it is not considered advisable to increase furosemide.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0064

Renin Levels Are Higher in Patients with AKI and Associate with Mortality and Major Adverse Kidney Events

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Background: Renin is a marker of tissue perfusion and may be useful in predicting mortality in critically ill patients. Renin might also reflect structural kidney damage in heterogeneous AKI settings. We examine if renin levels are different in patients with vs. without AKI and if renin levels associate with adverse outcomes in critically ill patients.

Methods: Multicenter observational study utilizing blood samples of critically ill patients (KLAKI) and patients undergoing cardiac surgery (TRIBE-AKI). Renin was measured by ELISA in serum from 296 critically ill patients at 24-48 h of AKI diagnosis (KDIGO ≥2) or ICU admission (controls), and peroperative in plasma from 105 patients undergoing cardiac surgery (35 with AKI [≥0.3 mg/dL increase or ≥50% increase in serum creatinine from baseline preoperative level to postoperative level] and 70 controls without AKI). The association of renin levels with hospital mortality and major adverse kidney events at hospital discharge (MAKE: composite of death, need of renal replacement therapy or patients to recover more than 75% of baseline eGFR) was evaluated in the critically ill group.

Results: Renin levels were higher in critically ill patients with AKI vs. ICU controls without AKI (median [IQR], 67.9 [21.7-343.7] vs 22.2 [6.4-73.0] pg/mL, p<0.001). Similarly, patients undergoing cardiac surgery who developed postoperative AKI had pre and postoperative renin levels differentially higher than those without AKI, sustained from POD1 to POD3 (157.9 [80.0-390.8] vs. 68.9 [20.6-149.9] pg/mL at POD1 in AKI vs. no AKI, p=0.003). In adjusted models, higher renin levels independently associated with increased risk of hospital mortality (OR: 1.27, 95%CI: 1.02-1.58 for every 1-unit increase in renin vs. no AKI, 3.44, 95%CI: 1.08-11.02 when the highest tertile was compared to the lowest tertile). Further, every 1-unit increase in renin increased the risk of MAKE by 16% (95%CI: 1.33%-18%).

Conclusions: Renin levels are differentially higher in patients with heterogeneous AKI when compared to controls without AKI. Renin levels associate with hospital mortality and MAKE in critically ill patients and therefore its risk-stratification should be further explored in this vulnerable population.

PO0066

Biomarker and Safety Results from a Phase 1b Study of RBT-9 in Healthy Volunteers and Subjects with CKD Stage 3/4

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Background: Acute kidney injury (AKI) remains a major unmet medical need without any FDA approved preventive or therapeutic options. Safe administration of pharmacologic agents that can prevent AKI in the hospital setting have great potential given the high rate of AKI-related morbidity and mortality. Organ preconditioning to elicit a state of induced cytoprotection prior to insult, such as cardiac surgery, is a mechanism by which the drug RBT-1 has been shown to be protective in various animal models of AKI including glycercyl-induced rhabdomyolysis, maleate-induced hypoxic/ischemic renal injury, and ischemia reperfusion injury. RBT-1 is composed of proprietary formulations of stauromycin prolymphoprotein (RBT-9) and iron sucrose (RBT-3). We conducted three phase 1 clinical trials to study the effect of RBT-1, RBT-3, and RBT-9 on biomarkers of cytoprotection observed in experimental animals and on clinical safety. Herein, we report results from the Phase 1b study of RBT-9 in both healthy volunteers and subjects with CKD Stage 3/4.

Methods: Forty-two subjects were enrolled and received a single dose of RBT-9 at 9 mg (N=6), 27 mg (N=18), and 90 mg (N=18). None of the subjects in the 9 mg group had CKD; 12 subjects (67%) in each of the 27 and 90 mg groups had CKD. Mean age was 59.5 years.

Results: The highest dose of RBT-9 dose-dependently induced cytoprotective biomarker responses (heme oxygenase-1 [HO-1], ferritin, NADPH dehydrogenase [quinone 1] [NQO1], and interleukin-10 [IL-10]) in both healthy volunteers and CKD subjects. Treatment-emergent adverse events (TEAEs) were reported in 20 subjects (47%), the majority of which were photosensitvity events and largely confined to the 90 mg treatment group. TEAEs were generally mild in severity. Only 3 TEAEs were moderate; no TEAEs were severe. No serious adverse events were reported. All TEAEs resolved during follow-up. There was no evidence of renal injury, as assessed by albuminuria and various biomarkers of renal tubular injury (KIM-1, NGAL, cystatin C, NAG).

Conclusions: We conclude that RBT-9 was safe and well tolerated in healthy volunteers and subjects with CKD. Adverse events were generally mild and related to photosensitivity reactions. Dose-dependent cytoprotective protein responses were observed that have previously corresponded with AKI protection in experimental animals.

Funding: Commercial Support - Renibus Therapeutics

PO0067

Analysis of AKI in Patients with Systemic Lupus Erythematosus

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Background: Renal involvement is commonly seen in systemic lupus erythematosus (SLE). The goal of our study is to analyze the impact and burden of acute kidney injury (AKI) on patients with SLE.

Methods: We analyzed the Healthcare Cost and Utilization Project Nationwide Inpatient Sample from the years 2012 to 2014. We included patients aged 18 years or older with either a primary or secondary diagnosis of SLE. Descriptive analyses were performed with a focus on patient characteristics and comorbidities. We used weighted multivariable survey regression methods to assess outcomes. Statistical analysis was performed using STATA 16.0. We considered a P value of <0.05 as statistically significant.

Results: We identified a total of 101,615 hospitalizations with SLE, of which 9,475 (9.3%) had AKI. Patients with a diagnosis of AKI were younger (mean age 39.3 vs. 45.4), more likely to be male (16.5% vs. 8.9%), black (45.5% vs. 33.5%), discharged from a teaching institution (72.2% vs. 65.4%). Patients with AKI had a higher prevalence of chronic kidney disease (53.2% vs. 10.1%), hypertension (74.5% vs. 47.5%). After adjustment with the patient and hospital level of confounder, the presence of AKI was independently associated with increased overall in-hospital mortality in patients with SLE (adjusted odds ratio [aOR] 12.1, 95% confidence interval [CI] 6.5-22.4, p<0.001). Length of stay (LOS) was 5.0 days longer (95% CI 4.5-5.6, p<0.001) in patients with AKI, and total hospital costs were $124,856 more than in patients without AKI (95% CI 106,556-143,152, p<0.001).

Conclusions: Patients with AKI were more likely to die in the hospital, had a longer length of stay, higher inpatient care costs. Thus, the presence of AKI poses a significant burden on patients with SLE. Close monitoring and early treatment are warranted in this population.
Efficacy Evaluation of Neutrophil Gelatinase-Associated Lipocalin and Cystatin C in Urine as Biomarkers in Early Diagnosis of AKI in Preterm

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Background: To investigate the value of neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C in urine in the early diagnosis of acute kidney injury in preterm and the efficacy of these two biomarkers in urine.

Methods: A prospective study was conducted on 98 preterm admitted to the NICU, including 55 males and 43 females. According to the diagnostic criteria for neonatal AKI published by the Acute Kidney Injury Network and the Kidney Disease Improving Global Outcomes (KDIGO), the serum creatinine is 1.5 times of the basic level or the urine volume is less than 1.5 ml/(kg*h) ≥24 h, 10 cases of AKI and 88 cases of non-AKI were confirmed on the first day of inclusion, 3 cases of AKI and 95 cases of non-AKI were confirmed on the seventh day of inclusion. Urine samples were collected on the day1, day7 of inclusion and the day of urine volume significant decrease (urine volume < 1.5 ml/(kg*h)), urine NGAL (uNGAL) and urine cyst-C were measured by ELISA, meanwhile serum creatinine were measured. The study was approved by the ethical community board and written consent was obtained from the kids’ parents.

Results: Among 98 cases, 10 cases were separated in AKI group and 88 in non-AKI group on the admission day, uNGAL and urine cyst-C in the AKI group were significantly higher than those in the non-AKI group (P < 0.05). On day 7, 3 cases were diagnosed AKI and 95 cases in non-AKI group. uNGAL and urine cyst-C in the AKI group were significantly higher compared with those in the non-AKI group (P < 0.05). Receiver operating characteristic curves (ROC) for the diagnosis of AKI on day 1 and day 7 were drawn, the area under the curve(AUC) of urine cyst-C on day1 and day 7 was 0.922 vs. 0.849, the sensitivity was 0.900 on day (when the critical value for AKI as 25.19ng/ml), and the sensitivity on day7 was 1(When the critical value was set 23.16ng/ml), and the specificity of urine cyst-C on day1 vs. day7 was 0.975 vs. 0.737 separately. The area under the curve(AUC) of uNGAL for AKI diagnosis was 0.860(day1) and 0.867(day7). When the critical value for AKI diagnosis was 100.12 g/L, the sensitivity for uNGAL was 1, and the specificity was 0.695. The positive value for uNGAL on day1 and day7 were 96% and 100% separately.

Conclusions: NGAL and cyst-C in urine can be used as biological indicators for the diagnosis of AKI in premature infants.

Funding: Government Support - Non-U.S.

AKI in Sickle Cell Disease

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Background: Sickle cell disease may cause acute injury to the kidney, especially during sickle cell crisis. Which mainly related to underlying stress-induced renal vasculopathy and alterations in glomerular hemodynamics. There is a paucity of national-level evidence showing the effect of acute kidney injury (AKI) on patients hospitalized with sickle cell disease. We aim to quantify the relationship between AKI and mortality and resource utilization in patients with sickle cell disease.

Methods: We analyzed adult patients admitted from 2012 to 2014 with a primary or secondary diagnosis of sickle cell disease using the Nationwide Inpatient Sample (NIS). The NIS is the largest publicly available inpatient database in the United States (U.S.). It contains data from approximately 8 million hospital stays each year, representing a 20% stratified sample of all U.S. non-federal hospitals, and is sponsored by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project (HCUP). The International Classification of Diseases, Ninth Revision, Clinical Modification Coding System (ICD-9-CM) was used to identify comorbidities. Survey multivariate regression analysis was performed using STATA 16.

Results: We included 240,550 admissions with sickle cell disease, majority of them were black patients (93%), 10,825 (4.5%) of sickle cell disease patients had AKI. Patients with AKI were older (mean age 41.3±12.5 vs. 31±10.4, p<0.001), more likely to be male (53.1% vs. 44.4%, p<0.001). Sickle cell disease patients had higher prevalence of hypertension (49.9% vs. 16.8%, p<0.001), coronary artery disease (6.3% vs. 2.1%, p<0.001), congestive heart failure (22.5% vs. 4.4%, p<0.001), diabetes mellitus (9.8% vs. 3.5%, p<0.001). After adjusting for patient and hospital-level confounders, patients with AKI had higher odds of mortality (adjusted odds ratio [aOR] 11.3, 95% confidence interval 7.04–18.34, p<0.001), a longer length of stay (2.6 days, 95% CI: 1.2–2.93 days, p<0.001), higher costs (S6707.2; 95% CI: $5816.2–$7598.3, p<0.001).

Conclusions: The demographic characteristics were significantly different between patients with or without AKI. Sickle cell nephropathy imposes a burden on both individual and health care systems. Randomized controlled trials are needed to investigate the role of vaso-occlusive events on AKI development.

Combining Renal Arrest and Damage Biomarkers to Predict the Progression of AKI in Patients with Sepsis

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Background: Septic AKI accounts for approximately half of all AKI in ICU, and up to 40% of mild or moderate septic AKI would progress to more severe AKI which is associated with significantly increased risk for in-hospital death and later CKD/ESRD.

Conclusions: NGAL and cyst-C in urine can be used as biological indicators for the diagnosis of AKI in premature infants.

Funding: Government Support - Non-U.S.
Early identifying high risk patients for AKI progression might help physicians to enhance individualized monitoring and personalized management in patients with septic AKI.

Methods: This is a prospective, multicenter cohort study which enrolled adult septic patients who initially developed stage 1 or stage 2 AKI in the ICU from January 2014 to March 2018. Sepsis was diagnosed based on the 2016 Sepsis-3 criteria, and AKI was diagnosed and staged according to 2012 KDIGO-AKI guidelines. Renal arrest biomarkers (urinary TIMP2*IGFBP7 [u TIMP2*IGFBP7]) and renal damage biomarkers (urinary KIM-1 [uKIM-1] and urinary IL-18 [uIL-18]) were measured at a time of AKI clinical diagnosis, and the utility of biomarkers for predicting septic AKI progression alone or in combination were evaluated. The primary outcome was AKI progression defined as worsening of AKI stage. The second outcome was receiving dialysis or death during ICU stay.

Results: A total of 149 septic patients with stage 1 or stage 2 AKI were included, 63 patients developed progressive AKI. 49 patients received dialysis or died during ICU stay. uTIMP2*IGFBP7, uKIM-1 and uIL-18 independently predicted the progression of septic AKI in which uTIMP2*IGFBP7 showed the greatest AUC (0.745; 95%CI, 0.667-0.823) as compared to uKIM-1 (AUC 0.719; 95%CI 0.638-0.800) and uIL-18 (AUC 0.619; 95%CI 0.525-0.731). Combination of uTIMP2*IGFBP7 with uKIM-1/uIL-18 further improved the performance of predicting septic AKI progression with AUCs of 0.752 (uTIMP2*IGFBP7 with uKIM-1) and 0.747 (uTIMP2*IGFBP7 with uIL-18), respectively. uTIMP2*IGFBP7, alone or combined with uKIM-1/uIL-18, improved the risk reclassification over the clinical risk factor model alone both for the primary and secondary outcomes, as evidenced by significant category-free net reclassification index.

Conclusions: Combination of renal arrest and damage biomarkers enhanced the prediction of AKI progression in patient with sepsis and improved risk reclassification over the clinical risk factor model alone.

Funding: Government Support - Non-U.S.

PO0072
Bicarbonate May Not Be the Best Treatment for Rhabdomyolysis: A Retrospective Cohort Study
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Background: It is controversial whether the use of bicarbonate solution, which has been traditionally attempted to treat rhabdomyolysis, has the beneficial effect of reducing acute kidney injury (AKI) and mortality, compared with the use of non-bicarbonate solution. The purpose of this study is to analyze whether bicarbonate therapy versus non-bicarbonate therapy may be effective in preventing AKI and death in patients with rhabdomyolysis.

Methods: We collected 4077 hospitalized patients with creatinine kinase (CK) > 1000 U/L and divided them into 2 groups: patients who received fluid with bicarbonate and who received fluid without bicarbonate. Patients were subgrouped into low (<2ml/kg/hr), middle (2-4ml/kg/hr) and high (>4 ml/kg/hr) amounts of fluid to receive in first 72 hours of admission. Cox regression analysis models were used to identify risks for dialysis and mortality. Safety profiles were assessed by volume overload and electrolyte imbalances.

Results: In a total of patients with a mean age of 57.9 years (male 66.7%), bicarbonate-containing solution was used in 61.1% of the participants. The proportion of the subjects were 34.6%, 36.5%, and 28.9% for the low, middle, and high fluid group, respectively. The bicarbonate group showed higher incidence rate of AKI (OR 4.5), higher 1-year mortality (OR 3.1) and longer hospital stay (26.6 ± 54.4 vs. 22.0 ± 22.7 days) than the non-bicarbonate group. Patients high given amount of fluid therapy showed higher incidence rate of AKI (OR 3.1), higher rate of dialysis dependency (OR 2.7) and higher 1-year mortality (OR 1.4), compared with low fluid group, regardless of the use of bicarbonate. The use of bicarbonate (adjusted HR [aHR] 1.55), volume overload (aHR 1.28) were associated with higher mortality while the use of furosemide (aHR 0.8) showed the preventive effect. Baseline CK or peak CK were not related to the risk of dialysis or death. Volume overload was significantly higher in the bicarbonate group compared with the non-bicarbonate group.

Conclusions: We showed bicarbonate therapy or high-volume fluid management in patients with rhabdomyolysis were not beneficial in preventing AKI and death, compared with the non-bicarbonate therapy or low-volume fluid management. It suggests that limited use of bicarbonate and adjustment of fluid volume may improve the short-term and long-term outcome of rhabdomyolysis.

Funding: Clinical Revenue Support

PO0073
Plasma Metabolites Do Not Change Significantly After 48 Hours in Patients on CRRT
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Background: Continuous renal replacement therapy (CRRT) is used in critically ill patients with hemodynamic instability. One of the primary aims of CRRT is to remove solutes that accumulate due to impaired kidney function. Surprisingly, few studies have assessed plasma solute levels during CRRT, and the duration of CRRT necessary to achieve adequate solute removal is unknown.

Methods: To assess the effect of CRRT on plasma solutes, metabolites were determined via targeted ultra-high pressure liquid chromatography coupled to mass spectrometry (UHPLC-MS) in 13 critically ill patients requiring CRRT. Metabolites were assessed on plasma collected prior to CRRT initiation, and on plasma and effluent collected on days 1, 2, and 3 thereafter.

Results: A total of 101 annotated metabolites were evaluated. Plasma levels of 22 metabolites (21.8%) were significantly reduced by Day 1 of CRRT, and included creatinine, phosphate, lactate, and the amino acids alanine, proline, and cysteine. Only 2 metabolites (2.0%) were significantly reduced between Day 1 and Day 2, and none were reduced between Day 2 and Day 3. Figure 1 demonstrates that marginal changes in solute levels decrease as CRRT progresses. All metabolites were detected in the effluent, and the sieving coefficients for metabolites that were reduced versus not reduced after CRRT were not statistically different.

Conclusions: No further reduction in plasma metabolites occurred after 48 hours of CRRT. Since the median CRRT treatment time is 4-7 days nationwide, with some patients treated substantially longer, these data bring into question the utility of prolonged, uninterrupted CRRT therapy, and have major potential implications for the duration of CRRT in the ICU population.

Figure 1. PLS-DA Scores Plot

PO0074
Sustained-Low-Efficiency Dialysis with Regional Citrate Anticoagulation and a Standard Hemodialysis Machine in Critically Ill Patients with AKI Francesco Di Mario,1 Filippo M. Fani,2 Paolo Greco,1 Caterina Maccari,1 Elisabetta Parenti,1 Tommaso Di Motta,1 Maria Teresa Farina,1 Giuseppe Regolisti,1 Enrico Fiacchadori,1 1UO Nefrologia, Azienda Ospedaliera-Universitaria Parma, Parma, Italy, Parma, Italy; 2UO Nefrologia e Dialisi, Ospedale San Giovanni di Dio, USL Toscana centro, Firenze, Italy.

Background: Sustained-Low Efficiency Dialysis (SLED) is an increasingly used Kidney Replacement Therapy (KRT) modality in critically ill patients with Acute Kidney Injury (AKI); in this setting regional citrate anticoagulation (RCA) is a rational approach to avoid extracorporeal circuit clotting. The present study was aimed at evaluating the safety and efficacy of a simplified RCA protocol for SLED with a conventional hemodialysis machine.

Methods: SLED was performed for 8-12 hours (daily or every other day) with a Sutural X Nipro® hemodialysis machine and a cellulose triacetate filter (Sureflex-19L, 1.9 m2, KUF 19 ml/mmHg/h). Blood flow was set at 200 ml/min and dialysis fluid flow at 100 ml/min. Citrate was infused in pre-dilution as ACD-A solution (citrate 2.2%, 112.9 mmol/L) at 200-400 ml/h rates (estimated pre-filter citrate concentration 2.4 mmol/L). Treatment was monitored by serial evaluations of ionized calcium (Ca++) and ACT at the beginning, at the 2nd hour and at the end of SLED session. Blood in the extracorporeal circuit was recalcified by the dialysis fluid itself (Ca++ 1.5 mmol/L) through Ca++ backfiltration; i.e. calcium supplementation was started only if patient Ca++ at the 2nd hour was <0.9 mmol/L.

Results: 41 SLED sessions were performed in 12 critically ill patients with AKI (mean age 69 ± 18 SD, mean APACHE II 22). Average pre- and post-SLED urea values were respectively 94 and 32 mg/dL. Most sessions (38/41, 93%) were completed for elapsed prescribed time. No statistically significant differences were observed between systemic ACT values measured during SLED as compared to baseline values. Ca supplementation
(10% Ca gluconate at fixed rate 5 ml/hour) was needed in 10/44 treatments, with rapid normalization of serum Ca. No new cardiac arrhythmia episode or hemorrhagic events were observed.

Conclusions: Our preliminary data suggests that a simplified RCA protocol for SLED using a conventional dialysis machine is easy and safe, also ensuring a good match between prescribed and actual dialysis dose administered.

PO0075 Prediction of AKI in Inpatient General Medical Ward Units Cassandra Chiao, Rachel Urban, Fauzia Osman, Tripti Singh. University of Wisconsin System, Madison, WI.

Background: Acute kidney injury (AKI) is common in hospitalized patients (A). A few scoring systems have been proposed to predict the risk of developing AKI in certain populations such as cardiac catheterization patients (B, C, D, E, F). However, there is no scoring system for predicting AKI in patients on the general medical wards. Our aim is to predict the development of AKI in acute general medical patients.

Methods: Retrospective single center study of all adult patient admitted to a tertiary care university hospital between July 2016-July 2018. AKI was defined by the KDIGO definition of AKI and all stages of AKI were included. We used chi-squared tests, ANOVA, and Kruskal Wallis to determine statistically significant factors. We calculated odds of AKI using logistic regression models. All analyses were conducted using STATA SE 15.

Results: A total of 10,981 were included in the study, 1,573 (14.3%) with AKI and 9,408 (85.7%) without AKI. Baseline demographics were significantly different between the two groups including age, race, length of hospital stay (p<0.001). In the univariate analysis, history of cancer and diabetes, proteinuria, admission BUN, hemoglobin (HGB), and hypotension during admission were predictive of AKI. After adjustment for significant univariable factors, age (OR 0.97 [0.96–0.99], p<0.001), admission BUN (OR 1.02 [1.01–1.04], p<0.001), and HGB (OR 0.79 [0.73–0.85], p<0.001) were significant in the multivariable analysis (Table 1).

Conclusions: We found that the age, admission BUN, and HGB were predictive of AKI in inpatient general medical units. These criteria can be used in acute general medical patients to create a scoring system to determine the likelihood of developing AKI and therefore prevent AKI and its downstream complications in these patients.

PO0076 Is Procalcitonin a Reliable Marker of Bacterial Infection in Patients with AKI? Mariam Charkviani, Sumit Sohal, Natia Murvelashvili, Maria Yanez Bello, Daniela Trelles, Alisha Sharma. Amita Saint Francis Hospital, Evanston, IL.

Background: Procalcitonin (PCT) is a biomarker that helps to distinguish bacterial infections from other causes of infection or inflammation and can be used as a helpful adjunct to clinical judgment for resolving diagnostic uncertainty. Limited data is available about the diagnostic value of PCT in patients with acute kidney injury (AKI). We aimed to assess the diagnostic usefulness of serum PCT level as a marker of bacterial infection in patients with AKI and assess the correlation of serum creatinine clearance to serum PCT level.

Methods: This retrospective case-control observational study involved patients admitted to the hospital during the study period and had PCT checked. Patients were categorized into proven, possible, and no bacterial infection groups. We compared PCT level in AKI group with proven bacterial infection vs no bacterial infection and PCT level during proven and no bacterial infection groups with AKI vs non-AKI. Patients with end-stage kidney disease and other causes of elevated PCT (pancreatitis, cancer, sepsis, etc.) were excluded.

Results: 379 patients were analyzed, 24 patients were excluded from the study. 66 patients classified into the AKI group and 226 into the non-AKI group. 107 patients were in a proven bacterial infection group and 98 Patients in no bacterial infection group. The mean value of PCT was significantly higher with confirmed bacterial infection compared to no bacterial infection in all patients despite their renal function (4.98±7.75 vs 1.66±4.88, p<0.001). PCT level was higher in the AKI group than in the non-AKI group (10.99±12.24 vs 2.39±2.93, p<0.001) in patients with a proven bacterial infection. Patients with no infection had much higher PCT level in the AKI group as compared to the non-AKI group (5.76±14.67 vs 0.71±1.39, p<0.003). PCT level was also significantly higher during confirmed bacterial infection vs no bacterial infection in patients with AKI (9.2±11.05 vs 0.7±2.17, p<0.04). There was a weak positive correlation between creatinine clearance and PCT level (correlation coefficient 0.125, p<0.15).

Conclusions: Higher cutoff level of PCT is needed in patients with AKI to use it as a marker of infection. The specificity of PCT may decrease in patients in AKI if current reference cutoff values are used to guide clinical decisions.


Background: While multiple studies have used statistical models to predict outcomes after AKI, no studies have compared these models to physician intuition at the time of AKI consult. We studied the accuracy of physicians in predicting outcomes after AKI and compared it to the strength of predictive statistical models.

Methods: Our pilot study focuses on the prediction of 3 outcomes after AKI: Recovery, progression to dialysis and mortality. Postgraduate years 4 and 5 level Nephrology providers were asked, at the time of initial renal consult, to forecast outcomes at 3 timepoints: 24hr, 48hr and 7 days. We compared physician prognosis to a gradient boosted trees model trained using retrospective EHR data. Our primary measure of performance was area under the receiver operating characteristic curve (AUCROC) at each time point.

Results: Data was captured from 56 patients with stage 2 AKI. Nephrology providers (<7) were good at predicting dialysis at all three timepoints and death at 48 hours and 7 days. In contrast, their ability to predict recovery of AKI was relatively poor. The statistical model performed significantly better at predicting death at all timepoints, however was poorer at predicting dialysis (Figure 1.0).

Conclusions: Both physician clinical acumen and our statistical model showed good performance in predicting need for dialysis and death after AKI, however performed poorly when predicting recovery. This highlights the need to conduct further in-depth analysis into this area and implement strategies to enhance prediction of recovery after AKI.

Funding: Other NIH Support - NIH R01DK113191

PO0078 Short-Term Prognosis of Patients with Cardiorenal Syndrome Type 1-Induced AKI Requiring Continuous Renal Replacement Therapy Yusuke Watanabe, Kei Sugiyama, Daichi Fukaya, Hiroaki Amano, Tsutomu Inoue, Hirokazu Okada. Saitama Medical University, Iruma-gun, Japan.

Background: Cardio-renal syndrome (CRS) type 1 is a condition wherein an acute heart failure (AHF) leads to the development of acute kidney injury (AKI). Continuous renal replacement therapy (CRRT) is used to remove excess solutes and fluids in CRS type 1 patients who have diuretic resistance. However, little is known about the outcomes of CRS type 1 patients who undergo CRRT.

Methods: We reviewed the clinical data of 74 consecutive CRS type 1 patients treated with CRRT from 2012 to 2015. Patients who underwent cardiovascular surgery and those who had chronic kidney disease stage 5 prior to admission were excluded. The primary outcome examined was in-hospital mortality.

Results: The mean age of patients was 70.6 ± 13.6 years old. The causes of AHF were ischemic heart disease (51.4%), valvular disease (13.5%), and other diseases. At the time of the CRRT initiation, the mean serum creatinine was 2.8 ± 1.0 mg/dL. The in-hospital mortality rate was 77.0%. Compared with non-survivors, the survivors had fewer number of previous hospitalizations for heart failure (50.9% vs. 23.5%, p = 0.046), higher systolic blood pressure (97.7 ± 22.2 mmHg vs. 112.3 ± 21.1 mmHg, p = 0.02), better ejection fraction (31.4 ± 17.9% vs. 42.0 ± 15.7%, p < 0.03), smaller inferior vena cava (IVC) diameter (18.0 ± 5.8 mm vs. 14.8 ± 4.4 mm, p = 0.04), less respiratory variations in the IVC diameter (59.6% vs. 49.9%, p = 0.04), lower serum vasopressor requirement (96.5% vs. 31.9%, p = 0.001), and lower respiratory support (36.1% vs. 23.5%, p = 0.02) at CRRT initiation. The survivors required a shorter CRRT duration over the non-survivors (6.1 ± 6.9 days vs. 11.7 ± 12.4 days, p = 0.03). Through the multiple logistic regression analysis, certain factors were associated with a poor short-term prognosis. These factors were history of previous hospitalizations for heart failure, vasopressor requirement upon start of CRRT, and the need for respirator support at CRRT initiation.

Conclusions: In our single-center experience, the use of CRRT for treating AKI caused by CRS type 1 was associated with a high in-hospital mortality rate. Patients with a history of previous hospitalization for heart failure, those who required vasopressors, and patients needing respirator support at CRRT initiation had an especially poorer prognosis.
PO0079

Roux-en-Y Gastric Bypass Is the Most Common Current Cause of Biopsy-Proven Oxalate Nephropathy

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Background: The objective of this study was to analyze patient characteristics and outcomes of biopsy-proven oxalate nephropathy likely due to an enteric cause at a single large tertiary health system.

Methods: Cases of oxalate nephropathy were identified based on documented kidney biopsy findings between 2009-2019 in patients with an associated enteric process likely to cause fat malabsorption.

Results: A total of 30 cases were identified (mean age of 65.2±8.56 years; 18(60.0%) female) with a median follow-up of 5 months; Risk factors included hypertension in 21(70%), diabetes in 14 (46.7%), chronic kidney disease (CKD) stage 3A or greater in 16(53.3%) and prior kidney stones in 6(20%). The most common enteric causes were Roux en Y gastric bypass (RYGB) in 17(56.7%), pancreatic insufficiency in 6(20%), inflammatory bowel disease in 4(13.3%), and recurrent C. difficile infection in 3(10%). At the time of diagnosis, acute kidney injury (AKI) stage II and stage III were present in 9 (30%) and 15 (50%) respectively, while 11(36.7%) required dialysis. Urinalysis revealed proteinuria in 16(53.2%), oxalate crystals in 10(33.3%), and hematuria in 9(30%). Median plasma oxalate at the time of biopsy was 18.3 (reference <2.01) μmol/L in 26 patients and median 24 hour urine oxalate excretion was 53 (reference [9.7-40.5]) mg/24 hrs in 17 patients. RYGB patients had a higher plasma oxalate compared to patients with other enteric causes (median 24.6 vs 16.5 μmol/L; p=0.03). Renal biopsy and clinical outcomes are shown in table1. Patients with acute tubular injury had greater number of tubules with calcium oxalate crystals by biopsy (median 19 vs 4), as did patients with CKD5 at last follow-up (20 vs 6). Features at the time of biopsy predictive of CKD5 at follow-up included AKI severity (p=0.002), dialysis at diagnosis (p=0.0008), and the presence of moderate to severe tubulointerstitial atrophy (p=0.001).

Conclusions: In this series RYGB was the most common enteric cause of biopsy-proven oxalate nephropathy. Severity of AKI at presentation and degree of tubulointerstitial fibrosis were both associated with worse renal outcome. The amount of renal crystal deposits at diagnosis associated with the short and long term renal injury.

Renal Histology (A) & Outcome (B)

PO0080

Impact of AKI on In-Hospital Outcomes in Chinese Patients with Community-Acquired Pneumonia

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Background: Acute kidney injury (AKI) is common in community acquired pneumonia (CAP). However, the impact of AKI on in-hospital outcomes of patients with CAP in the population of Chinese remains largely unknown.

Methods: Multiple Cox regression models were employed to identify the association between AKI and in-hospital mortality and 30-day mortality.

Results: 4213 patients were included, and 950 (22.5%) patients were AKI. The independent risk factors for AKI were age, male, hypertension, cardiac dysfunction, diabetes, chronic kidney disease, acute respiratory failure, diuretic, vasoactive drugs, and CURB-65. After multivariable Cox regression, independent risk factors of in-hospital mortality and 30-day mortality were similar: AKI, ACEI/ARB, hypertension, CURB-65, acute respiratory failure, and using vasoactive drugs. Patients developed AKI had worse in-hospital outcomes. Patients with AKI had increased 1.31-fold (HR 1.31, 95 % CI, 1.04–1.66, p< 0.001), non-invasive mechanical ventilation (25.9% vs. 5.8%; P < 0.001), invasive mechanical ventilation (25.4% vs. 7.1%; P < 0.001), and had a longer length of hospital stay (14 days vs. 10 days; P < 0.001) than those without AKI.

Conclusions: AKI was common in Chinese patients with CAP. Patients with CAP who developed AKI had worse in-hospital outcomes.
PO0082

Mortality Prediction of Serum Neutrophil Gelatinase-Associated Lipocalin in Patients Requiring Continuous Renal Replacement Therapy
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Background: We investigated whether serum neutrophil gelatinase-associated lipocalin (NGAL) can predict mortality in patients with acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT).

Methods: This study enrolled 169 patients who underwent serum NGAL testing at CRRT initiation from June 2017 to January 2019. The predictive power of serum NGAL level for 28-day mortality was compared to the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score and Sequential Organ Failure Assessment (SOFA) score via area under the receiver operating characteristic curve (AuROC) value.

Results: There were 55 survivors and 114 non-survivors at 28 days post-CRRT initiation. Median serum NGAL level was significantly higher in the non-survivor group than in the survivor group (743.0 vs. 504.0 ng/mL, P=0.003). The AuROC value of serum NGAL level was 0.640, which was lower than APACHE-II score and SOFA score values (0.767 and 0.715, respectively). However, in the low APACHE-II score group (<27.5), AuROC value of serum NGAL was significantly increased (0.698), and it was an independent risk factor of 28-day mortality (hazard ratio 2.405, 95% confidence interval (1.209-4.783), P=0.012).

Conclusions: In patients with AKI requiring CRRT, serum NGAL levels may be useful for predicting short-term mortality in those with low APACHE-II scores.

Funding: Government Support - Non-U.S.

PO0084

Prevalence, Length of Stay, and Hospitalization of AKI in Patients with and Without Sjogren Syndrome
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Background: Acute Kidney Injury (AKI) has emerged as a significant cause of morbidity and mortality in patients with autoimmune diseases. However, this has not been examined in patients with Sjogren’s syndrome (SJS). To achieve this, we examined the prevalence, mortality, outcomes, Length of Stay (LOS), and hospital charges in patients with AKI with SJS compared to patients without SJS from a National Inpatient Sample database in the period 2010-2013.

Methods: Data retrieved from the National Inpatient Sample (NIS) for adult patients admitted with a principal diagnosis of acute kidney injury between 2010 and 2013, using the respective ICD-9 codes. The study population divided into two groups, with and without Sjogren’s disease. Multivariate and linear regression analysis conducted to adjust for covariates.

Results: The study population represented 97,055 weighted patient discharges with acute kidney injury. Analysis revealed acute kidney injury patients with Sjogren’s compared to patients without Sjogren’s had statistically significant lower hyperkalemia rates (adjusted Odds ratio (OR)0.65, CI 0.46 to 0.92; p =0.017). There was no statistically significant difference in mortality, length of stay, hospital charges, and other outcomes. Moreover, The charges of hospitalization and length of stay were found to be statistically insignificant by the adjusted linear regression model. In addition, nearly three quarters of patients had Medicare, followed by privately insured patients with the least number being on Medicaid. More than half of the population have received their treatment in a tertiary center hospital. Charlson’s index reported more than two-thirds of study subjects to have two or more co-morbidities.

Conclusions: At present, our study is unique as it has examined the prevalence, mortality, and outcomes of Sjogren’s in patients with acute kidney injury. Patients with Sjogren’s has significantly lower hyperkalemia during the hospitalization. Further research is needed to identify the underlying protective mechanisms associated with Sjogren’s that resulted in lower hyperkalemia.

PO0085

Clinical Characteristics and In-Hospital Outcomes for 1519 Consecutive Patients with AKI
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Background: Acute kidney injury (AKI) occurs in about 15% of hospitalized patients. Patients who recover from AKI have a higher long-term risk of end-stage kidney disease and death. The aim of this large single center study was to report differences in lab testing findings and short-term hospital outcomes in relation to cause of AKI in consecutive patients in a nephrology department.

Methods: We conducted a retrospective chart review of patient data obtained via an electronic database created as part of the MRC’s program in conjunction with the health system’s electronic health record. Descriptive statistics were utilized to describe baseline characteristics. We restricted analyses to participants without end stage kidney disease on admission and those who survived at least 24 hours to allow for development of AKI. Kaplan-Meier plots were utilized to show death free survival by AKI category. All analyses were conducted using the R Statistical Computing Environment.

Results: We obtained data for 116 patients in the time period since 2015. Among the 116 patients, 55 patients had AKI defined as doubling of creatinine within 7 days but did not require RRT. Of the remaining 61 patients, 28 developed AKI requiring RRT. Patients who developed AKI or AKI requiring RRT had a mortality of 70% at 30 days. The remaining 33 patients who did not develop AKI had a mortality of 52% at 30 days. Regarding electrolyte derangements, cooling was associated with hypokalemia and hypophosphatemia with 64% percent of patients with potassium less than 3 mmol/L and 57% of patients with phosphorus less than 2 mg/dL.

Conclusions: AKI is associated with a high rate of mortality in this unique patient population, and additionally there is marked hypokalemia and hypophosphatemia in the setting of therapeutic cooling. Given the high mortality, this study raises questions regarding optimal treatment strategies for patients who develop AKI, including timing and delivery of RRT and the ideal approach to volume and electrolyte management.
Methods: All patients diagnosed with AKI between 2009 and 2018 and admitted to the nephrology department at Danderyd University Hospital, Stockholm, Sweden, were included. Relevant laboratory and physiological measures were registered. Patients on dialysis treatment were excluded. Patients were followed until discharge or death, whichever came first. 

Results: In 1519 AKI patients, the majority (n=687) was of prerenal, followed by combined (defined as chronic kidney disease combined with any type of AKI) (n=536), renal (n=166), and postrenal (n=130) etiology. Patients with renal AKI were younger, had longer duration of stay, and had higher bicarbonate levels on admission. 63.2% of patients had a sCr decrease of at least 30% from admission during their stay. Most of these had prerenal followed by postrenal etiology. There was no statistically significant difference in mortality between the four etiologies of AKI.

Conclusions: This study provides data from a large, contemporary AKI patient cohort under nephrology care. We confirm that patient characteristics as well as short-term outcomes differ substantially in patients of variable AKI etiology. Greatest in-hospital reduction of sCr was seen in patients with prerenal and postrenal AKI, whereas patients with renal combined AKI had poorer renal recovery. These findings have important implications for prognostic evaluation upon admission and further resource planning. 

Funding: Private Foundation Support

Characteristics of study population

PO0086

Traditional and Non-Traditional Risk Factors and Their Influence on In-Hospital Mortality in Community- vs. Hospital-Acquired AKI

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Background: Many studies compare hard outcomes in Community Acquired (CA-AKI) vs. Hospital Acquired AKI (HA-AKI), but few works contrast how various risk factors (RF) impact in-hospital mortality risk in both groups.

Methods: Retrospective study of in-patients with AKI. AKI was classified by KDIGO-2012 Stages. CA-AKI occurred in the first 48h, and HA-AKI >48h after admission. We compared clinical and epidemiological features, and the traditional RF (age, Charlson’s Index (ChI), ICU entrance, and AKI severity). We analyzed hyponatremia (Na) should be explored and modifiable factors should be tackled in order to prevent etiologies between cohorts. We conclude that these novel associations (e.g. anemia and AKI type, probably due to diverse baseline characteristics, evolution time, and AKI etiologies between cohorts). We conclude that these novel associations (e.g. anemia and haematocrit (Ht), had longer hospital stay, were less frequently admitted to medical wards, and less HD dependent at discharge. Mortality was significantly higher among HA-AKI vs. CA-AKI (31% vs.18% p<0.001). See Table 1. Traditional RF correlated with higher risk of death in both groups. Hypertension, heart failure and anaemia Max were associated with mortality in CA-AKI but not in HA-AKI. On the other side, HA-AKI had a higher risk of death associated with HtNa, which was not significant among CA-AKI patients. See Figure 2. 

Conclusions: We found that HA-AKI is more deadly than CA-AKI (consistent with previous studies), but shows lesser HD dependence at discharge. The traditional RF: older age, higher ChI, ICU admission, and AKI stage 3 influenced in-hospital mortality in both groups. Non-traditional RF showed an heterogeneous influence on outcomes according to AKI type, probably due to diverse baseline characteristics, evolution time, and AKI etiologies between cohorts. We conclude that these novel associations (e.g. anemia and HtNa) should be explored and modifiable factors should be tackled in order to prevent AKI mortality.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO0087

One-Year AKI Stage 3 Outcome in Elderly Patients at a Secondary Care Hospital in the United Kingdom

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Background: Elderly patients are prone to Acute Kidney Injury (AKI) 3 due to multiple co-morbidities and frailty. The short term and long term outcome and mortality in this group of patients is unclear.

Methods: We prospectively collected data on patients aged over 70 years with AKI 3 from the daily e-alert sent by the hospital biochemistry lab. 117 patients attended or admitted to secondary care hospital in West Kent, UK over 6.5 months between 13 December 2018 and 26 May 2019 were analysed and followed up for next 12 months. AKI 3 was defined as per KDIGO Criteria. Data was collected for age, co-morbidities, serum creatinine at admission, peak, discharge and 12 months, cause of AKI 3 and mortality. Exclusion criteria: AKI stage 1, stage 2 and patients on regular dialysis.

Results: 57% patients had community acquired and 43% developed AKI 3 while as in-patient. The mean age was 80.1 ± 6.2 years with co-morbidities of Chronic Kidney Disease (>3) 64.7%, Cardiovascular disease (CVD) 50%, Diabetes Mellitus 42.2% and Malignancy 8.7%. The stable baseline, peak and discharge s. creatinine (mean ± std dev) were 127.7 ± 85.6, 420.9 ± 222.7 and 248.5 ± 184.5 umol/L respectively. 59.5% patients were reviewed by nephrologists and 20.7% were transferred under renal care. 30.4% had oliguria at presentation. The reasons for AKI 3 were classified as pre-renal (59.48%), uraemic obstruction (11.2%) and renal that included sepsis (13.79%), cardio-renal syndrome (3.45%), drug induced nephrotoxicity (2.6%), other including ATN (9.70%). Renal function recovery was complete in 44.8%, Partial in 22.4% whereas 32.8% did not have any recover. 6 (5.17%) patients needed acute haemodialysis, of these 2 died and 4 (66.6%) were discharged off dialysis and were alive at 12 months. 47.4% patients were alive at discharge with s.creatinine of 173.2 ± 143.2 umol/L while only 32% of the overall patients were alive at 12 months with s. creatinine (eGFR) (mean ± std dev) 161.5 ± 172.1 (48 ± 28 ml/min) with mean follow up of 331 ± 112 days. All patients that did not recover from AKI died.

Conclusions: We conclude that short and long term outcome in patients with AKI 3 aged more than 70 years has high mortality at discharge (52%) and 12 months (68%). AKI 3 is common in patients with co-morbidities of CKD, CVD and Diabetes mellitus. Outcome of acute haemodialysis is effective in select group of patients.

PO0088

Urine Analysis and Urine Electrolytes Among Patients with COVID-19 Infection and AKI


Background: Determining intravascular volume status for patients who have COVID-19 infection and AKI is critical for guiding decisions about fluid management and treating AKI. In this study, we present data on urinalysis and urine electrolytes among patients with COVID-19 infection who developed AKI at our hospital.

Methods: This is a consecutive patients with COVID-19 who were diagnosed with AKI at our center in Spring of 2020 and had a urinalysis performed within 48 hours of diagnosis of AKI. When applicable we used Mann-Whitney test to compare groups.
**PO0089**

**Recovery of Renal Function Among Left Ventricular Assist Device Patients with Severe AKI Requiring Renal Replacement Therapy: A Meta-Analysis**

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**University of Mississippi Medical Center, Jackson, MS, Mayo Clinic Rochester, Rochester, MN.**

**Background:** Acute kidney injury (AKI) is a common and severe complication after left ventricular assist devices (LVAD) implantation with an incidence of 37%; 13% of which requiring renal replacement therapy (RRT). Severe AKI requiring RRT in LVAD patients is associated with high short-term and long-term mortality, compared with those without RRT. While recovery of renal function is associated with better outcomes, the rates of recovery of renal function among LVAD patients with severe AKI requiring RRT are unclear.

**Methods:** Ovid MEDLINE, EMBASE, and the Cochrane Databases were systematically searched from database inceptions through January 2020 to identify studies evaluating the rates of recovery from severe AKI requiring RRT after LVAD placement, which is defined by regained kidney function resulting in the discontinuation of RRT. Random-effects and generic inverse variance method of DerSimonian-Laird were used to combine the effect estimates obtained from individual studies.

**Results:** A total of 268 patients from 14 cohort studies with severe AKI requiring RRT after LVAD were enrolled. Follow-up time ranges from hospital discharge up to 12 months. 78.5% of renal recovery occurred at the time of hospital discharge or within 30 days. Majority (85%) of patients used continuous-flow LVAD. Overall, the pooled estimated rates of AKI recovery among patients with severe AKI requiring RRT was 50.5% (95%CI: 34.0%-67.0%), respectively. While the data on pulsatile-flow LVAD were limited, subgroup analysis of continuous-flow LVAD demonstrated the pooled estimated rates of AKI recovery among patients with severe AKI requiring RRT of 52.1% (95%CI: 36.8%-67.0%). Meta-regression analysis did not demonstrate a significant association between study year and AKI recovery rate (p = 0.08). There was no publication bias as assessed by the funnel plot and Egger’s regression asymmetry test in all analyses.

**Conclusions:** Recovery from severe AKI requiring RRT after LVAD occurs approximately 50.5%, and it has not significantly changed over the years despite advances in medicine.

**PO0090**

**Early Nephrologist Interventions to Avoid Kidney Replacement Therapy in AKI**

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**Background:** It is well known that early nephrologist involvement in patients with AKI improve outcomes. Determine which intervention has a greater impact on avoiding the need for KRT will be an important advance.

**Methods:** Our objective was to Identify which nephrologist intervention decrease the need of KRT. We analyze age, gender, comorbid conditions, cause of AKI, pharmacology therapy, cause of KRT, early interventions: fluid, antibiotic and nutritional adjustment, nephrotoxic withdrawal and removal of hyperchloremic solutions and death. Kaplan Meier survival analysis. Multivariable logistic regression model was performed. P< 0.05 which is significant.

**Results:** From 2017 to 2020 288 patients with AKI where analyzed prospectively with a 10 days follow-up, 45 (15%) patients die, overall survival of 84.4% (IC 95%:0.80 – 0.88) (Figure1). Only fluid adjustment decreases the risk of KRT (OR 0.75, 95% CI 0.68-0.81, p < 0.001) while having AKI KDIGO 3 increases the risk (OR 1.12, 95% CI 1.05-1.20, p<0.001)beingbelongtooverloadhemancauseofKRT(OR1.67,95%CI,53-1.82,p<0.001). Between all interventions, just fluid adjustment avoid progression to AKI KDIGO 3 (OR 0.76, 95% CI 0.65-0.89, p < 0.001). (Table1)

**Conclusions:** In AKI, fluid adjustment was the most important nephrologist intervention to avoid KRT.
PO0091

Usefulness of the Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in Community-Acquired AKI

Background: The neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) ratios have been identified as markers of inflammation and endothelial dysfunction. To date, its usefulness as prognostic markers in community-acquired acute kidney injury (CA-AKI) has not been evaluated.

Methods: We established a cohort of patients with CA-AKI admitted to our Nephrology service from January 2010 to February 2015. NLR and PLR ratios were obtained with the first analysis performed.

Results: We studied 308 patients with CA-AKI, 58% were men, mean age 75.22. Etiology of CA-AKI: prerenal 69.5%; renal 23.1%; obstructive 7.5%. AKI KDIGO stages: I, 14.6%; II, 11%; III 74.4%. CKD was detected in 68.8% 17.15% of cases required hemodialysis and 12.3% died. Mean NLR was 9.14 ± 8.47. Mean PLR was 236.99 ± 228.41. NLR according to etiology was: prerenal 8.55±8; renal 9.73±9.8; obstructive 13.99±14.82 (significant differences between obstructive and prerenal). PLR according to etiology: prerenal 228.31±216.34; renal 236.15±233.77; obstructive 320.37±304.89 (non-significant differences). Within the group prerenal, 79 cases were complicated by acute tubular necrosis (ATN). These cases presented a higher NLR (10.7±10.28 vs NLR 7.8±5.6; p=0.026). There were no significant differences between the PLR of both groups. The NLR showed a significant correlation with the peak creatinine (r=0.186; p=0.001) and the length of hospital stay (multiple linear regression analysis). Through correlations (r=0.134, p=0.018 and r=0.165, p=0.07). The NLR, but not the PLR, was associated with the length of hospital stay (multiple linear regression analysis). Through a multivariate binary logistic regression analysis, the variables that were independently associated with mortality during admission were the Liaño individual severity index and the NLR (OR 1.060; IC 95% 1.014 – 1.108). The best cut-off point of the NLR to predict mortality was 6.68 (AUC 0.584; sensitivity 0.60; specificity 0.58; Youden index 0.178)

Conclusions: In our CA-AKI patients cohort, the NLR was associated with the morbidity and the mortality. More studies are need to confirm this finding, but the easiness of obtaining it and its economic cost make it cost-effective, giving the NLR a leading role in assessing the risk of CA-AKI.

PO0092

Clinical Characteristics and Histologic Descriptions of Acute Tubular Injury: A Systematic Review
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Background: The term acute tubular injury (ATI) represents histopathologic renal tubular injury and often manifests clinically as acute kidney injury (AKI). Studies systematically summarizing the clinical presentation and histologic changes in human ATI are limited.

Methods: We comprehensively searched human studies of ATI from 1936 to July 2019. We extracted study characteristics, clinical characteristics and histologic descriptions of ATI by bright field, immunofluorescence or electron microscopy (EM) and by immunohistochemistry. We also compared histology of tubular cell injury as a function of tissue procurement timing and etiologies.

Results: We included 292 studies comprising of 1987 patients. The majority of studies (76%) were single center case reports. The mean age of patients included was 47 years old. 39.3% of patients had hypertension and 24.9% of them had diabetes mellitus. Baseline, peak and lowest creatinine were 1.29 mg/dL, 7.04 mg/dL and 1.86 mg/dL respectively. 48.9% of studies were native kidney biopsy cases, of which 86.7% were performed after serum creatinine peaked. There were significant amount of missing data in these clinical characteristics reported across studies. We identified 16 histologic criteria used to determine ATI. Criteria include the presence of any AKI on day 7 or, if death occurred before 7 days, death without AKI recovery. The Chi-square test was used to compare distributions between groups, if p<0.05 then a pairwise comparison between groups was made using the Chi-square test adjusted with Bonferroni correction.

Results: We found a total of 633 patients with severe AKI (53.6%) within 24h. The rate of severe AKI at 24h was different across phenotypes being highest in the delta and beta phenotypes (80.8% and 73.6% respectively), and lowest in the alpha phenotype (30.1%, overall p<0.0001). Greater CKD was most common in the beta phenotype (52.8%, overall p<0.0001) while in the others was lower (31.4% in alpha, 26.8% in gamma, and 35.0% in delta). The highest prevalence of AKI with CKD was again in the beta phenotype (52.0%, overall p<0.0001). AKD occurred more often in the delta (57.4%) and beta (50.0%) phenotypes compared to alpha (25.0%), gamma (26.6%), or delta (34.8%, p<0.0001). AKD occurred more often in the delta (57.4%) and beta (50.0%) phenotypes compared to alpha (32.7%) and gamma (40.1%, p=0.0002).

Conclusions: Severe AKI was significantly more common among patients with beta and delta phenotypes. However, the beta phenotype had a higher level of underlying CKD that predisposed to new AKI. Alpha and gamma phenotypes not only had lower rates of AKD, but these cases were less likely to progress to AKD.

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PO0094
Comparison of Clinical Characteristics of AKI in Patients with Glyphosate and Glufosinate Herbicide Poisoning
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Background: This study aimed to investigate the clinical characteristics of acute kidney injury in patients with glyphosate and glufosinate herbicide poisoning.

Methods: From 2008 to 2019, 230 patients admitted to our hospital after glyphosate or glufosinate intoxication were included in this study. Clinical characteristics, laboratory data, and medical outcomes were analyzed. Patients were divided into two groups: glyphosate and glufosinate groups. The study was limited to patients with acute kidney injury (AKI) and excluded patients with diabetes or chronic kidney disease. Demographic data, laboratory data, and medical outcomes were compared between the two groups.

Results: The study included 230 patients, of which 133 were in the glyphosate group and 97 were in the glufosinate group. The incidence of AKI was 13.9% in the glyphosate group and 10.3% in the glufosinate group. The glufosinate group had a higher prevalence of AKI compared to the glyphosate group (p=0.04). There were significant differences in the levels of serum creatinine, blood urea nitrogen, and serum potassium between the two groups. The glufosinate group had higher levels of serum creatinine and blood urea nitrogen, and lower serum potassium levels compared to the glyphosate group.

Conclusions: Glyphosate and glufosinate herbicide poisoning have different clinical characteristics, and the glufosinate group has a higher incidence of AKI.

PO0095
Clinical Significance of Hypoalbuninemia for AKI in Patients with Scrub Typhus
In O Sun, A young Cho. Presbyterian Medical Center, Jeonju, Jeollabuk-do, Republic of Korea.

Background: The aim of this study is to investigate the clinical significance of hypoalbuninemia for acute kidney injury in patients with scrub typhus.

Methods: From 2009 to 2018, 611 patients were diagnosed with scrub typhus. We divided the patients into two groups (normalalbuminemia vs. hypoalbuninemia) based on the serum albumin level of 3.0 g/dL. We compared the occurrence of AKI, clinical characteristics, and severity of acute kidney injury based on RIFLE classification between the two groups.

Results: Of the total 611 patients, 78 (12.8%) were categorized as hypoalbuminemia group. Compared with patients in normalalbuminemia group, patients in hypoalbuminemia group showed higher incidence of AKI (26.5% vs. 11.5%, p<0.01), and higher total leukocyte counts (10.2 × 10^3/mL vs. 6.7 × 10^3/mL, p<0.01). Hypoalbuminemia group showed significantly longer hospital stay (9.6 ± 6.1 vs. 6.1 ± 3.0, p<0.01) and higher incidence of complications in respiratory system (50% vs. 14%, p<0.01), cardiovascular system (28% vs. 11%, p<0.01), neurologic system. Furthermore, acute kidney injury (58% vs. 18%, p<0.01) was also developed in hypoalbuminemia group. The overall incidence of acute kidney injury was 23.1%; of which, 14.9%, 7.0% and 1.2% were classified as Risk, Injury and Failure, respectively. The serum albumin level correlated with acute kidney injury severity (3.4 ± 0.5 vs. 3.0 ± 0.5 vs. 2.6 ± 0.3, p<0.05). In a multivariate logistic regression analysis for predicting acute kidney injury, age, presence of co-morbidities such as chronic kidney disease, diabetes, or hypertension, total bilirubin, leukocytosis and hypoalbuminemia were significant predictors of acute kidney injury.

Conclusions: Hypoalbuminemia was closely associated with scrub typhus associated with acute kidney injury.

PO0096
Risk Factors for Patient Subgroups with Distinct Health Utility Profiles Following AKI
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Background: Health-related quality of life (HRQOL) after dialysis initiation for acute kidney injury (AKI) is low. We sought to determine patient subgroups with distinct health utility profiles at 60 days after diagnosis of AKI and evaluated the potential risk factors associated with subgroup membership.

Methods: The Biologic Markers of Renal Recovery for the Kidney (BioMaRK) study is an observational cohort of patients nested within the Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network study. Clinical characteristics and biomarkers of inflammation were collected from 817 patients with AKI around the time of hospital admission. The serum bicarbonate level was lower in glufosinate intoxication than in glyphosate intoxication (19.8 ± 4.3 vs. 21.5 ± 3.9, p<0.01). In comparison with patients of glyphosate intoxication, patients with glufosinate poisoning experienced increased inflammation (59.6% vs. 19.7%, p<0.01) and intensive care unit admission (66.8% vs. 38.2%, p<0.01) more frequently. The overall incidence of acute kidney injury was 38.3% in this study, and there was no difference between two groups (35.8% vs. 45.6%, p=0.123).

Results: Patients with glufosinate intoxication showed more severe type of clinical manifestation and intensive care unit admission rates than glyphosate intoxication.

Conclusions: Patients with glufosinate intoxication showed more severe type of clinical manifestation and intensive care unit admission rates than glyphosate intoxication.
PO0099
Design of START: A Phase 2 Study Evaluating the Safety and Efficacy of RBT-1 on Preconditioning Response Biomarkers in Subjects Undergoing Cardiac Surgery
Bluhpinder Singh,1,2 Philip T. Lavin,1 Andreas Orfanos,2 Stacey Ruiz,2 Donald J. Keyser,1 Alvaro F. Guilleum,2 Richard A. Zager,3,4 Navdeep Tangri,3 Jean-Claude Tardif1,5 University of California Irvine, University of California Irvine, Irvine, CA, US, Department of Medicine, Irvine, CA; 1Renibus Therapeutics, Southlake, TX; 2Montreal Health Innovations Coordinating Center, Montreal, QC, Canada; 3Fred Hutchinson Cancer Research Center, Seattle, WA; 4University of Washington Department of Medicine, Seattle, WA; 5University of Manitoba, University of Winnipeg, MB, Winnipeg, MB, Canada; 4Institut De Cardiologie de Montreal, Montreal, QC, Canada; 4Boston Biostatistics Research Foundation, Framingham, MA.

Background: Cardiac surgery is associated with an increased risk of acute kidney injury (AKI). RBT-1 induces non-ischemic tissue preconditioning that has shown organ protective effects in several animal models of AKI. Markers of cytoprotection observed with RBT-1 treatment in animals were also found to be upregulated in a Phase 1 study of RBT-1 in healthy volunteers and subjects with Stages 3 and 4 chronic kidney disease (CKD). Based on these data, we have designed a Phase 2, placebo-controlled, double-blind, randomized, multicenter study that will assess the effect of RBT-1 on preconditioning response biomarkers in subjects scheduled to undergo cardiac surgery.

Methods: Study Design: This study will enroll 126 subjects scheduled to undergo coronary artery bypass graft (CABG) and/or cardiac valve surgery. Eligible subjects will be randomized to receive a single dose of RBT-1 or placebo via intravenous infusion between 24 and 48 hours prior to scheduled cardiac surgery. Subjects will be followed through Day 90. Inclusion/Exclusion Criteria: Subjects eligible for enrollment include adults who are scheduled to undergo non-emergent, on-pump coronary artery and/or cardiac valve surgery. Major exclusion criteria include CKD with eGFR ≤ 20 mL/min/1.73m2 or need for dialysis.

Results: Objectives: The primary objective of this study is to evaluate the efficacy of RBT-1 on preconditioning response biomarkers from baseline through Day 3 post-cardiac surgery. Based on preclinical data, plasma heme oxygenase-1 (HO-1), ferritin, and interleukin-10 (IL-10) have been identified as the relevant biomarkers for this study. Secondary objectives include change in tubular injury biomarkers and incidence of AKI based on KDIGO classification. Exploratory objectives include the occurrence of major adverse kidney events (MAKE) through Days 30 and 90.

Conclusions: The multinational START study will assess the cytoprotective preconditioning response to RBT-1 in subjects undergoing cardiac surgery.

Funding: Commercial Support - Renibus Therapeutics

PO0100
Acute Peritoneal Dialysis During the COVID-19 Pandemic in New York City
Nina J. Caplin,1,2 Manish Tandon,1,2 Olga Zhdanova,1 Richard Amerling,3 Nathan Thompson,1 NYU Langone Health, New York, NY; 2Bellevue Hospital Center, New York, NY; 3Saint George’s University, Saint George, Grenada.

Introduction: The dramatic spread of COVID-19 in March 2020 threatened to overwhelm ICU capacity. At the peak we had more than 120 patients in the ICU. About 40% of the ICU patients required RRT due to AKI. Our ability to provide RRT with CVVH and IHD was severely limited by critical shortages of equipment and personnel. We rapidly established an acute PD program at Bellevue Hospital for AKI patients. The acute PD program turned out to be instrumental in the BH response to COVID-19.

Case Description: Patients
All patients who needed RRT in the ICU were eligible for PD. PD was performed manually every 1-2 hours. Eventually we acquired 18 cyclers which greatly improved to 24 hours per day. Exchanges were initially performed manually every 1-2 hours. Eventually we acquired 18 cyclers which greatly eased the workload. Outcomes
As of May 8, 2020 63 patients were evaluated, 38 PD catheters were placed with 35 used for exchanges. 2 patients had catheters placed but recovered renal function prior to starting PD. I/38 was nonfunctioning and changed to IHD. 15/38 survived >30 days; 8 recovered renal function; 20 expired <30 days.

Discussion: Because of the shortage of our typically used dialysis modalities we were compelled to start an acute PD program. No patient on PD required additional dialytic support with BID or CVVH. PD was well tolerated by ventilated patients with hemodynamic instability. Acute PD more than adequately filled the gap in treatment options during this unprecedented crisis.

PO0101
Novel Prescription of Continuous Venovenous Hemodialysis Dialysate Na+ in a Patient with Cerebral Edema and Severe Hypernatremia
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Introduction: AKI necessitating dialysis is difficult in patients with traumatic brain injury. Slow clearance and increased dialysate Na+ are recommended. Yet, barriers in adjusting dialysate Na+ may occur with premixed commercial dialysate. We present a unique method of prescribing CVVHD to prevent Na+ overcorrection in a patient with cerebral edema and severe hypernatremia.

Case Description: An 18 year old male presented with polytrauma after a motor vehicle accident. His injuries included multiple intracranial bleeds. On day 13, nephrology was consulted for AKI, BUN > 150 mg/dl, and refractory hypekalemia. Head CT scan showed known bleeds and diffuse cerebral edema. At consult, IV 3% saline had already resulted in plasma Na+ ranging 161-166 meq/L for > 3 days. Our hospitals perform CVVHD via NStage with commercial dialysate bags with Na+ fixed at 140 meq/L. To prevent Na+ overcorrection, a custom commercial bag with 3% saline was in-circuit. Initially, clearance goals were set by dialysate flow rate. Then, separate IV pump for 3% saline was Y connected to the pre-pump dialysate line, and IV pump rate was calculated to adjust final dialysate Na+. Final dialysate flow equal to IV pump flow plus residual draw from commercial bags. Our initial goal dialysate Na+ was 160 meq/L. Dialysis solution bags steadily showed adjusted Na+ of about 158 meq/L at initiation. Changes to other dialysate factors (i.e. K+, HCO3-) were negligible. CVVHD was started with titration of the dialysate-attached 3% saline IV pump to control of Na+. All other 3% saline was discontinued. Though the patient ultimately died from overall injuries, change in plasma Na+ was slow and controlled (10 meq in 7 days).

Discussion: We present a new method for adjusting dialysate Na+ using in-circuit mixing of commercial dialysate and 3% saline. Our method used readily available solutions, was easy to titrate, depended solely on dialysis, and did not require manipulation of commercial bags. We suggest consideration of our method in CVVHD, brain trauma, and hypernatremia.
increased to 60 mg/dl. Kidney function did not improve even after 2 months and re-biopsy revealed ongoing interstitial inflammation in IgAN. Consequently, the patient was given a trial of azathioprine 200 mg daily with reduced prednisolone dose (40 mg/dl). Creatinine levels decreased moderately after 2 weeks to 1.70 mg/dl due to which the prednisolone dose was further tapered to 20 mg/dl.

Discussion: In past, azathioprine has shown promise in treatment of lupus nephritis and IgA nephropathy. To our knowledge, this is the first reported case of successful treatment of steroid resistant severe drug induced AIN with azathioprine. As it has lesser side effects and better compliance than steroids, it is suggested that azathioprine may be considered as initial or alternative form of treatment for AIN. Larger, randomized clinical trials need to be conducted in order to establish optimal dosing and long term effectiveness of azathioprine in treating AIN.

**P00103**

The Successful Treatment of Bile Cast Nephropathy with Plasma Exchange

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Introduction: Bile cast nephropathy is a condition of renal dysfunction in the setting of hyperbilirubinemia. There are very few cases of this condition reported in literature, and there is a lack of established treatment guidelines. We report the successful management of two patients with bile cast nephropathy using therapeutic plasma exchange (TPE).

Case Description: CASE 1: A 59 year old man with stage 3 colon carcinoma on Capecitabine developed chemotherapy-induced liver toxicity resulting in severe cholestasis and biopsy-proven bile cast nephropathy. He underwent TPE. CASE 2: A 69 year old African American woman with PSC and colon cancer post a remote colectomy was admitted with pruritus and acute kidney injury (AKI). CT abdomen without contrast showed a 6 cm liver mass with bile duct dilatation, a biopsy proven metastasis from his previous colon cancer. A kidney biopsy confirmed bile cast nephropathy. The patient was started on hemodialysis (HD), and a biliary stent was placed. He was treated with TPE. He opted for hospice due to cancer CASE 3: A 38 year old man was admitted with severe acute alcoholic hepatitis and AKI. A kidney biopsy confirmed bile cast nephropathy. He underwent TPE and a total of four sessions of HD. The clinical course in our patients with biopsy proven bile cast nephropathy post and after TPE therapy is noted in Table 1.

Conclusion: Bile cast nephropathy is a rare entity, presenting a challenge in management. Thrombocytopenia, hepatic insufficiency, coagulopathy, and antiphospholipid antibodies are common with this condition, posing a challenge in case management. In our series, the patients had acute liver and kidney failure with no underlying chronic liver disease. 1-2 plasma volume exchange was performed with each procedure with a combination of plasma and 5% albumin. A good response to TPE in decreased total bilirubin level and improvement in renal function was noted. There were no serious adverse events and all procedures were tolerated well by the patients. Medical management of bile cast nephropathy such as steroids and cholestyramine have shown limited or no benefit. Renal replacement therapy has also been shown to be of limited benefit and should be mainly instituted for the treatment of AKI. In bile cast nephropathy, TPE may help in the clearance of bile acid crystals and reduction of proinflammatory molecules which contribute to acute liver and kidney injury. In this small case series, institution of TPE appeared to improve the clinical course of patients with bile cast nephropathy.

**P00104**

An Unusual Case of IgA Nephropathy Associated with Parvovirus B19

Laila S. Lakhan, Hashim Abbas, Mohamed G. Atta. Johns Hopkins University, Baltimore, MD.

Introduction: Parvovirus is known to cause upper respiratory infections in children and the immunosuppressed. It's association with kidney disease has been sporadically reported in literature, mostly causing lupus like glomerulonephritis with endocapillary and the immunosuppressed. It's association with kidney disease has been sporadically reported in literature, mostly causing lupus like glomerulonephritis with endocapillary and the immunosuppressed.

Case Description: A 23 year old African American female with a history of Hemoglobinopathy due to maternal sickle cell disease presented with a 1 week of generalized edema and malaise. Initially, she was found to have non-oliguric AKI with Creatinine 2.5 mg/dL (baseline Cr: 0.6 mg/dL). Serologies were notable for normal Complements, negative ANA, anti-cardiolipin-IgM and direct antiglobulin. The serum and urinary Immunofixation and serum cryoglobulinemia tests were all negative, while the serum κ to λ light chain ratio was depressed to 0.231. A renal biopsy conducted on day 9 revealed a diffuse proliferative glomerulonephritis with intracapillary pseudo-thrombi formation with orderly arranged microtubular structures of 20-35 nm in diameter in the subendothelial and mesangial area on electron microscopy. The patient developed on day 13 symmetrical finger-tip numbness and tingling with weaknesses in her hands and legs. She was started on hemodialysis (HD), and a biliary stent was placed. He was treated with TPE.

Conclusion: Parvovirus B19 is an RNA virus and is known to cause conditions such as Parvovirus IgM and detectable Parvovirus DNA. She was started on Pulse dose steroids; azathioprine 200 mg daily with reduced prednisolone dose (40 mg/dl). Creatinine levels decreased moderately after 2 weeks to 1.70 mg/dl due to which the prednisolone dose was further tapered to 20 mg/dl.

Discussion: In past, azathioprine has shown promise in treatment of lupus nephritis and IgA nephropathy. To our knowledge, this is the first reported case of successful treatment of steroid resistant severe drug induced AIN with azathioprine. As it has lesser side effects and better compliance than steroids, it is suggested that azathioprine may be considered as initial or alternative form of treatment for AIN. Larger, randomized clinical trials need to be conducted in order to establish optimal dosing and long term effectiveness of azathioprine in treating AIN.

Discussion: This case provides an example of AKI associated with Parvovirus infection. Parvovirus B19 is present in 3% of American Blacks but only 0.3% of African Americans were included in the cohort on which the Oxford Classification was coined. The improvement in acute kidney injury with a short course of steroids is suggestive of Parvovirus related process more than the typical endocapillary proliferation related to IgAN. The extension of Oxford Classification in the African American population can thus be challenging and potentially misleading as seen in this case. A repeat renal biopsy may be warranted to assess the underlying diagnosis of IgANephropathy and should be treated based on findings.
between an uncommon genetic mutation and a rare diagnosis. In this patient, the fact of him being homozygous for PAI-1 4G allele led to arterial occlusion. The patient was transferred to CCU and started on clevidipine and heparin blood. Creatinine was 1.6 and the baseline was unknown. CTA showed right renal artery occlusion. The patient was transferred to CUC and started on clevidipine and heparin drip. Arteriogram and directed thrombolysis were performed. Despite these interventions, his creatinine trend peaked at 2.85, whereas hemoglobin started dropping substantially. High rate IV fluids, a workup for malignancy, and hypercoagulable were started with subsequent stent placement for reperfusion. After 3 days of directed thrombolysis, he was transferred to wards. Urine output decreased and a Foley catheter was placed. The patient was started on clonidine, amlopidine, and labetalol. After 10 days of hospitalization, all workup was unremarkable. PAI-1 4G/5G study was homozygous for 4G allele. The patient’s medical condition improved. He was discharged and advised to follow up as an outpatient.

Case Description: A 53 years old male with hypertension, presented to the emergency room complaining of abdominal pain and pink urine for 3 days. His BP was 186/120 mmHg and pulse 100/min. Physical exam was consistent with right flank tenderness. Urinalysis showed high gravity, high amount of protein and blood. Creatinine was 1.6 and the baseline was unknown. CTA showed right renal artery occlusion. The patient was transferred to CCU and started on clevidipine and heparin drip. Arteriogram and directed thrombolysis were performed. Despite these interventions, his creatinine trend peaked at 2.85, whereas hemoglobin started dropping substantially. High rate IV fluids, a workup for malignancy, and hypercoagulable were started with subsequent stent placement for reperfusion. After 3 days of directed thrombolysis, he was transferred to wards. Urine output decreased and a Foley catheter was placed. The patient was started on clonidine, amlopidine, and labetalol. After 10 days of hospitalization, all workup was unremarkable. PAI-1 4G/5G study was homozygous for 4G allele. The patient’s medical condition improved. He was discharged and advised to follow up as an outpatient.

Discussion: Studies have proven the link between PAI-1 4G and thrombotic events, however, most of the evidence shows a link between PAI-1 4G and venous thrombosis. In this patient, the fact of him being homozygous for PAI-1 4G allele led to arterial thrombosis. Therefore, it might be prudent to include a PAI-1 workup in prothrombotic studies. In renal artery thrombosis, a cause must be established. Although there are other common causes of arterial thrombosis, PAI-1 4G should be considered as a potential cause in patients with few or no risk factors. This case report glimpses the relationship between an uncommon genetic mutation and a rare diagnosis.

Discussion: Cannabinoids are found in natural marijuana and contain many active compounds, but delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) are of most interest. THC is the primary ingredient in marijuana that makes people “high”. Synthetic cannabinoids are analogs of natural occurring cannabinoids that are chemically synthesized. This synthetic compound is added to the natural marijuana or other herbs to appear as a natural product. The clinical effects can be like natural marijuana which include tachycardia, conjunctival injection, slurred speech, and increase appetite due to the partial or full agonistic effect at the cannabinoid receptors. Compared to cannabis, synthetic cannabinoids have a greater risk for serious neuropsychiatric toxicity and severe acute kidney injury. We need more clinical research to identify the specific nephrotoxic agents.

Discussion: Synthetic cannabinoids (SC), “Ganja”, have been used as recreational drugs with increasing frequency among young adults but have significant toxicity. We present a case of acute kidney failure in a relatively healthy young male individual after using marijuana pills.

Case Description: 31-year-old Hispanic male with no known past medical history presented to the emergency room with nausea and vomiting for 2 days. He stated that he has recently started taking “Ganja” pills to help with relaxation after losing work due to the Covid-19 pandemic. Vital signs were within normal limits and physical findings were unremarkable. Laboratory data were significant for serum creatinine of 10.14 mg/dl, blood urea nitrogen of 91 mg/dl, estimated glomerular filtration rate of 8 mL/minute per 1.73m², and serum potassium of 7 meq/l. Urine toxicology was positive for cannabinoids. Complements and serologies were all negative. Renal ultrasound was unremarkable. A renal biopsy showed acute tubular injury with tubular dilatation, cytoplasmic simplification and vacuolization (image). Interstitial hemodilution was initiated but later discontinued after renal recovery. On discharge, serum creatinine was 1.2 mg/dl.
PO0110

The Emerging Role of Bedside Doppler Ultrasound for Precise Assessment of Venous Congestion in Cardiorenal Syndrome
Abhilash Koratala,1 Saqib Mahmud,1 Olanrewaju A. Olaoye,2 Amir Kazory,2 1Medical College of Wisconsin, Milwaukee, WI; 2University of Florida, Gainesville, FL.

Introduction: Congestion is an integral component of cardiorenal syndrome and the primary reason for hospitalization in patients with heart failure (HF). Making it a key target in the management of these patients. Routinely used parameters to monitor response to decongestive therapy such as physical examination, B-type natriuretic peptide changes in weight and net fluid balance, even inferior vena cava ultrasound (IVC US) are all error prone. Doppler ultrasonography (DUS) of the portal, hepatic and when possible, intrarenal veins is an attractive alternative that can be used at bedside to accurately assess the degree of congestion and guide management strategies.

Case Description: A 55-year-old man with a history of HF with reduced ejection fraction of ~25%, hypertension and chronic kidney disease stage 3 presented with acute kidney injury of uncertain etiology. Serum creatinine (Scr) was 3.5 mg/dL for a baseline of 1.6 mg/dL. He had no symptoms except for his usual dyspnea on exertion. Physical examination was significant for crackles at lung bases and mild pitting pedal edema. Bedside US revealed increased extravascular lung water and a dilated but collapsible IVC. DUS revealed stigmata of severe congestion with a pulsatile portal vein and systolic flow reversal, and a hepatic vein with only diastolic (D) component below the baseline. Therefore, the diagnosis of congestive renal failure due to acute cardiorenal syndrome was made and high dose intravenous diuretics were initiated. The follow up DUS on days 3 and 5 showed remarkable improvement (reversal of waveforms to normal pattern) indicating progressive decongestion [Figure]. His diuretic therapy was titrated based on these findings and Scr improved to 2 mg/dL at discharge.

Discussion: Bedside DUS assessment of hepatic and portal veins aids in management of patients with HF by non-invasively monitoring the efficacy of decongestive therapy, and serves as a valuable adjunct to conventional clinical evaluation.

PO0111

Furosemide: An Unusual Cause of Acute Interstitial Nephritis Requiring Hemodialysis: First Case Report
Hassan Alhalabi, Dallas Nephrology Associates, Irving, TX.

Introduction: Furosemide, a loop diuretic, is widely used for volume control and is a known cause of acute interstitial nephritis. However, AIN due to furosemide is not typically associated with abrupt and severe acute kidney injury (AKI). Here we report a patient who developed severe AKI requiring hemodialysis shortly after receiving furosemide.

Case Description: A 65 year old male with a history of hypertension was started on oral furosemide 20 mg daily for edema in his legs. One week later he presented to the emergency room complaining of oliguria and worsening edema. Laboratory findings were significant for a serum creatinine of 37.8 mg/dl and potassium 7.8 mmol/L. Patient required emergent hemodialysis for volume control, clearance and hyperkalemia, and continued to require HD every other day. Serologic work-up included a normal C3, C4, ANA, ANCA, anti-GMB, and SPEP/UPEP. Urinalysis showed small blood, no protein, 12-15 RBC’s, 10 WBC’s. Renal ultrasound was normal. A kidney biopsy was deferred. After starting levothyroxine, complete renal recovery was seen in 2 patients and partial recovery in one within 8 weeks (Table 1).

Discussion: AIN has been reported in patients with severe hypothyroidism, and most cases were suspected to be due to rhabdomyolysis and had rapid normalization. Few cases of slower and incomplete recovery have been noted in cases with prolonged periods of severe hypothyroidism. In our series, normal urinalysis, absence of myoglobin, and normal or modest elevation of CPK makes rhabdomyolysis unlikely. The AKI could be due to hypothyroidism induced changes in renal hemodynamics. Our study relies on eGFR for renal function, and extent to which this reflects true changes in GFR is unclear. Hypothyroidism is a reversible cause of AKI and should be evaluated in cases with unexplained AKI. These patients can attain normal renal function with prompt initiation of levothyroxine therapy.

PO00112

Hypothyroidism-Induced AKI: A Case Series
Spoonri Ramini, Varun Kumar Bandi. Dr. Pinnamaneni Siddhartha Institute of Medical Sciences & RF, Gannavaram, India.

Introduction: Thyroid hormones affect the development and various functions of the kidney. Such effects are partly mediated by direct renal action and partly by cardiovascular and systemic effects.

Case Description: We present a series of 3 patients who presented with unexplained acute kidney injury (AKI). All patients were male, and one was hypertensive on amlopidine. Investigations showed blood urea levels ranging from 20 to 88 mg/dl, serum creatinine between 1.3 to 3.65 mg/dl with estimated glomerular filtration rate (eGFR) of 17.88 to 63.18 mL/min/1.73m2. Urine routine and ultrasound abdomen did not reveal any abnormalities. The patients had features suggestive of hypothyroidism and thyroid evaluation was done. Thyroid stimulating hormone (TSH) was elevated in all patients and T3 and T4 were decreased. The TSH levels ranged between 88.4 to 100 mIU/L. Creatine phosphokinase (CPK) level was modestly elevated in only one case, with absent urine myoglobin in all cases. A possibility of hypothyroidism induced AKI was considered and renal biopsy was deferred. After starting levothyroxine, complete renal recovery was seen in 2 patients and partial recovery in one within 8 weeks (Table 1).

Discussion: AKI has been reported in patients with severe hypothyroidism, and most cases were suspected to be due to rhabdomyolysis and had rapid normalization. Few cases of slower and incomplete recovery have been noted in cases with prolonged periods of severe hypothyroidism. In our series, normal urinalysis, absence of myoglobin, and normal or modest elevation of CPK makes rhabdomyolysis unlikely. The AKI could be due to hypothyroidism induced changes in renal hemodynamics. Our study relies on eGFR for renal function, and extent to which this reflects true changes in GFR is unclear. Hypothyroidism is a reversible cause of AKI and should be evaluated in cases with unexplained AKI. These patients can attain normal renal function with prompt initiation of levothyroxine therapy.

Characteristics of patients

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PO00113

Glomerular Congestion Secondary to Renal Vein Stenosis After Kidney Transplant
Muna Alnimiri. University of California Davis Department of Internal Medicine, Sacramento, CA.

Introduction: Renal vein stenosis (RVS) post kidney transplant is uncommon complication, especially when it causes severe glomerular congestion, and AKI. We present a case of RVS 3 months post kidney transplant with kidney biopsy showing severe glomerular congestion

Case Description: 33 y old male CKD secondary to HTN underwent LKT, smooth post op course discharged with a creatinine of 1.1 mg/dl presented for 3 months protocol biopsy with creatinine of 1.5mg/dl, kidney biopsy showed severe glomerular congestion. No rejection figure1, Doppler US showed suspicion for renal vein stenosis. Renal venogram demonstrated narrowing of the transplant renal vein at the anastomosis with the right common iliac vein figure 2 Successful 10 mm angioplasty balloon was inflated along the narrowed segment follow up creatinine back to 1.1mg/dl

Discussion: Transplant RVS is a rare vascular complication after renal transplantation that may cause graft dysfunction. Correction of RVS with either angioplasty or stent placement is safe and effective approach. Our patient presented with AKI and severe glomerular congestion that warranted doppler US, the finding of RVS and glomerular congestion from back pressure warranted urgent venogram and angioplasty with excellent results. Conclusion: in evaluating AKI post kidney transplant ureteral obstruction, rejection, CNI toxicity and renal artery stenosis should be ruled out if all negative RVS should be evaluated.
AKI Clinical, Outcomes, and Trials - 2

Brain Got Spongy at Angry Kidneys

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Introduction: Brain edema is a rare complication of acute kidney injury in patients who have not received renal replacement therapy. Immunologic and pro-inflammatory cascades mediate brain edema that is not dependent on the uremia, and instead, it is due to crosstalk between the kidneys and brain in the so-called reno-cerebral reflex. We are presenting an 88-year-old female with a history of hypertension and hyperthyroidism with acute colitis that developed acute kidney injury and cerebral edema. We want to raise awareness of the need for early diagnosis and treatment to prevent severe clinical outcomes.

Case Description: 88-year-old female with a past medical history of hypertension, hyperthyroidism came to the ER complaining of green-colored non-bloody diarrhea for 2 days. Examination remarkable for left lower quadrant tenderness, tachycardia, altered, awake, oriented to person only, cooperative and following commands. Labs were remarkable for leukocytosis with neutrophilia, fecal leukocyte positive, and metabolic alkalosis. Abdominal CT showed acute colitis localized to descending colon and sigmoid. The patient was admitted with acute colitis. On day 2 of admission creatinine went up to 2.35 from 1.07. On urine, sediment was evident with renal tubular epithelial cells and oxalate crystal. Renal sonogram with no renal abnormality. On day 3 the creatinine continued increasing doubled to 4.4. The patient’s mental status started declining, and metabolic acidosis was present. Renal replacement therapy was advised, but the patient’s family refused it and signed off DNR. The mental status started declining, and metabolic acidosis was present. Renal replacement therapy was advised, but the patient’s family refused it and signed off DNR. The patient was initiated on hemodialysis. Evaluation of AKI with hepatitis B and C serologies, HIV, complement levels and ANA was unremarkable. Kidney ultrasound showed increased echogenicity without hydronephrosis. An abdominal CT scan with IV contrast done for worsening fever and leukocytosis showed diffuse areas of non-enhancement involving bilateral renal cortices consistent with acute renal cortical necrosis.

To note, throughout his presentation and admission, the patient was not hypotensive. He remained dialysis dependent for three months with oliguria that eventually improved and dialysis was discontinued with a stable eGFR of 1.73ml/min. He has remained off dialysis for the past five months and is undergoing transplant evaluation.

Discussion: RCN is thought to be an irreversible cause of AKI secondary to decreased perfusion, vasoospasm and endothelial injury resulting in sclerosis. It is frequently associated with hypotension but in our case the patient was normotensive. The mechanism leading to RCN associated with pancreatitis remains poorly understood. Acute pancreatitis, on the other hand, has been associated with other vasoocclusive ischemic complications (e.g. Purtscher’s retinopathy). RCN is a devastating complication that often leads to dialysis dependence. Despite our patient showing signs of recovery, his prognosis remains poor. Further study is needed to understand its pathophysiology and potentially mitigate its consequences.

Severe Vancomycin Nephrotoxicity

Jefferson L. Tiziozi, Layth Al Attar, Maryam K. Saeed, Jingyin Yan, Bryan M. Tucker. Baylor College of Medicine, Houston, TX.

Introduction: We report a case of acute kidney injury with biopsy-proven changes related to a vancomycin level of 136.6 mg/L. From our review of the literature, this is the highest vancomycin level ever recorded.

Case Description: A 60-year-old female with type 2 diabetes mellitus, hypertension, Sjogren’s disease not requiring immunosuppression, baseline normal kidney function, and left ankle osteomyelitis on home intravenous vancomycin presented with vertigo. Workup revealed oliguric acute kidney injury with sub-nephrotic range proteinuria (blood urea nitrogen 56 mg/dL, creatinine 6.70 mg/dL, urine protein to creatinine ratio 0.98) and an elevated random vancomycin level (136.6 mg/L). A comprehensive evaluation including physical examination, serologic testing, and renal imaging was unremarkable. Due to high vancomycin levels and minimal improvement in renal function despite resuscitation with intravenous crystalloids, hemodialysis was initiated via a tunneled dialysis catheter. A renal biopsy was then obtained, which demonstrated acute tubuloepithelial injury, morphologically consistent with acute tubular necrosis. There was also mild arterial sclerosis, minimal interstitial fibrosis and tubular atrophy, and no immune-mediated glomerulonephritis.

Discussion: Vancomycin is renally-eliminated by glomerular filtration and, to a lesser degree, excretion in the proximal tubule. Various mechanisms of renal injury are reported, including acute tubular necrosis and interstitial nephritis. Accrual of vancomycin-uromodulin complexes lead to inflammation. In this case, a comprehensive workup and kidney biopsy was important to rule out other causes of renal failure and support the diagnosis of vancomycin-induced nephrotoxicity. Renal recovery often occurs with discontinuation of vancomycin therapy. Severe cases, however, are frequently exacerbated by oliguria and require high-flux hemodialysis for effective drug removal by approximately thirty percent. Prolonged exposure to high levels of vancomycin increases the risk of permanent renal failure. This patient developed vancomycin nephrotoxicity despite drug monitoring, dosing based on creatinine clearance, and using the minimum inhibitory concentration required. Further research to establish precise mechanisms of vancomycin-induced nephrotoxicity is needed.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
DRESS Syndrome and Acute Interstitial Nephritis Relapse: A Case for Caution


**Introduction:** The syndrome of drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but potentially life-threatening drug-induced type IV hypersensitivity reaction that usually occurs 2-6 weeks after drug initiation. Typical findings include skin eruption, fever, hematologic abnormalities, and visceral organ involvement. Prolonged corticosteroid treatment is often required as relapse after initial improvement is not uncommon.

**Case Description:** A 62-year-old woman with a history significant for right total hip arthroplasty complicated by a prosthetic joint infection requiring hardware explantation and antibiotic spacer placement initially presented to the ED with fever, rash, and pruritus. She was treated with cefepime and vancomycin for possible intra-operative bacterial cultures. Urinalysis showed pyuria (51-100/hpf) and eosinophils (1-5%). Skin biopsy showed a drug reaction. She was diagnosed with DRESS syndrome and acute interstitial nephritis (AIN) secondary to the antibiotics, which were then changed to aztreonam and daptomycin. She was treated with systemic and topical steroids and was discharged on oral prednisone (80 mg daily) and had clinical improvement. She was seen again the ED 5 days after discharge with fever and worsening rash and pruritus. Physical examination was notable for mild facial swelling and scattered pink macules coalescing into patches on both upper and lower extremities and on the groin. Laboratory studies revealed leukocytosis with peripheral eosinophilia [7.35x10⁹/L] (on discharge: 0.87), elevated serum creatinine of 4.8 mg/dL, and elevated LFTs, ESR, and CRP. She was diagnosed with DRESS syndrome and AIN relapse secondary to rapid steroid taper. She was started on a higher dose of oral prednisone (80 mg daily) and had clinical improvement. She was then discharged with plan to taper by 10 mg every 2 weeks over 4 months.

**Discussion:** Long-term supra-physiologic doses of steroids are necessary to treat DRESS syndrome even after patients appear to have improved. Relapses do occur and frequently follow treatment discontinuation or rapid steroid taper, leading to increased morbidity and mortality. In such cases, a more prolonged steroid treatment is needed, which can cause well-known adverse events and complications. Close monitoring is thus required.

Rivaroxaban-Induced Anticoagulant-Related Nephropathy


**Introduction:** Anticoagulant-related nephropathy (ARN) is a rare and newly recognized cause of acute renal failure (ARF). A lack of serologic studies and hesitancy to perform high risk biopsies due to concerns for thrombosis or hemorrhage, make ARN a challenging diagnosis. The pathophysiology is believed to be from diffuse glomerular hemorrhage which manifests as numerous RBC casts. These RBC casts obstruct and damage tubular epithelial cells resulting in renal failure. We will examine a case of ARN.

**Case Description:** An 83-year-old Caucasian female presented with complaints of lower extremity weakness and was found to have ARF on laboratory investigation (Cr 5.18mg/dL from 1.1mg/dL one month prior). The patient was recently started on rivaroxaban after being diagnosed with a stroke caused by atrial fibrillation. The patient was admitted for evaluation and management of olugic ARF, requiring the initiation of HD. Initial evaluation was significant for hyperkalemia (5.6 mEq/L), hyperphosphatemia (5.0 mg/dL), hypocalcemia (Ca 8.6 mg/dL) and high LDH in addition to oliguric AKI with serum creatinine (2.5 mg/dL, baseline 0.8 mg/dL). Surprisingly Uric acid level was low (1.8mg/dL) as patient had been on prophylactic Allopurinol. Patient did not have any signs of hypovolemia or post renal obstruction. Urine microscopy was bland. Urgent Hemodialysis (HD) session was provided for malignant hyperkalemia. AKI was assumed to be hyperphosphatemia-induced rather than urate nephropathy in TLS. Renal biopsy was considered but deferred due to high risk of bleeding. Hyperkalemia resolved with one session of HD, but hyperphosphatemia rebounded with worsening of creatinine. So CVH was initiated and carried out for 72 hours. It lowered serum phosphate level to normal range with resolution of AKI.

**Discussion:** With the broad use of heparin agents, calcium phosphate deposition, rather than hyperuricemia is becoming the leading cause of AKI in TLS. Choosing an appropriate dialysis modality is crucial to prevent further phosphate nephrotoxicity. Intermittent HD followed by CVH may be an effective approach. CVH should be considered as a preferred modality to achieve a sustained lowering of phosphate level and prevent rebound hyperphosphatemia. Our case is an excellent example when HD followed by CVH helped in early renal recovery by effectively lowering serum phosphate levels.

Continuous Venousous Hemofiltration for Hypouricemic Tumor Lysis Syndrome and Extreme Hyperphosphatemia Complicated by AKI

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**Introduction:** Tumor lysis syndrome (TLS) is an oncological emergency and can cause Acute Kidney Injury (AKI) mostly by acute urate nephropathy. We present a case of hypouricemic TLS and severe hyperphosphatemia leading to AKI, effectively managed by Continuous Veno-Venous Hemofiltration (CVVH).

**Case Description:** 44-year male with newly diagnosed Burkitt’s lymphoma and currently receiving first cycle of da-EPOCH chemotheraphy, was found to have clinical TLS per Cairo-Bishop definition. Laboratory studies were significant for hyperkalemia (K 6.4 mEq/L), hyperphosphatemia (Phosphate 13.0 mg/dL), hypocalcemia (Ca 6.9 mg/dL) and high LDH in addition to oliguric AKI with elevated serum creatinine (2.5 mg/dL, baseline 0.8 mg/dL). Surprisingly Uric acid level was low (1.8mg/dL) as patient had been on prophylactic Allopurinol. Patient did not have any signs of hypovolemia or post renal obstruction. Urine microscopy was bland. Urgent Hemodialysis (HD) session was provided for malignant hyperkalemia. AKI was assumed to be hyperphosphatemia-induced rather than urate nephropathy in TLS. Renal biopsy was considered but deferred due to high risk of bleeding. Hyperkalemia resolved with one session of HD, but hyperphosphatemia rebounded with worsening of creatinine. So CVH was initiated and carried out for 72 hours. It lowered serum phosphate level to normal range with resolution of AKI.

**Discussion:** With the broad use of hypouricemic agents, calcium phosphate deposition, rather than hyperuricemia is becoming the leading cause of AKI in TLS. Choosing an appropriate dialysis modality is crucial to prevent further phosphate nephrotoxicity. Intermittent HD followed by CVH may be an effective approach. CVH should be considered as a preferred modality to achieve a sustained lowering of phosphate level and prevent rebound hyperphosphatemia. Our case is an excellent example when HD followed by CVH helped in early renal recovery by effectively lowering serum phosphate levels.
PO0121

Use of Continuous Venous Hemodialysis and Plasmapheresis to Treat Simultaneous Iron and Acetaminophen Overdose

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Introduction: Iron may fatally exacerbate toxicity in polypharmacy overdoses, including acetaminophen overdose. We present a case of intentional acetaminophen and iron overdose and treatment with continuous veno-venous hemofiltration (CVVH) and plasmapheresis.

Case Description: 31-year-old male with history of schizophrenia and previous suicide attempts presented to an outside hospital with abdominal pain and emesis 1.5 hours after ingestion of 100 tablets each of 325 mg acetaminophen and 325 mg ferrous sulfate. Vitals on admission were BP 121/83 mmHg, pulse 93 bpm, RR 18/min, G 2 saturation 98% on RA. Labs showed bicarbonate 23 mEq/L, anion gap (AG) of 14, BUN 16 mg/dL, creatinine 1 mg/dL, total bilirubin 0.7 mg/dL, AST 24 units/mL, ALT 16 units/mL, iron 356 μg/dL, and acetaminophen 269.8 μg/mL. Patient was started on IV acetylcysteine. Repeat labs 12 hours later revealed iron level 4526 μg/dL, total bilirubin 4.8 mg/dL, AST 476 units/mL, ALT 855 units/mL. IV deferoxamine was initiated. Patient became lethargic and hypotensive and required intubation. He was transferred to our hospital for further management. Labs upon arrival showed AG of 16, bicarbonate of 12 mEq/L, creatinine 1.98 mg/dL, ALT 13129 units/mL, AST 476 units/mL, and ALT 855 units/mL. IV deferoxamine was started. Patient was unresponsive, euolemic, and NG tube drain was bloody. CVVH was started via left femoral dialysis catheter with blood flow rate of 250 mL/min and replacement fluid rate of 3500 mL/hour. 6 hours after CVVH, labs revealed an iron level of 362 μg/dL, and an acetaminophen level of 100 μg/mL. Due to continued deterioration including hemodynamic instability and persistent acidoses, plasmapheresis was initiated. Labs 2 hours later showed iron level of 20 μg/dL and acetaminophen level of 91 μg/mL. The patient’s clinical status continued to decline despite removal of iron and acetaminophen and he died after 24 hours due to fulminant liver failure.

Discussion: In this case of simultaneous massive iron and acetaminophen overdose, CVVH was effective in removal of iron (60%) and acetaminophen (44%) over 6 hours. Plasmapheresis may be considered as an additional modality to remove excess free iron from the blood.

PO0122

Severe AKI Associated to Acquired Autoimmune Hemolytic Anemia and Hemophagocytic Syndrome: A Case Report

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Introduction: Autoimmune hemolytic anemia (AIHA) is a rare entity with an annual incidence of 1-3/100,000. Secondary AKI is associated to lymphoproliferative disorders (LD), autoimmune diseases, drugs, and less frequently to infections, being an unusual cause of AKI. Hemophagocytic syndrome (HLH) is an uncommon syndrome of excessive immune activation that can be triggered by infection that disrupts immune homeostasis. Herein, we present a very rare case of a patient with AKI requiring RRT associated to severe AIHA and HLH.

Case Description: A 46-year-old Caucasian man was admitted with fever, anuria and severe anemia. Three days prior to admission he had vomiting, diarrhoea and oliguria. Physical examination revealed normal BP, fever and pale skin. Blood tests showed SCr 8.8mg/dL (baseline 0.9mg/dL), metabolic acidosis and urine dipstick Hb3+. He had AIHA with Hb 6.7g/dL, LDH 1194U/L, haptoglobin<30mg/dL, total bilirubin 1.35mg/dL, and positive Coombs test. Blood smear revealed atypical lymphocytes and rare blasts; platelet count was normal. HLH was diagnosed based on clinical (fever, splenomegaly) and laboratory criteria, with high ferritin (46833mg/L), tricylglycerides 308mg/dL, high levels of IL2 receptor (13547pg/mL). Sedimentation rate was 85mm/h and CRP 19mg/dL.

Infection was negative for acute bleed but concerning for cerebral edema. RRT was switched to another. We describe a patient with Pheochromocytoma who developed AKI requiring renal replacement therapy (RRT). Our patient experienced an acute hypertensive crisis followed by cardiovascular collapse likely precipitated by intravenous glucocorticoids given for presumed myocarditis. Glucocorticoids increase catecholamines; the excess causes cardiotoxicity which in turn leads to ischemic AKI. Patient was able to tolerate iHDF therapy. However, as the Phenoxybenzamine was up titrated, the fluctuations included hypertensive episodes and was worsened on dialysis. Given the unpredictable fluctuations in blood pressure and the possibility of associated hypertensive encephalopathy and/or

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cerebral edema in the setting of Pheochromocytoma, it may be prudent to choose CRRT when RRT is warranted, though there are no guidelines regarding which modality is superior in these patients.

PO0125
Blast from the Past: A Rare Case of AKI from Sulfadiazine-Induced Nephrolithiasis

Introduction: Sulfadiazine has been used for the treatment of neutropenoplasmosis in patients with HIV infection. Nephrolithiasis is a known complication of high dose sulfadiazine therapy. However, this complication is rarely seen in HIV patients due to improved antiretroviral therapy. We present a rare case of sulfadiazine-induced nephrolithiasis in a patient with AIDS.

Case Description: A 55-year-old female with DM and HTN was hospitalized for worsening mental status and CT scan finding of frontal lobe mass. During hospital stay, pt. also found to have HIV infection and a very low CD4 count. Antiretroviral therapy and high dose intravenous sulfadiazine 1,500 mg every 6 hours was initiated for presumed neutropenopathy. On admission, serum creatinine (Scr) was 0.68. Seventeen days after initiation of sulfadiazine therapy, Scr increased to 2.42. Urinalysis revealed microscopic hematuria. Kidney sonogram showed left hydronephrosis and echogenic foci in both kidneys concerning for kidney stones. Sulfadiazine was discontinued and patient was started on sodium bicarbonate infusion to alkalinize her urine but Scr continued to worsen, peaking at 4.73 within few days. Serial kidney sonograms revealed alternating fullness of the collecting systems of both kidneys. Urology team was consulted and patient underwent cystoscopy with bilateral ureteral stent placement. Scr subsequently returned to normal limits within one week of ureteral stent placement.

Discussion: Our patient developed severe but reversible post-obstructive AKI secondary to high-dose sulfadiazine-induced nephrolithiasis. In the modern era of antiretroviral therapy, sulfadiazine-induced nephrolithiasis is a very rare occurrence in clinical practice. Hence, clinical and nephrology care providers should be aware of this rare cause of AKI in patients with HIV infection.

PO0126
Rhabdomyolysis as Initial Presentation of COVID-19
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Introduction: Rhabdomyolysis has infectious etiology including Mycoplasma pneumoniae infection, Legionella, and Influenza. To date, there has been one case report from Wuhan China of a patient who developed rhabdomyolysis from COVID-19 during their hospitalization. We report a case where acute kidney injury and rhabdomyolysis was the initial presentation.

Case Description: A 57 year old African American male with history of HTN for more than 10 years, presented with complaints of decreased urine output for 3 days associated with dark urine that progressed to anuria, fever for 11 days, decreased appetite and oral intake and generalized muscle weakness. Labs on admission were notable for acute kidney injury (creatinine 1.77mg/dL) which progressed rapidly to a peak creatinine of 11.10mg/dL within 72 hours, and other electrolyte abnormalities including mild hyperkalemia and acidosis. His CPK was ~92,000U/L on admission and COVID-19 PCR was positive. Other labs included: peak AST 1692 U/L and ALT 291U/L, ferritin 1436 mg/ml, 4.86mg/dL, DDimmer 2330 DDU, urinalysis specific gravity 1.030 with large blood, 10RBCs, 20WBCs, urine spot protein/creatinine 2.1 and random urine sodium 65. Serologic workup was negative for glomerular etiology. He was presumed to have acute tubular necrosis (ATN). He was treated with initial admission for anuria and worsening of renal function. He was maintained on hemodialysis with minimal ultrafiltration three times a week, intravenous fluid resuscitation along with intermittent doses of bumex. He received total of five hemodialysis treatments until he became normo-oliguric and started showing signs of recovery. He was taken off dialysis approximately three weeks after his initial presentation. His creatinine decreased and is 1.4 mg/dL one month after being taken off of hemodialysis.

Discussion: COVID-19 has its usual presentation of fevers, shortness of breath, dry cough and myalgias. This case highlights the importance that rhabdomyolysis can be one of the presenting features of COVID-19. Chances CPK levels should be an initial part of not only acute kidney injury workup in the COVID-19 patient but also for any COVID-19 newly diagnosed case as this diagnosis requires prompt and specific treatment.

PO0127
Lymphomatous Infiltration of the Kidney: A Sonographic Diagnosis
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Introduction: The purpose of this case study is to illustrate the sonographic findings seen in kidney infiltration by lymphoma.

Case Description: A 56-year-old man with a history of hypertension, diabetes mellitus type 2 and follicular lymphoma with transformation to diffuse large B-cell lymphoma presented with worsening fatigue, headache and diplopia. MRI of the brain demonstrated central nervous system involvement by the lymphoma. He was also found to have worsening renal function with a serum creatinine of 4.5 mg/dl (baseline: 1.6-2 mg/dL). A renal sonogram (RUS) was performed, which demonstrated bilateral enlarged kidneys (~14.5 cm each) with irregular outlines and multiple parenchymal hypoechogenic to heterosexual lesions. No internal vascularity was noted on color Doppler. These findings are consistent with lymphomatous infiltration of the kidneys, confirmed later by PET (positron emission tomography) scan [Figure]. The renal function continued to worsen despite supportive care, and he required initiation of hemodialysis. Acute kidney injury was initially attributed to poor oral intake and mild hypercalcemia, but lymphomatous infiltration likely contributed to his renal impairment as well. Renal biopsy was not undertaken due to progression of the lymphoma and limited life expectancy.

Discussion: Kidney is the most common extra-renal site of leukemic and lymphomatous infiltration, and tumor-cell infiltrates in the kidney are seen in up to 30% of patients with lymphoma. Rarely, renal involvement may be the first manifestation of lymphoma. The kidneys may appear normal on RUS because of the small size of the nodular infiltrates or with the typical findings described above. Unilateral and perirenal infiltration with lymphoma has also been described. Hemophagocytosis may be noted on RUS if there is compression of the renal hilum or ureters by the lymphomatous tissue. Nephrologists performing point of care ultrasound may be aware of these findings. These patients will require a prompt referral to the Hematology & Oncology team when renal ultrasonography leads to a new diagnosis of lymphoma.

PO0128
Minimal Change Nephrotic Syndrome Superimposed on Anti-Glomerular Basement Membrane Antibody Glomerulonephritis: A Case Report
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Introduction: Background : The renal prognosis of anti-GBM glomerulonephritis (anti-GBM GN) is extremely poor as renal dysfunction often progresses acutely before the initiation of treatment. It is also known that once the disease activities are controlled by aggressive treatment, its recurrence is rare. Here we experienced a case of anti-GBM GN that improved from severe renal dysfunction but later relapsed. A possible cause was thought to be a rare complication of minimal change nephrotic syndrome (MCNS).

Case Description: A 50-year-old man was admitted to our hospital because of general malaise, fever, oliguria and renal dysfunction. The patient’s laboratory data showed serum creatinine as high as 6.6 mg/dl and severe inflammation (C-reactive protein 20.6mg/dl). Anti-glomerular basement membrane antibody (anti-GBM Ab) was detected in his serum, leading to a diagnosis of anti-GBM GN. Treatment was initiated with high-dose glucocorticoid (GC) and plasma exchange therapy (PE), and the patient’s renal function and oliguria improved rapidly and he was discharged 40 days after admission. Renal biopsy findings showed cellular crescents associated with linear IgG deposits along the glomerular tufts compatible with anti-GBM GN, but only about one-third of the glomeruli was involved, suggesting that it still remained an early stage of the disease. However, two months after discharge, he had a relapse and was re-admitted due to severe proteinuria associated with positive anti-GBM Ab. On the second admission, he was treated with high-dose GC and PE combined by intravenous cyclophosphamide, and complete remission was achieved a few weeks later. Electron microscopy of the renal biopsy that returned later showed significant foot process effacement on podocytes in the apparently normal glomeruli without electron dense deposits.

Discussion: Considering clinical course and renal pathology findings, it is suggested that the present case was a rare complication of an early stage of anti-GBM GN and MCNS. Although the cause of concurrent development of anti-GBM GN and MCNS associated with anti-GBM antibody titers is unclear, it may have been precipitated by influenza infection or some unknown factor.

PO0129
Thrombotic Microangiopathy with Acute Interstitial Nephritis Secondary to Trimethoprim-Sulfamethoxazole

Introduction: Thrombotic Microangiopathy (TMA) and Acute Interstitial Nephritis (AIN) are well recognized entities that individually cause significant morbidity and mortality. The relationships with several medications have been described, but the two conditions coexisting are rare.

Case Description: 28-year-old man with no significant past medical history presented with bilateral lower extremity edema, excoriations, discharge, and weakness for one week. He initially presented to an outpatient clinic and was discharged on trimethoprim-sulfamethoxazole (TMP/SMX). His symptoms progressed leading to admission. Physical
examination revealed an obese man with bilateral lower extremity edema, eczematous rashes, and ascites on both feet. Initial laboratory results were significant for a creatinine of 5.2 mg/dl and oliguria. Urinalysis revealed proteinuria, hematuria, and pyuria. He then developed thrombocytopenia and anemia. Haptoglobin and lactate dehydrogenase were elevated, and schistocytes were identified on peripheral smear consistent with microangiopathic hemolytic anemia. He also had eosinophilia. Work-up for autoimmune inflammatory, and connective tissue diseases was ordered and results were unremarkable. ADAMTS13 activity was decreased to 42%. The patient started hemodialysis and a kidney biopsy was performed with findings of acute tubular necrosis, thrombotic microangiopathy, and acute interstitial nephritis. TMP/SMX was discontinued and he was started on steroids. His renal function improved, and he was discharged home without need for further dialysis.

Discussion: TMA is characterized by endothelial damage causing microangiopathic hemolytic anemia, thrombocytopenia, and end-organ damage. TMA can be attributed to genetic and acquired autocrine causes, or may emerge secondary to medical diseases. AIN is a common cause of kidney injury and is associated with multiple drugs. This case demonstrates the unique coexistence of TMA and AIN in a patient receiving TMP/SMX, which has been related to decreased creatinine clearance, bone marrow suppression, hyperkalemia, and hypersensitivity reactions. This case supports the cessation of the offending drug and the use of steroid treatment as an option for TMA and AIN. In conclusion, TMA and AIN may occur simultaneously as an adverse drug reaction.

PO0130
Rhabdomyolysis in SARS-CoV-2 infection
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Introduction: Acute kidney injury (AKI) is a common complication of SARS-CoV-2 infection. Multiple mechanisms have been proposed including acute tubular necrosis (ATN) due to shock, cytokine release syndrome, hypoxia or vascular injury and thrombosis. Direct viral injury to tubular epithelial cells and podocytes has also been described. Rhabdomyolysis has been reported in infection with SARS-CoV, Respiratory Syncytial Virus and Influenza A. Although muscle CK elevation was reported in cohorts of patients with COVID-19 and there is a single case report of late onset rhabdomyolysis, overt rhabdomyolysis has not been described. To our knowledge this is the first patient with presented with signs and symptoms of severe rhabdomyolysis and AKI that was likely secondary to SARS-CoV-2 infection.

Case Description: A 51 year-old male with hypertension and diabetes, presented with five days of diffuse myalgia and mild dry cough with shortness of breath. He denied trauma, new medications, changes in diet, strenuous exercise or illicit drug use. Physical exam notable for fever and tachypnea, but no hypoxia. Labs were clear and all muscles groups were soft and non-tender. Polymerase chain reaction was positive for SARS-CoV-2. Serum creatinine was 2.4 mg/dl (baseline 1.3 mg/dl), Urinalysis showed 3+ blood, 2+ protein and 1-2 RBC per high power field. Initial serum creatinine kinase was 340,000 U/L and peaked at 464,000 U/L on day 4. Serum and urine myoglobin levels were elevated at 15,175 mg/L and >5000 mg/L, respectively on day 5. He received isotonic intravenous (IV) fluids but developed oliguria on day 2, requiring diuresis to maintain urine output. BUN and creatinine increased to 130 and 19 mg/dl, respectively by day 8 and hemodialysis was initiated. Renal clearance and urine output then slowly improved, and dialysis was discontinued by day 15.

Discussion: Myalgia and fatigue are common symptoms of COVID-19 infection. In addition, diastolic hematuria is reported in up to 10% of patients. Thus diagnosis of rhabdomyolysis and myoglobinuria requires a high index of suspicion. Early consideration and timely diagnosis of rhabdomyolysis and the treatment of myoglobinuria with intravenous fluids is extremely important to prevent ATN. However, administration of IV fluids may be challenging in COVID-19 patients at risk of hypoxia and acute respiratory distress syndrome.
fever and eosinophilia, and is usually a diagnosis of exclusion. On renal biopsy (Bx), DI-AIN usually presents with interstitial inflammation rich with eosinophils and neutrophils cast without glomerular injury. Immunofluorescence with negative IgG, IgA, IgM, C3, C1q, fibrinogen, albumin, kappa and lambda light chains. Electron microscopy was unremarkable. Cr at 3rd day peaked at 4.7mg/dL, then trended down. Upon discharge BUN/Cr 58/3.6. One week after at renal clinic visit her kidney function came back to her baseline. We continued steroids for 3 weeks due to suspicion of AI renal imaging and urine culture remained negative.

Discussion: This is a rare case where Zosyn was promptly stopped and prednisone was initiated early in the course of AIN despite neutrophil infiltration on renal Bx. DI-AIN can present with predominant neutrophilic infiltration; however, this makes the diagnosis more challenging. High suspicion, prompt antibiotic discontinuation and early institution of steroid can prevent further kidney injury or potential chronic kidney disease.

Case of Paraneoplastic Pauci-Immune Glomerulonephritis
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Introduction: This case highlights the importance of complete systemic evaluation for patients presenting with rapidly progressive glomerulonephritis (RPGN).

Case Description: 58 year old male with history of DM type 2 and hypothyroidism presents with acute kidney injury (AKI). Notable findings include a rash which was biopsied and due to leukocytoclastic vasculitis. Baseline Cr 0.59 mg/dL and continued to increase rapidly leading to patient becoming hemodialysis dependent. Urine showed an active sediment; serology including ANCA and anti-GBM were all negative. Patient was empirically started on steroids for possible Immunoglobulin A glomerulonephritis and also due to diagnosis of adrenal insufficiency. Renal biopsy subsequently showed pauci-immune crescentic glomerulonephritis with 89% og glomeruli with crescents, 74% with fibrinoid necrosis and 52% with segmental necrosis. Patient was started on Cytoxan. However further work up revealed a submass which was biopsied and found to be Hodgkin’s lymphoma. Patient was started on chemotherapy however did not make any renal recovery and remains dialysis dependent.

Discussion: This case highlights the importance of thorough evaluation in patients presenting with rapidly progressive glomerulonephritis. Although oftentimes it is due to a primary renal or renal/pulmonary disorder, paraneoplastic conditions should not be overlooked and need further investigation.

Renal Abnormalities in Patients with e-Cigarette, or Vaping, Product Use-Associated Lung Injury (EVALI)
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Background: The use of electronic cigarettes is linked to the development of lung injury. There are no reports to date of renal injury secondary to vaping. Animal studies suggest that vaping could be associated with renal injury (1,2).

Methods: A retrospective chart review of the first twenty cases of patients with EVALI was performed. We present the urinary abnormalities noted in patients with EVALI.

Results: Twenty patients admitted for EVALI underwent urinalysis as part of their laboratory workup. None of these patients had known pre-existing renal disease. All patients except for one had normal creatinine on admission. Proteinuria was seen in thirteen patients (65%) and microscopic hematuria (~4 RBC/hp) was seen in five patients (20%). All patients with microscopic hematuria also had proteinuria. However further work up revealed a vaginal mass which was biopsied and found to be Hodgkin’s lymphoma. Patient was started on chemotherapy however did not make any renal recovery and remains dialysis dependent.

Conclusions: EVALI can be associated with hematuria and proteinuria. In animal studies, E-cigarette vapor is hypothesized to diminish airway barrier function, release inflammatory protein into the circulation creating systemic inflammation leading to distant organ injury and dysfunction (2). There are several limitations to this study. This is a retrospective chart review and long term outcome is unknown as data is lacking. Nevertheless the high prevalence of urinary abnormalities on admission in patient with EVALI calls for further investigation. While the pathogenesis of vaping-associated renal injury is unclear, urine analysis should be considered in all patients presenting with EVALI (Ref 1). Impact of a cigarette refill liquid exposure on rat kidney Golli NE et al. Regul Toxicol Pharmacol 2016 Jun;77:109-16. 2. Chronic inhalation of e-cigarette vapor containing nicotine disrupts airway barrier function and induces inflammation and multiorgan fibrosis in mice Crotty Alexander et al Am J Physiol Regul Integr Comp Physiol. 2018 Jun 1;314(6):R834-R847.

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Kidney Biomarkers and Major Adverse Kidney Events in Critically Ill Patients

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Background: Several biomarkers of acute kidney injury (AKI) have been examined for their ability to predict AKI earlier than serum creatinine. Few studies have focused on using kidney biomarkers to better predict major adverse kidney events (MAKE), an increasingly used composite outcome in critical care nephrology research.

Methods: Single-center prospective study collecting blood and urine samples from critically ill patients with AKI KDIGO stage 2 or above, and matched controls from a single, tertiary care intensive care unit. Samples were collected at 24-48 hours after AKI diagnosis (cases) or ICU admission (controls), 5-7 days later, and 4-6 weeks following discharge for AKI patients. The primary outcome of interest was MAKE at hospital discharge.

Results: Serum/urinary neutrophil gelatinase-associated lipocalin, serum/urinary cystatin C, and urinary kidney injury molecule-1 early in the AKI or ICU course were all significantly higher in patients with MAKE compared to those not experiencing MAKE. Serum cystatin C, and to a lesser extent serum NGAL, significantly improved upon a clinical prediction model of MAKE as assessed by the area under the receiver operating characteristic curve. Patients without MAKE experienced a greater decline in serum NGAL from initial measurement to second measurement than those patients experiencing MAKE.

Conclusions: Early values of kidney biomarkers in critically ill patients are associated with MAKE. This relationship appears to be greatest with serum NGAL and cystatin C, which display additive utility to a clinical prediction model. Trending serum NGAL may also have utility in predicting MAKE.

Funding: NIDDK Support, Private Foundation Support

Poster

Urine Biomarkers and Risk of Long-Term Kidney Outcomes After Cardiac Surgery: the TRIBE-AKI Study

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Background: The urine biomarkers epidermal growth factor (EGF) and monocyte chemotactic protein-1 (MCP-1) show promise as biomarkers of chronic kidney disease (CKD) progression in settings such as diabetes mellitus, but their role in the transition from AKI to CKD remains unclear. EGF is produced specifically by renal tubular epithelium of the thick ascending limb and MCP-1 is extensively studied as a marker of kidney inflammation. We evaluated the associations of urine EGF and MCP-1 with CKD incidence or progression after cardiac surgery.

Methods: In this sub-study of the prospective TRIBE-AKI cohort, we evaluated 865 adult patients who underwent cardiac surgery from 2007–2010 at two sites in Canada and the US. We tested the association of first post-operative urine EGF and MCP-1, and the ratio EGF/MCP-1, with the composite outcome of CKD incidence or progression. We assessed for interaction by peri-operative AKI status.

Results: Over a median (IQR) follow-up of 5.8 (4.2-7.1) years, 266 (30.8%) patients developed the composite outcome at an event rate (95% CI) of 55.4 (49.2-62.5) per 1,000 person-years. Elevated levels of first post-operative urinary EGF and MCP-1 were each independently associated with the composite outcome, in opposing directions (Table 1), and the ratio (EGF/MCP-1) was strongly associated with decreased risk of CKD incidence or progression in both continuous and categorical analysis (aHR 0.50 [0.33-0.74] for T3 compared to T1). There was no interaction by AKI status.

Conclusions: Urine EGF and MCP-1 may be useful for risk prediction of future CKD outcomes after peri-operative injury in cardiac surgery.

Funding: NIDDK Support

Poster

Higher Plasma KIM-1 Is Associated with Increased Mortality and Decreased Renal Recovery in Patients with AKI Requiring Renal Replacement Therapy

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Background: Plasma kidney injury molecule-1 (KIM-1), a protein synthesized by renal proximal tubular cells, increases during periods of ischemia and thereby acts as a sensitive marker for AKI severity. We hypothesized that higher plasma KIM-1 levels assessed prior to commencing renal replacement therapy (RRT) would associate with higher mortality and RRT dependence in critically ill patients with severe AKI.

Methods: We measured plasma KIM-1 levels in 806 Day 0 samples from participants in Acute renal failure Trial Network (ATN) trial, a randomized controlled trial of intensive versus less-intensive RRT. For our primary analysis we used a logistic regression model to assess the risk of 28-day mortality and an inverse probability weighted logistic regression model to assess the odds of 28-day renal recovery, per doubling in log-transformed Day 0 KIM-1. Both models were adjusted for components of the ATN trial mortality risk score (age, chronic hypoxemia, CVS disease, malignancy, immunosuppressive therapy, ischemic AKI, post open surgery and vital signs at RRT initiation).

Results: Higher levels of plasma KIM-1 were associated with an increased risk of death within 28 days (adjusted odds ratio 1.15; 95% CI 1.03-1.29; p = 0.02) per doubling in log-transformed plasma KIM-1. Higher levels of Day 0 plasma KIM-1 were also associated with an increased risk of persistent RRT dependence at 28 days (adjusted odds ratio 0.76; 95% CI 0.66-0.87; p = 0.001) per doubling in log-transformed plasma KIM-1.

Conclusions: Higher plasma KIM-1 levels measured prior to initiation of RRT are independently associated with higher 28-day mortality and lower probability of 28-day renal recovery in critically ill patients with severe AKI.
PO0141
Estimated vs. Measured Glomerular Filtration Rate in Acute Decompensated Heart Failure
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Background: Kidney function is closely monitored in patients with acute decompensated heart failure (ADHF). Recent studies indicate that rise in endogenous filtration markers (serum creatinine (Scr) or cystatin c (Cys)) is neither associated with tubular injury nor with adverse outcomes when accompanied by efficient decompensation. The imperfections of Scr or Cys to estimate GFR in non-steady state could contribute to misjudgment of renal failure in ADHF. In this study we measured GFR (mGFR) in patients treated for ADHF and correlated them with estimated GFR dynamics.

Methods: In a prospective cohort study in 50 hospitalized subjects treated for ADHF, mGFR was measured using a two-component intravenous visible fluorescent injectate (VFI) at two timepoints 48h apart. Serum concentrations of a high molecular weight dextran component of VFI were measured 15 and 60 min after injection to quantify plasma volume (PV) using indicator-dilution principle. Concentrations of a low molecular weight component of VFI were measured to determine mgFR based on PV-normalized plasma pharmacokinetics. Pearson’s r, Bland-Altman plots, precision, accuracy and bias were calculated for 4 established equations (CKD EPI r, CKD EPI c, CKD EPI c+c, sMDRD) and kinetic GFR (kGFR, Chen et al., JASN 2013). 38 subjects had complete serial mGFR data.

Results: GFR calculated by any estimating equation correlated significantly with measured GFR (CKD EPI r, r=0.81; CKD EPI c, r=0.81; CKD EPI c+c, r=0.84; sMDRD, r=0.81; kGFR r=0.81, p<0.0001). CKD EPI c+c had the best overall performance with an accuracy (P30) of 75%. However, changes in mGFR during 48h of ADHF treatment were not adequately reflected in corresponding changes of eGFR. KDIGO SCR-based AKI criteria frequently failed to detect relevant decreases of mGFR (Sensitivity 55%).

Conclusions: In patients hospitalized for ADHF undergoing decompangement, GFR estimates based on Scr and CC display substantial deficits in estimating GFR. In particular, changes of Scr- and CC-based GFR displayed a remarkable disconnect from mGFR dynamics. KDIGO SCR criteria displayed a poor sensitivity in detecting relevant decreases of mGFR, indicating a need for improved diagnostic approaches to identify true worsening renal function in ADHF.

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PO0142
Multiple Beneficial Effects of Renal Exosomes on Ischemic Injury
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Background: Ischemic injury to the kidney and other organs is deadly and expensive. We have demonstrated the effectiveness of adult cell-based therapies in multiple models of renal failure. Given the large benefits of relatively few cells, we hypothesized that exosomes from transplanted cells were the therapeutic effector. We and others have shown benefit with exosomes in renal injury models. To define the mechanisms of benefit from renal exosomes, the effects of exosomes from platelets and dermal epithelia were compared to those of renal exosomes.

Methods: The hypothesis that renal exosomes improve multiple pathways of injury postischemia and contain anti-oxidant and anti-inflammatory cargo was tested in a renal ischemia model. Exosomes from post-ischemic kidneys, platelets or skin were isolated by serial centrifugation. Renal function was estimated from serum creatinine. Oxidative stress and inflammation were assessed by immunostaining for 4-hydroxyneonal and neutrophils, respectively. Anti-inflammatory cytokine levels were measured by enzyme-linked immunoassay.

Results: We found significant improvements in renal function (figure) and structure with renal exosomes, given 24 hours postischemia, when renal failure was present. Exosomes from skin epithelia or platelets were not effective. Renal, but not skin or platelet, exosomes decreased evidence of oxidative stress in post-ischemic kidneys by 67%, with preservation of catalase and superoxide dismutase. Significantly less renal neutrophil infiltration was found in the renal exosome group as compared to postischemia groups that received vehicle or skin or platelet exosomes. Anti-inflammatory IL-10 levels were significantly higher in post-ischemic kidneys in the renal exosome group.

Conclusions: Exosomes derived from kidney cells effect multiple pathways of injury to improve postischemic kidney function.

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PO0144
Point-of-Care Prevention and Treatment of AKI with Adipose-Derived Stem Cells: Efficacy and Cost Advance over Culture-Expanded Bone Marrow-Derived Mesenchymal Stem Cells
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Background: Our pre-clinical studies (AJP 2005) and a Phase I Clinical Trial (Nat Rev Neph 2010) show that administration of bone marrow-derived, culture expanded, allogeneic Marrow Stromal Cells (MSC) is effective in the prevention and hastened recovery from experimental AKI, and safe and renoprotective in on-pump cardiac surgery patients at high risk for post-op AKI. Significantly, MSC treated unlike historical control on-pump cardiac surgery patients did not develop Chronic Kidney Disease (CKD) long term (>7 years). Expansion and banking of MSCs is expensive and time consuming. To address these limitations, we compared treatment with syngeneic, culture-expanded MSCs or vehicle to treatment with either syngeneic, minimally manipulated allogeneic Adipose Derived Stem Cells (ASCs) or autologous Stromal Vascular Fraction (SVF) immediately isolated from fat, containing ASCs, endothelial precursor and other cells for efficacy in preventing AKI. ASCs share therapeutically critical activities with MSCs and are in sufficiently high numbers/gm fat to present an alternative to culture-expanded MSCs.

Methods: ASCs and SVFs were isolated by minimal processing from abdominal fat harvested from male Fisher344 (F344) rats. IRI AKI was induced (bilateral renal pedicle clamping x 40 min) in 50% of male F344 rats (~200 g wt; n=7 each). Upon reflow, groups were infused (supraprenal aorta) with either (1) 1x106 ASCs, (2) 1x105 autologous SVF cells, (3) 1x106 syngeneic, cultured MSCs, (4 and 5) vehicle in animals with or without fat harvest.

Results: Outcomes were compared to those of sham treated animals (n=7). Renal function assessed by serum Cr (SCr) in ASC or SVF treated animals was significantly better protected, and recovery more rapidly achieved compared to vehicle and MSC treated rats.

Conclusions: Our data suggest therefore that autologous ASCs and the SVF, obtained by minimal manipulation from a patient’s lipop罗斯ate, have the potential to treat that same patient with an efficient, inexpensive and safe point-of-care protocol to prevent or treat AKI and prevent subsequent progression to CKD. (No University of Utah resources were used for this work.)

Funding: Commercial Support - SymbioCellTech, LLC

PO0145
Administration of Exosomes from Mesenchymal Stem Cells Provides Effective Survival Benefits and Functional Rescue from Severe, Progressive Ischemia-Reperfusion Injury-Induced AKI in Rats
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Background: While administration of Mesenchymal Stem Cells (MSCs) has been demonstrated clinically to prevent Acute Kidney Injury (AKI) such as that caused by cardiac bypass surgery, administration 48 hrs post-injury was found to be ineffective or potentially damaging, likely because the introduction of large cells (~50μm) into the compromised microvasculature may impair renal function. MSCs’ renoprotection is mediated by their paracrine release of anti-inflammatory and trophic cytokines and their exosomes. Exosomes signal, post uptake by target cells, through the lateral transfer of mRNAs, miRNAs, DNA, proteins, and lipids. Since MSC-derived exosomes can prevent AKI we tested whether their small size and ability to move through the compromised renal microvasculature might allow them to provide effective rescue therapy for late stage AKI.

Methods: Exosomes from Sprague Dawley (SD) rat MSCs were isolated post 24 hr culture, purified using the ExoQuick-TC kit, and characterized for size (nanosize), protein and gene expression of relevant markers. 1/R AKI (52 min bilateral renal pedicle clamp) was induced in female SD rats. If the SCr value on Day 2 was greater than that on Day 1, demonstrating progressive AKI, then rats were infused via left carotid artery either 1 ml of Vehicle (PBS; n=9), Exosomes (200 μg protein-equivalent; ~4x10e10 exosomes; n=6), or MSCs (2x10e6; n=6) on Day 3.

Results: Versus controls, all 3 cell types significantly protected renal function and histology from AKI (SCr levels, tissue injury scores); but within 14 days, each treatment elicited a significant IgG antibody response (57-99%) against the infused cell type. Rats inoculated i.p. with hASCs and confirmed to have positive immunity to hASCs were no longer renoprotected by hASCs when treated with them for IRI AKI.

Conclusions: While xenogeneic use of MSCs/ASCs is renoprotective, the demonstrated induction of an immune response makes such applications unsafe/ineffective in pre-clinical studies. Caution is advised in interpreting results of studies using cell lines containing xenogenic expression vectors for genes meant to enhance MSCs’ clinical efficacy. (Not U of Utah work)

Funding: Commercial Support - SymbioCellTech, LLC
Glomerular Filtration Fails to Increase During Pregnancy After Renal Ischemia-Reperfusion Injury
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Background: Renal demands are increased during normal pregnancy due to the large increase in plasma volume and cardiac output, with a corresponding increase in glomerular filtration rate and decreased blood pressure (BP). Recent studies in our laboratory have reported that pregnancy after recovery from ischemia reperfusion (IR) injury results in poor maternal and fetal outcomes, including decreased fetal weight, increased fetal mortality, and tissue damage. The gene encoding KIM-1 (IRI) by enabling TECs to bind and engulf dying neighbouring cells, limiting inflammation and immunogenic contents into the extracellular milieu, exacerbating inflammation. Kidney injury, however, is absent in this model, leading to decreased placental perfusion and poor fetal growth.

Methods: Female Sprague Dawley rats (10 weeks of age, n=3) were implanted with telemetry devices and placed into a flooded fetal and maternal cage during pregnancy. Three groups were studied: control rats that did not undergo ischemia (C), rats that underwent 45 minutes of ischemia (I), and rats that underwent 45 minutes of ischemia followed by 1 month of recovery (IR). Two groups of rats were used for analysis: one group was sacrificed at gestational day 20, and the second group was sacrificed at gestational day 20 after the 1 month recovery period. Glomerular filtration rate was calculated using creatinine clearance (using 24 hour urine collection from gestational days 19-20 and plasma creatinine on gestational day 20).

Results: BP decreased to a similar extent (7±1.2mmHg in control vs 8±1.2mmHg in IR dams) by gestational day 20, however the decrease in BP was delayed in the IR dams, resulting in an overall higher pressure load as determined by the area under the curve analysis (2080±33 vs 2184±16, p<0.05, t-test). Glomerular filtration rate was significantly higher (2080±33 vs 2184±16, p<0.05, t-test) in control rats compared to IR rats. The decrease in BP was delayed in the IR dams, leading to an increased pressure load and poor fetal growth.

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Myeloid Lactate Dehydrogenase A (LDHA) Regulates Macrophage Polarization and Promotes Fibrosis in AKI
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Background: Renal ischemia/reperfusion injury (IRI), a major cause of AKI, is characterized by an initial decrease in blood flow, followed by its subsequent restoration. IRI facilitates infiltration of proinflammatory macrophages as well as proliferation of intrarenal resident macrophages that, upon activation, undergo glycolytic switch, and can further exacerbate injury by inducing excessive inflammation. LDHA, a key enzyme involved in the glycolytic switch, catalyzes the conversion of pyruvate to lactate, regenerating NAD+ from NADH. Here we investigate the role of LDHA in myeloid cells and its effect on AKI.

Methods: To test the hypothesis that myeloid LDHA expression regulates macrophage polarization, LDHA-expressing bone marrow derived macrophages (BMDM) from wild-type and LDHA knockout (LDHA KO) mice grown in M-CSF for 7 days and then polarized with IFN-γ were used. LDHA deficiency in macrophages attenuates systemic inflammatory response and iRIR. Phenotypic alterations in splenic macrophages might play critical roles in the protection against iRIR.

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PO0152
PD-1 Regulates Metabolic Fitness of Tregs in Protection from Kidney Ischemia-Reperfusion Injury
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Background: Regulatory T cells (Tregs) protect the kidney in models of ischemia reperfusion injury (IRI). Previous studies suggested programmed cell death protein 1 (PD-1) expression by Tregs is required for their protective function in AKI. However downstream mechanisms of PD-1 signaling in Tregs in AKI is not clear. We aimed to investigate the role of PD-1 in Tregs with respect to mitochondrial function in AKI.

Methods: We induced AKI in male C57Bl/6 mice with 26 min bilateral renal IRI. CD4-CD25+ Tregs were isolated from PD-1+/+ and PD-1-/- Foxp3-GFP mice and then injected (100,000 cells/200ul) via tail vein into recipient mice 24h prior to ischemia reperfusion surgery. Kidney function was determined by measuring creatinine and tissue KIM-1 and (100,000 cells/200ul) via tail vein into recipient mice 24h prior to ischemia reperfusion surgery. Kidney function was determined by measuring creatinine and tissue KIM-1 and NAG mRNA expression levels. Histological damage was assessed by light microscopic analysis of H&E stained kidney sections. In different set of experiments to understand the metabolic fitness of Tregs, we treated isolated T-cells from PD-1+/+ and PD-1/- mice and incubated them overnight with anti-CD3/Ab to mimic antigenic stimulation or with high concentration of IL-2, which is critical for Treg survival and function. Mitochondrial membrane potential of Tregs was measured with TMRE to monitor the mitochondrial fitness. FACS-sorted Tregs from PD-1+/+ and PD-1/- mice were also analyzed for the expression of genes involved in mitochondrial dynamics and biogenesis.

Results: In the mouse kidney IRI, PD-1+ Tregs offered no protection from AKI. Compared to PD-1+/+ mice, PD-1-/- Tregs had reduced mitochondrial mass and mitochondrial membrane potential. In FACS-sorted Tregs, expression of markers of mitochondrial function, antioxidant pathways as well as those for mitochondrial dynamics were remarkably attenuated in the Tregs from PD-1-/- mice as compared to PD-1+/+ mice.

Conclusions: Ability of Tregs to protect kidney from IRI-induced AKI is dependent on PD-1 expression by Tregs. Mitotracker green and TMRE experiments suggest that in the absence of PD-1, Tregs have reduced mitochondrial number and/or function. Tregs require mitochondrial fitness for their development and optimal function. Additionally, these genes may regulate cytokine rearrangement and microtubule movement related to cell motility, granule release and cell division.

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PO0154
Toll-Like Receptor 4 Blockade Ameliorates Kidney Ischemia-Reperfusion Injury

Background: Renal ischemia-reperfusion injury (IRI) is a key mechanism in various clinical conditions including sepsis and transplantation, and animal studies have demonstrated that toll-like receptor 4 (TLR4) is a key mediator of IRI. Since few study have tried the pharmacologic inhibition of TLR4 in renal IRI, we investigated the effect of TLR4 blockade on this condition with the goal of pursuing better therapeutic options.

Methods: We subjected C57BL/6 mice to 23 minutes of renal pedicle clamping following an intraperitoneal injection of TLR inhibitory peptide (TIP1), a TLR4 inhibitor, or vehicle. Sham mice underwent only a flank incision. Then, the kidneys were harvested after 24 hours of reperfusion for histology, western blot, RT-PCR, and flow cytometry. We also performed primary mouse renal tubular cell culture to assess the effects of TLR4 inhibition on tubular epithelial cells under hypoxia and subsequent reoxygenation.

Results: TIP1 pretreatment lowered the magnitude of an increase in serum creatinine levels and attenuated tubular injury. In addition, TIP1 administration decreased mRNA expressions of inflammatory cytokines, and apoptotic cells, and lowered oxidative stress in postischemic kidneys. The kidneys pretreated with TIP1 also showed less infiltration of macrophages and T helper 17 cells. In primary mouse tubular cells subjected to hypoxia and reoxygenation, the addition of TIP1 into culture media ameliorated the magnitude of an increase in mRNA levels of KIM1 and inflammatory cytokines.

Conclusions: Our data demonstrated that inhibition of TLR4 with TIP1 reduced tubular injury and an inflammatory and immune response in a mouse model of IRI.

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we injected adeno-associated viral vector serotype 9 (AAV9)-Six1 into uninjured renal pellets before IR injury, then assessed morphologic and functional parameters and genes expression in injury related tissues.

Results: We demonstrated that Six1 promoted cell proliferation by upregulating cyclin and glycolytic genes, and that cell migration through increasing the expression of matrix metalloproteinases (MMPs) in the cell model. Notably, the overexpression of Six1 could suppress inflammation through NF-κB-mediated pathway. Six1 target the promoters of amino-terminal enhancer of split (AES) and translocated in liposarcoma (TLS), which are cofactors of NF-κB subunit RelA, and then inhibit the transactivation function of RelA in a negative feedback circuit. Six1 overexpression resulted in inhibiting inflammation and promoting cell proliferation to reduce kidney damage of mice from IR injury in vivo.

Conclusions: Our studies suggested that Six1 promoted kidney recovery and regeneration through proliferation/migration and anti-inflammation which might be a potential therapeutic target that can be used to improve kidney repair after IR injury.

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PO0156

IRF8-Dependent Regulation of Kidney Dendritic Cells in Ischemic AKI

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Background: Ischemic acute tubular necrosis is a common cause of acute kidney injury (AKI), which involves a greater functional diversity of mononuclear phagocytes (MPCs) such as dendritic cells (DCs). The deletion of DCs induce more kidney injury and impair the recovery of AKI. The hematopoietic transcription factor IRF8 mediates the phenotype of DC. However, the role of IRF8 dependent mechanism during AKI is not well known. Hence, we hypothesized that the dynamically altered expression of IRF8 in DCs could contribute to AKI.

Methods: AKI was induced by transient renal pedicle clamping in C57BL6/J. Kidneys, lymph nodes and spleens were collected on D1, D3 and D7. MPCs were identified by Flow cytometry. Expression of IRF8 and MHC II were quantified by IHC. The knockdown of IRF8 was performed by transfecting siRNA in bone marrow-derived DCs (BMDCs). BMDCs were stimulated with necrotic supernatant from tubular epithelial cells and histones and analyzed by phagocytosis assay, T-cell differentiation assay, RT-PCR or flow cytometry.

Results: In vivo, we identified four distinct phenotypically MPCs with diverse expression status in response to AKI injury. The phenotypes of MPCs in response to AKI injury implies that selective targeting of IRF8 DCs may provide an effective strategy to induce immune-modulation of the progression of AKI.

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PO0157

VNN1 Mediates Renal Maladaptive Repair after AKI by Inducing Premature Senescence of Renal Tubular Cells

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Background: Renal maladaptive repair can lead to the failure of acute kidney injury (AKI) to chronic kidney disease. Sustained renal interstitial damage catalyzes accelerated senescence of renal tubular cells leading to renal fibrosis after AKI. VNN1/1 (VNN1) is an extracellular enzyme with panthenthamelaminic activity that indirectly reduces the synthesis of glutathione, causing oxidative stress. This study aimed at investigating the role of VNN1 in senescence of renal tubular cells after renal ischemia reperfusion (IR) injury.

Methods: Thirty male wild BALB/c mice were randomly divided into control group, sham group and I/R group. In the I/R group, bilateral renal pedicles were clamped for 35 min and reperfusion was performed. The expression of VNN1 were detected. Furthermore, the degree of renal damage and the senescence of renal tubular cells were compared in wild type mice and VNN1 knockout mice after I/R injury.

Results: Scr, BUN and renal injury score increased significantly at the early stage (3d) of renal injury after I/R. Renal fibrosis was observed in the advanced stage (28-42d).

The expression of VNN1 in renal tubular cells of I/R group increased after I/R injury. The protein levels in VNN1 KO mice were significantly lower than those in wild type mice at 7-28 d after renal reperfusion. The renal interstitial fibrosis level was significantly higher in VNN1 KO mice than that of wild type mice at 42d after reperfusion. The results suggest that VNN1 KO promotes renal repair of AKI. It is found that 50% of the VNN1 up-regulated genes after IR renal injury were stress-related genes through mRNA microarray analysis. The ratio of P16 positive tubule cells in VNN1 KO mice was significantly higher than that in wild type mice at 7d after renal reperfusion. The expression levels of phosphorylated Rb1 in VNN1 KO renal tubular cells were significantly higher than those in the wild type renal tubular cells after hyposxia/reoxygenation, suggesting that VNN1 could promote the senescence of renal tubule cells through P16-Rb1 pathway during AKI repair.

Conclusions: VNN1 mediates renal maladaptive repair after AKI by inducing premature senescence of renal tubular cells through P16-Rb1 pathway.

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The Proximal Tubule Is a Source of De Novo NAD+ Synthesis, the Metabolites of Which Are A Valuable Predictor of AKI

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Background: Reduced NAD+ is reported to increase the susceptibility of AKI. De novo synthesis pathway from tryptophan is an important source of NAD+ in the liver and probably kidney. In the present study, we characterized the expression of the enzymes of de novo NAD+ synthesis pathway in the human kidney. We then examined the association of the urine metabolites in this pathway and AKI development in patients who received high-dose methyltrexate (HDMDTX) chemotherapy or liver transplantation (LT) and analyzed their predictive value for AKI.

Methods: The expression of the enzymes of de novo NAD+ synthesis pathway was examined by immunohistochemistry. To examine the predictive value of urine tryptophan metabolites in AKI, 71 patients who received a total of 191 HDMDTX treatments were prospectively enrolled as a discovery cohort and 49 patients receiving LT were enrolled as a validation cohort. Urine samples were collected within 72 hours before chemotherapy/surgery. AKI was defined by KDIGO criteria. Urine tryptophan metabolites were measured by LC-MS and adjusted by creatinine. The performance of these metabolites to predict AKI after HDMDTX/LT was analyzed.

Results: Enzymes of de novo NAD+ synthesis pathway including KMO, KYNU, HAAO, QPR, and ACMSD were detected in renal tubules that were positive for LTL, but not labeled by AQP2, NCCT, nor THP, consistent with proximal tubule expression. A total of 191 HDMDTX treatments were included in the discovery cohort and AKI developed after 35 HDMDTX treatments (18.5%). In those who developed AKI, the urine level of 3-hydroxyanthranilic acid (3-OH AA) was significantly higher while the level of quinolinic acid (QA) was significantly lower compared with those who did not develop AKI (3-OH AA: 4.42 [2.74-9.32] vs 3.57 [1.86-5.73], p = 0.002; QA: 13.43 [9.69-22.34] vs 20.64 [14.80-32.05], p = 0.004). The area under the receiver operating characteristic curve (AUC) of urine QA/3-OH AA for AKI prediction was 0.748. The discrimination ability of the urine QA/3-OH AA on AKI susceptibility was validated in LT cohort, with the AUC as 0.729.

Conclusions: The proximal tubules are an important source of de novo NAD synthesis. Reduced urine QA/3-OH AA ratio is associated with development of AKI. The present study suggests that urine QA/3-OH AA ratio is a potential biomarker to predict AKI and NAD+ synthesis pathway is a potential therapeutic target.

Dietary Omega-3 Fatty Acids After the Lipid Mediator Profile and the Fatty Acid Composition of Membrane Phospholipids but Is Not Enough to Improve Renal Insufficiency

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Background: The efficacy of omega-3 fatty acids on ischemia-induced AKI has been reported, but the underlying mechanisms remain poorly understood. There have been no reports that demonstrated how dietary omega-3 fatty acids influenced the components of membrane phospholipids in the kidney. In this study, we focused on the effect of dietary omega-3 fatty acids on the membrane phospholipids components in the kidney, and examined the disease course of ischemia-induced AKI in the presence of the lipid mediator alterable by dietary omega-3 fatty acids.

Methods: Male 4-week-old wild-type Sprague-Dawley rats were fed for 2 months on AIN-93M, which contains 4% soy oil, or modified AIN-93M, which contains 4% perilla oil instead of soy oil. AKI was induced by unilateral ischemic reperfusion with right nephrectomy. Left renal ischemia was induced by using non-traumatic vascular clamps for 30 min. At 24 h after reperfusion, left kidneys and serum were collected. The fatty acid composition of membrane phospholipids and lipid mediators were quantified by HPLC-tandem mass spectrometry (HPLC/MS/MS).

Results: In the kidney of omega-3 diet fed rats, the levels of arachidonic acid-derived proinflammatory lipid mediators, except for 5-HETE, were not reduced compared with omega-6 fed rats. Eicosapentaenoic acid (EPA) and EPA-derived lipid mediators were significantly increased in the kidney of omega-3 diet fed rats. Furthermore, membrane phospholipids which contained EPA and docosahexaenoic acid (DHA) were significantly increased in the kidney of omega-3-fed diets. However, there was no significant difference in serum creatinine, blood urea nitrogen or histological damage between omega-3 diet fed rats and omega-6 diet fed rats.

Conclusions: Dietary omega-3 fatty acids altered the lipid mediator profile and the fatty acid composition of membrane phospholipids, but was not enough to improve renal insufficiency or histological damage.
PO0164
Kidney Functional Improvements by a Novel Potent and Selective Vasopressin V1a Antagonist After Ischemia-Reperfusion Injury (I/RI) in Rats
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**Background:** Alteration in renal perfusion is a key pathologic mechanism implicated in the development of ischemic acute kidney injury (AKI). We have reported that activation of V1a receptor decreases renal blood flow (RBF) and oxygenation in settings of increased vasopressin (AVP) levels. Here we studied the role of BAY 2327949, a recently identified potent and selective V1a antagonist, in a rat renal I/RI model.

**Methods:** In a first setting, rats were infused with BAY 2327949 (100 μg/min/kg i.v.) or vehicle and baseline measurements were determined for 20 min. Unilateral ischemia was induced by clamping of left kidneys for 15 min, followed by 20 min of reperfusion. RBF and intrarenal oxygenation (pO) were continuously measured via Laser Doppler Flowmetry. In a second setting, kidney function (creatinine, cystatin C, urea) was studied 24h after 45 minutes of ischemia in uninephrectomised male rats treated with BAY 2327949 (0.5, 1, and 3 mg/kg BID, i.v.).

**Results:** Unilateral clamping resulted in an immediate drop of RBF and pO, that partially recovered during reperfusion (figure). Treatment with BAY 2327949 significantly ameliorated the severity of ischemic hypoxia and resulted in an improved and almost complete restoration of RBF and pO during reperfusion (figure). In the second setting, preventive treatment with BAY 2327949 resulted in dose-dependent, significant improvements of kidney function parameters 24h post I/RI as compared to placebo treated rats.

**Conclusions:** BAY 2327949 is a novel potent and selective vasopressin V1a receptor antagonist blocking the detrimental effects of elevated vasopressin levels on renal perfusion and oxygenation. For these reasons, BAY 2327949 could become a viable treatment option in conditions of increased AVP levels, such as AKI and CKD.

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PO0165
Augmentor of Liver Regeneration Protects Kidney from Ischemia-Reperfusion Injury via Regulation of TLR4 Signaling Pathway
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**Background:** Toll-like receptor 4 (TLR4) expressed within the ischemic kidney is a crucial mediator of innate activation and inflammation. The augmenter of liver regeneration (ALR) is an immunoregulator which is highly expressed in kidney upon induction of renal I/R injury. It has been shown that exogenous ALR can protect kidney against I/R injury. However, whether ALR’s protective effect results from its immune regulatory function has yet to be determined. In this study, we show that treating renal I/R induced-rats with recombinant human ALR (rhALR) protects them from kidney I/R.

**Methods:** Rats were randomized into 4 groups as follows: sham-operated group; I/R group; I/R+rhALR1 group; I/R+rhALR2 group. TLR4, neutrophils and macrophages were detected by immunohistochemistry. ERK, JNK, and p38 proteins were tested by WB. mRNA of HMGB-1, Biglycan, HAS1, HAS2 and HAS3 was detected by real-time PCR. The cytokines and chemokines were measured by ELISA.

**Results:** This result is corroborated by less tubular damage on rhALR treated rats than those on untreated rats. rhALR treated rats have significantly less apoptosis in tubular epithelial cells, less tubulointerstitial infiltration by neutrophils (24 h) and macrophages (72 h), as well as lower levels of inflammatory cytokines compared to the untreated control rats. Furthermore, rhALR downregulated mRNA expression of endogenous ligands for TLR4 and restrain activation of TLR4 and downstream signaling molecules (ERK, JNK, and p38) on rats with renal I/R injury.

**Conclusions:** rhALR protects kidney from I/R injury by regulation of TLR4 signaling pathway

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PO0166
DPP-4 Inhibitor Attenuated Renal Vasoconstriction Following Ischemia-Reperfusion Injury in Cirrhotic Rats
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**Background:** Cirrhotic patients may develop esophageal varices to cope with portal hypertension. Variceal bleeding is usually associated with hypotension and ischemia-reperfusion injury (IRI) which may activate endogenous vasoconstrictors, leading to severe renal vasoconstriction and renal failure (so called hepatorenal syndrome). Previous studies reported that dipeptidyl peptidase-4 inhibitor (DPP4i) could attenuate the endothelin-1 (ET-1) induced vasoconstriction and increase vasodilation. The aim of this study is to delineate the effect of DPP4i in renal vascular reactivity of cirrhotic rats following IRI.

**Methods:** Male S-D rats were used for experiments. Biliary cirrhosis was created by common bile duct ligation (CBDL). Control group received sham surgery (SHAM). After surgery, Linagliptin (3 mg/kg/d) or distilled water (DW) was administered for 28 days. On the 29th day, bilateral renal pedicles were clamped with microvascular clamps for 45 minutes in IRI group. The clamps were then removed followed with 60 minutes of reperfusion. Kidneys were perfused in situ via right renal artery for continuous monitoring of renal perfusion pressure.

**Results:** There was no difference in mean arterial pressure, heart rate, portal pressure, and blood sugar between DW and DPP4i treated rats. IRI enhanced renal vascular response to ET-1 in both SHAM (p=0.027) and CBDL (p=0.025) rats, implying renal vasoconstriction. Compared with corresponding DW-treated rats, DPP4i treatment abrogated renal hyperreactivity following IRI in CBDL rats (p=0.036), but not in SHAM rats (p=0.737).

**Conclusions:** We concluded that DPP4i may attenuate the development of renal vasoconstriction following IRI in cirrhotic rats. The potentially mechanisms remained to be elucidated.
Concentration-response curves to ET-1 in perfused kidneys of SHAM (A) and BDL (B) rats.

PO0167

PTEN Protects Against Ischemia Reperfusion-Induced AKI via Regulating TNF-α Mediated Apoptosis

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Background: Recently, PTEN, a vital tumor suppressor, has been raised its role in kidney homeostasis. We previous demonstrated that podocyte-specific knock-in of PTEN alleviated albuminuria and glomerulosclerosis in diabetic kidney disease. However, whether PTEN involves in acute kidney injury (AKI) remains unclear.

Methods: The levels of PTEN in renal tissue and serum were detected in ischemia-reperfusion (IR)-induced AKI mice with different ischemia time. Expression of PTEN was also detected in IR-induced cultured HK-2 injury with different ischemia and reperfusion time using ATP/glucose depletion that concentration of antimycin A mimicked the severity of ischemia. Immunoprecipitation and mass spectrometry were combined to analyze differential PTEN-interacting proteins among control, IRI+LV-NC and IRI+LV-PTEN groups. PTEN intervention including knock-down (si-PTEN) and knock-in (lentivirus-PTEN) was performed in HK-2 to reveal the role and mechanism of PTEN in IRI-AKI.

Results: PTEN was significantly reduced in renal tissue and serum in AKI mice at bilateral renal artery occlusion for 28 min and 35 min, and reperfusion for 1 day compared with sham group (P<0.05). Concentration of serum PTEN was negatively correlated with level of serum creatinine (r=-0.87, 95% CI -0.94 to -0.71). PTEN was also downregulated in IR-induced HK-2 injury in an antimycin A concentration dependent manner (P<0.05). There were 23 upregulated (ACO2, BRCA1, USP30), and 20 downregulated (BIN1, pericentrin, SLC12A5) PTEN-interacting proteins in IRI+LV-PTEN group compared with IRI+LV-NC group. Gene Ontology enrichment analysis showed that overrepresentation of differential PTEN-interacting proteins functionally related to cytoskeleton, and ATPase activity. Pathway analysis showed a great role of differential PTEN-interacting proteins in apoptosis, and necroptosis. Knockdown of PTEN increased the expression of NGAL, Ctgf and TNF-α in IR-induced HK-2 injury (P<0.05), while overexpression of PTEN alleviated IR-induced injury (P<0.05).

Conclusions: PTEN was decreased in renal tissue and serum associated with severity of ischemia injury in IRI-AKI mice, suggesting that PTEN is promising to be a serum biomarker for early prediction and evaluation of AKI. PTEN protected HK-2 from IR-induced injury possibly via regulating cytoskeleton and TNF-α-mediated apoptosis signal.

PO0168

Endothelial Prolyl-Hydroxylase Domain Proteins Regulate Capillary Rarefaction Following Ischemic AKI and Reprogram Endothelial Metabolism

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Background: Endothelial cell (EC) metabolism has emerged as a new regulator of EC behaviour, but its role in capillary rarefaction, a common feature of progressive renal disease, remains unknown. Because EC sense oxygen and metabolic alterations through Prolyl hydroxylases 1 to 3 (PHD1-3), here we wished to define the impact of PHD inactivation on post-ischemic kidney injury outcomes, while in vitro studies focused on metabolic consequences.

Methods: Following the induction of renal ischemia-reperfusion injury (IRI), concurrent deletion of PHD1,2,3 was achieved by the Cdhs5(PACCreER) inducible system. Analysis was performed at day 14 post-IR. Furthermore, we examined the impact of DMOG, a PHD inhibitor on angiogenic capacities and global metabolic profiles of endothelial cells.

Results: Post-ischemic kidneys of PHD1,2,3−/− showed more fibrosis, as indicated by 68% increase in collagen area (P=0.005) and significant upregulation of profibrotic genes Loa12, Tgfβ and Acta2 (n=6-8, P<0.05) compared to controls. Quantitative analysis of endomucin staining showed 50% decrease in peritubular capillary density, associated with reduced endothelial proliferation as indicated by Ki-67 immunostaining (n=4, P=0.005). Notably, biochemical inactivation of PHDs by DMOG reduced EC proliferation in MTT assay (P=0.0001) while cell cycle analysis showed decrease of cells in S (~39%, n=3, P<0.05) and G2/M phases (~28%, n=3, P<0.05). Furthermore, DMOG reduced EC migration (50%, n=3, P<0.005) and tube formation. LC-MS analysis showed a profound effect of DMOG in glycolytic, TCA cycle, lipid and, nucleotide metabolites. Specifically, EC treated with DMOG showed an increase in lactate (1.46-fold, P<0.05) and significant reductions in citrate (2.2 fold, P=0.001), alpha-ketoglutarate (2.5 fold, P<0.001), malate (1.4-fold, P<0.05) and malate (1.3 fold, P=0.01). Supplementation with citrate partially rescued the proliferation defect induced by DMOG, suggesting that PHDs may affect angiogenic responses through alterations in mitochondrial metabolism.

Conclusions: Post-ischemic endothelial inactivation of PHDs promotes peritubular capillary rarefaction and fibrosis following AKI, a response which could involve alterations in mitochondrial metabolism.

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Poster

PO0169

Treprostinil Inhibits Mitochondria-Mediated Apoptosis During Renal Ischemia-Reperfusion Injury in Rats

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Background: Renal ischemia-reperfusion (IR) injury is a major factor that contributes to acute kidney injury, which is associated with high morbidity and mortality. Renal I/R injury compromises mitochondrial structure and function, further exacerbating renal tubular injury. Currently, there is no treatment for I/R injury available. We recently demonstrated the efficacy of treprostinil (Remodulin®), an FDA-approved prostacyclin analog, in reducing acute kidney injury during bilateral rat renal I/R injury. In this study, we investigated the role of treprostinil in reducing mitochondria-mediated apoptosis during rat renal I/R injury.

Methods: Male Sprague Dawley rats were randomly assigned to groups: control, sham, I/R, treprostinil or I/R-treprostinil and subjected to 45 minutes of bilateral renal ischemia followed by 1-72 hours reperfusion. Placebo or treprostinil (100 ng/kg/min) was administered subcutaneously via an osmic minipump. Blood and kidney tissue were collected for analysis.

Results: Treprostinil significantly reduced peak elevated Scr vs. placebo (0.6 ± 0.05 vs. 2.1 ± 0.2 mg/dl, p<0.001) at 24-hour post-reperfusion. Treprostinil also prevented I/R-mediated renal apoptosis at 6-hour post-reperfusion vs. placebo (1.0 ± 0.01 vs. 1.4 ± 0.01, p=0.001) relative to control, determined by TUNEL assay. Mitochondrial DNA (mtDNA) copy number was reduced by 23% in I/R-placebo group (p=0.067) from control, starting, following 1-hour post-reperfusion. In contrast, treprostinil preserved mtDNA content to control levels (p=0.01). In addition, placebo increased cytochrome c release into cytosol by 2.4-fold vs. control (p=0.05) at 1-hour post-reperfusion, which treprostinil prevented. Non-targeted semi-quantitative proteomics data using SWATH-MS showed decreased renal ATP levels in placebo, which were restored by treprostinil to that of control at 6-hour post-reperfusion (p<0.05).

Conclusions: Our results demonstrate that treprostinil reduces mitochondrial-mediated renal apoptosis, evidenced by reduced cytochrome c release, restored mtDNA copy number and ATP protein concentration to that of control kidney levels, thereby accelerating mitochondrial recovery and protecting renal tubules from I/R-induced apoptosis. These results suggest that treprostinil is a viable therapy to reduce renal I/R injury.

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PN00170

DNA Repair Factor KAT5 Acts Against Ischemia-Reperfusion Injury Through Promoted DNA Repair and KCC3-Dependent TGF Regulation in Proximal Tubular Cells

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Background: It is known that an episode of ischemia-reperfusion (IR) results in tolerance to subsequent IR, which is so-called “pre-conditioning (PC) effect”. However, the molecular mechanisms of the pre-conditioning effect have not been elucidated. We have recently discovered that DNA double strand break (DSB) repair tolerance factor KAT5 is essential for maintenance of podocyte integrity (Cell Rep. 2019). Here we investigated the role of KAT5 in PC effect.

Methods: Wild-type (WT) mice and proximal tubular epithelial cell (PTEC)-specific KAT5 knockout (KO) mice underwent IR injury by clamping bilateral renal arteries for 30 minutes followed by reperfusion. Ischemic pre-conditioning was performed 1 week prior to IR injury. In vitro studies using cultured human PTECs (HK2 cells) were conducted with ATP depletion by Antymicin A (AMA), an in vitro model of acute tubular cell damage.

Results: Serum UN, Cr, urine NGAL, DNA DSB marker γHAX and KAT5 expression of the PTECs were increased and chloride transporter KCC3 expression was decreased at 24 hours after IR. IR with PC showed an attenuated increase in serum UN, Cr urine NGAL and DNA DSBs with accelerated KAT5 and KCC3 expression. Mass spectrometry imaging of the kidney cortex following the first IR demonstrated elevated glomerular adenensine, which is used as a marker of accelerated tubule-glomerular feedback (TGF), whereas it was decreased after the second IR with PC in WT mice, suggesting attenuated TGF in the second IR. Therefore, increased chloride uptake through KCC3 in PTECs may contribute to the suppression of TGF, which maintained GFR. In KAT5 KO mice, PC effect was attenuated with increased DNA damage and decreased KCC3 expression. In vitro ATP depletion studies showed elevated KAT5 and KCC3 expression following second treatment with AMA. Chromatin accessibility assay showed promoted chromatin accessibility of the KCC3 promoter region after the second treatment with AMA. ChiP analysis revealed that KAT5-binding KCC3 promoter region was significantly increased after the second injury compared with the first injury, indicating that elevated KCC3 expression was caused by increased binding of KAT5 to the KCC3 promoter region.

Conclusions: PTEC KAT5 may act against IR injury through promoted DNA repair and regulation of TGF via KCC3 expression.

PN00172

Blocking the Histone Lysine 79 Methylation Transfer DTT1 Ameliorates AKI

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Background: The Disruptor of telomeric silencing 1-like (DOT1L) gene encodes a histone methyltransferase that methylates lysine-79 of histone H3 (H3K79). DOT1L-dependent H3K79 methylation plays an important role in various physiological and pathological processes, including transcriptional regulation, embryonic development and renal fibrosis. However, its role in acute kidney injury (AKI) tissue injury remains unknown.

Methods: AKI was induced in Male C57Bl/6 mice by bilateral ischemia-reperfusion (IR) or intraperitoneal injection with folic acid (FA). EPZ5676, a highly selective inhibitor of DOT1L (20 mg/kg) or an equal volume of vehicle was administered immediately after IR or FA injection and then daily for two days. Renal function and histology were assessed by serum creatinine and HE staining. Immunohistochemistry and Western blotting were performed to identify tubule injury (NGAL), apoptosis (TUNEL and cleaved Caspase 3), proliferation (PCNA and Cyclin D) and Wnt signaling activation (active β-catenin and β-catenin).

Results: Mice developed AKI at 48 h after IR injury or FA administration as shown by the upregulation of serum creatinine and NGAL expression levels. Pharmacologic inhibition of DOT1L with EPZ5676 resulted in less severe tubular injury as evidenced by reduced renal dysfunction, diminished NGAL expression. Furthermore, the administration of EPZ5676 significantly reduced the number of TUNEL-positive and cleaved Caspase-3 positive tubular cells in kidneys. Conversely, renal tubular cell proliferation was enhanced as indicated by increased expression of PCNA and cyclin D. Moreover, DOT1L inhibition by EPZ5676 up-regulated the expression of active β-catenin form and β-catenin.

Conclusions: Our data reveals that blocking DOT1L with EPZ5676 may protect against AKI in mice through inhibition of apoptosis and enhancement of kidney repair by a mechanism involved in the modulation of the canonical Wnt signaling pathway.

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PN00173

Triptolide Treats Renal Tubular Injury Induced by Renal Ischemia-Reperfusion Through Specific Delivery of Kidney-Targeting Nanoplatfrom

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Background: Triptolide (TP) has been proved to be effective in the treatment of a variety of kidney diseases. Unfortunately, its clinical application is limited because of its high toxicity and low specificity. Here, we report a novel and safe kidney-targeting nanoplatfrom for specific delivery of TP.

Methods: Nano-polymer MNPs-TP was synthesized by encapsulating TP in a mesoscale nanoparticles (MNPs) with kidney targeting ability. MNPs-TP was injected into mice via tail vein to evaluate its toxicity to organs and immune system, and compared with free TP. The targeting and mechanisms of MNPs-TP treatment were explored by organ imaging, Transwell and other experimental methods. Finally, the model of renal ischemia-reperfusion injury (IRI) in mice was established, and the protective effects and mechanisms of TP and MNPs-TP on renal tubules in different concentrations were compared.

Results: Toxicity test showed serious pathological changes in liver, testes and the proportion of CD4+/cd8+ in blood of mice in TP group, while MNPs-TP showed no toxic effect on these organs. In vivo study showed that TP and MNPs-TP (5 mg/kg) could protect the renal tubules by down-regulating the expression of kidney injury marker (NGAL), proliferation (PCNA and Cyclin D) and Wnt signaling activation in kidneys of mice with AKI. Western blotting was performed to identify renal tubule injury (NGAL), apoptosis (TUNEL and cleaved Caspase 3), proliferation (PCNA and Cyclin D) and Wnt signaling activation.

Conclusions: MNPs-TP showed superior therapeutic effect on renal ischemia-reperfusion injury in comparison with TP. Furthermore, MNPs-TP conjugated presented much lower hepatotoxicity and no adverse effect on the immune and genetic system. The kidney-targeting MNPs may provide a promising drug delivery platform of hydrophobic drugs for treatment of renal diseases.
of urine NGAL is from the plasma, our next step was to examine the renal handling of plasma NGAL.

Methods: Mice: C57Bl/6J. Interventions: bilateral kidney ischemia reperfusion (IR) - 27 minutes; maleic acid (MA) (400mg/kg pH 7.4 in saline, IPA); furosemide (4mg, IPA); uninvolved vehicle animals served as a control. Recombinant human (rh) NGAL (Sig, IV) was injected to determine the fate of circulating rhNGAL. Measurement: transmural glomerular filtration rate (GFR), rhNGAL and mouse (m) NGAL in the plasma and urine, megalin in the urine. To link proximal tubular (PT) function with plasma and urine NGAL levels, we calculated the fractional excretion of rhNGAL (FE-rhNGAL): FE-rhNGAL = ([urine rhNGAL] / [plasma rhNGAL] x [urine creatinine]) / 100.

Results: Uninvolved vehicle: mice had 100% GFR and low levels of plasma and urine (rh)NGAL. IR (ATI model) and MA (PT injury model): 1% and 29% GFR respectively, increased plasma and urine rhNGAL in both models. Furosemide (PT injury model): GFR – 30%, plasma and urine rhNGAL was slightly elevated, urine rhNGAL was similar to control. FE-rhNGAL was less than 1% in normal and PRA mice, and it was greater than 20% in IR and MA treated mice. mNGAL plasma and urine levels, and FE-mNGAL were similar to rhNGAL levels and FE-rhNGAL respectively. Urine concentration of megalin correlated with FE-rhNGAL in every intervention (see Figure). Megalin is expressed on the brush border of PT and is responsible for the resorption of most filtered proteins, including NGAL.

Conclusions: Our data suggest that normal PT function is required for the clearance of plasma NGAL. Consideration of plasma NGAL with FE-NGAL is important to interpret urine NGAL levels and PT function and effectively distinguishes PRA from ATI.

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PO0175
A Case Report of Vaping-Related Renal Thrombotic Microangiopathy

Introduction: Acute kidney injury (AKI) and hematuria have been reported in patients with e-cigarette use (vaping)-associated lung injury (EVALI) but exact renal pathology is not well understood. We report a case of biopsy proven renal thrombotic microangiopathy (TMA) in a patient with EVALI.

Case Description: A 40-year-old woman with history of vaping tetrahydrocannabinol (THC) and depression presented to emergency room with 2 days of fatigue, body aches, non-productive cough, and dyspnea on exertion. On admission, BP was 157/85 mmHg, hemoglobin 5.9, platelet count 239, serum creatinine (Scr) 1.76 with 10-30/hpf non-dysmorphic RBC and 2+ proteinuria on urinalysis. Patient failed initial treatment with diuretics and on day 3, was intubated for respiratory distress. By this time, Scr had increased to 4.68 and LDH was quite elevated (1456) but platelet count was normal (194), haptoglobin high (551) and peripheral stiichocytes only occasional. Her EVALI improved with standard cares in the next week but renal function further worsened, and hemodialysis was started on day 13. Renal biopsy revealed acute TMA with diffuse endothelial swelling, focal segmental glomerular and arteriolar thrombi and activation. Patient was not taking any medications known to cause TMA. Serologic and infection work up were negative including pneumococcus, HIV, antinuclear, anti-Scl70 and antiphospholipid antibodies. The ADAMTS-13 activity was 48% and serum homocysteine was low (3.8). Imaging studies showed no evidence of malignancy. Functional complement work-up did not reveal increased alternative complement pathway activity or autoantibodies. On day 20, patient was started on plasma exchange (PLEX) for 5 sessions followed by a slow renal recovery - last hemodialysis on day 22 and now, more than 1 month after last PLEX and after approximately 2 months of vaping cessation, most recent Scr is 2.57

Discussion: There is no clear association of kidney disease with marijuana use in large population studies but there are case reports of AKI with synthetic cannabinoid use including one report of biopsy proven TMA. Drug-induced TMA is usually a diagnosis of exclusion and temporal correlation. Given the lack of other evident cause of TMA, the diagnosis was made with renal biopsy. No evidence of malignancy, non-sepsis related infection, drug reaction or vasculitis was seen. The patient also had elevated antithrombin III and decreased factor V. TMA was likely related to vaping.

PO0176
A Rare Case of Obstructive Nephropathy with Intratubular Tamm-Horsfall Polyps Secondary to Acquired Hemophilia
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Introduction: Acquired hemophilia has been rarely implicated in obstructive nephropathy. We present a case of gross hematuria, bilateral hydropnephrosis, and biopsy-confirmed tubulointerstitial nephritis with intratubular Tamm-Horsfall Protein (TBP) polyps. These atypical pathological aggregations of urinary glycoproteins were previously described to be located in renal veins or lymphatics. Our case represents a rare etiology of obstructive nephropathy, with unique pathological findings, secondary to an acquired hemophilia.

Case Description: A 64-year-old man with hypertension and tobacco use presented with bilateral flank pain and gross hematuria. On physical examination, the patient had normal vital signs. He denied any recent surgeries. Urinalysis showed hematuria, pyuria, and proteinuria. He had oliguric acute kidney injury (AKI) with creatinine (Cr) of 3.2 mg/dL. Renal ultrasound showed bilateral hydronephrosis. Renal function deteriorated over 3 days to Cr of 7.4 mg/dL with proteinuria of 10 g/day. Serologic markers revealed mildly elevated PR3-ANCA. Pulse steroid therapy was begun and kidney biopsy was performed. Pathology report described acute tubulointerstitial nephritis with TBP polyps and interstitial non-caseating granulomas. Immunohistochemistry assay showed TBP polyps within markedly dilated renal tubules, consistent with obstructive nephropathy. No evidence for vasculitis or other vascular lesions was seen. After biopsy, the patient developed retroperitoneal hemorrhage requiring embolization. Further studies indicated the presence of a factor VIII inhibitor. He improved with transition from steroids to mycophenolate mofetil. A few months later, his renal function returned to normal with a bland urinalysis, proteinuria less than 100 mg/dL and resolution of hydronephrosis.

Discussion: We encountered a rare presentation of acquired hemophilia with macroscopic hematuria and AKI. We suspect that blander clots and associated intraluminal clots resulted in elevated tubular pressures causing obstructive nephropathy and the formation of intratubular TBP polyps. Administration of immunosuppressive therapy resulted in cessation of the polyps as well as factor VIII inhibitor production, reinforcing our hypothesis. Anti-factor VIII antibodies are a rare complication of solid tumors and urologic malignancy work-up is ongoing.

PO0177
Reflex Anuria: A Forgotten Urologic Etiology of AKI
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Introduction: Reflex anuria (RA) is a rare entity that can lead to severe acute kidney injury (AKI). It was defined by Hull and colleagues in 1980 as “cessation of urine output from both kidneys in response to irritation or trauma to one kidney or its ureter or severe painful stimului to other pelvic organs”. RA represents a gray area between nephrology and urology and should be considered in the differential diagnosis of AKI. We present a case of AKI and anuria where the prompt recognition and management of RA resulted in full recovery of kidney function and avoidance of renal replacement therapy and unnecessary testing.

Case Description: A 40-year-old male with Crohn’s disease status post prior right and left hemicolectomy was admitted with worsening abdominal pain and hematochezia consistent with Crohn’s flare. He underwent open abdominoperineal resection. Pre-operatively, urology performed cystoscopy and prolabolistic bilateral ureteral stent placement. Stents were removed without complication at the end of the case. On post-op day 1, he developed oliguria that progressed to complete anuria. This was associated with rapid rise in serum creatinine up to 5.5 from baseline of 0.6 (Figure 1). The differential diagnosis was broad, including acute tubular necrosis, vascular thrombosis and obstruction but because of the temporal relationship with recent procedures, RA was suspected as the etiology of AKI. Patient underwent urgent bilateral ureteral stent placement which was followed by brisk urine output (~11 L/24 hours) and normalization of serum creatinine.

Discussion: RA is a rare diagnosis that requires high index of clinical suspicion. It is a functional rather than parenchymal disease that can cause dramatic cessation of urine output and AKI. Neurovascular reflex leading to arteriolar vasocstriction and ureteric spasm is a proposed mechanism. This case illustrates that acute anuria and AKI after bilateral ureteral stent placement.

PO0178
AKI in a Patient with COVID-19, G6PD Deficiency, Acetaminophen Overdose, and Methemoglobinemia: What a Broad Differential!
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Introduction: Acute kidney injury (AKI) is a common complication in hospitalized and critically-ill patients. Prompt evaluation and subsequent management is warranted to avoid long term kidney dysfunction. However, a clear diagnostic pathway is not always possible. We present a case and the diagnostic analysis of intrinsic AKI in an unusual confluence of comorbidities.
Discussion: Our patient presented with significant abnormalities in multiple organ systems, including AKI. An analysis of comorbid conditions and typical AKI diagnostics allowed an expansive differential diagnosis (fig 1). One remaining interrogate was the value of a kidney biopsy. Although the etiology of his AKI would remain uncertain and presumably multifactorial, the lack of a clear therapeutic option and both hemodynamic instability and high risk of complications impeded a kidney biopsy. This case exemplifies the challenging but common scenarios and dilemmas that nephrologists face every day. AKI is a well-described entity, yet its diagnosis is complex and dynamic.

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CJ.7

PO0179
Catch 22: The Vicious Cycle of Malignant Hypertension and Worsening Renal Thrombotic Microangiopathy
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Introduction: Renal Thrombotic microangiopathy (TMA) may arise from multiple distinct etiologies. Malignant hypertension is one of these conditions that can precipitate and worsen renal TMA.

Case Description: 34-year-old woman with a history of gestational hypertension, presented to the ED with complaints of a viral URI and was found to be in an hypertensive emergency with an SBP in the 260's. She was a non-smoker and did not use drugs or alcohol. She denied having any other symptoms or any recent medication use. Her labs were notable for hemolytic anemia and acute kidney injury with a creatinine of 4.0 mg/dL. A peripheral smear confirmed schistocytes, along with a normal serum ADAMTS 13 activity at 89. Extensive work-up for atypical hemolytic uremic syndrome was negative and complement levels were normal. Renal ultrasound showed diffusely increased renal cortical echogenicity. Renal biopsy confirmed the diagnosis of acute on chronic renal function and 62 % of patients with poor outcome had glomerular crescents involving 43–75% of the glomeruli.

Discussion: This is a case of an elderly male patient who developed AKI with kidney biopsy that showed lupus nephritis; however, ANA and anti-dsDNA antibody were negative. Patient's renal function continued to worsen that he eventually required hemodialysis. On 6-month repeat chest CT showed resolution of bibasilar opacities, although with persistent upper lobe ground glass opacities consistent with smoking and vaping-related injury.

Renal Limited Lupus-Like Nephritis in an Elderly Male
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Introduction: Lupus nephritis is a major cause of morbidity in Systemic Lupus Erythematosus (SLE). 60% of SLE patients develop renal impairment, which is more common in age < 55 years old. SLE has a female predominance with a female-to-male ratio of 8:1. We report a case of an elderly male, who has negative serology and absence of extra-renal manifestations of SLE, diagnosed with renal limited lupus-like nephritis (RLLN).

Case Description: A 76-year-old Caucasian male with no previous history of renal or autoimmune diseases was admitted because of acute kidney injury (AKI). Patient had no history of joint pain and swelling, rash, or oral ulcers. He was not taking NSAID or Hydralazine. Laboratory test showed creatinine 2.7 mg/dL, serum albumin 2.1 g/dL, urine protein creatinine ratio 725mg/g, and urinalysis with dysmorphic RBC of >5 RBC/HPF. Serology showed negative anti-dsDNA, ANA titer <1:40 and undetectable complements C3 and C4. Human immunodeficiency virus, and rapid plasma reagin were also negative. Patient’s renal function continued to worsen that he eventually required hemodialysis. A renal biopsy was performed. Light microscopy revealed diffuse endocapillary hypercellularity and no crescent lesion. There was a full house with global granular mesangial and basement membrane staining for IgG, IgA, IgM, C1q, C3, free kappa and lambda light chains under immunofluorescence microscopy. Electron microscopy revealed mesangial and subendothelial dense deposit and segmental duplication. All these findings are consistent with RLLN.

Discussion: This is a case of an elderly male patient who developed AKI with kidney biopsy that showed lupus nephritis; however, ANA and anti-dsDNA antibody were negative and there were no clinical manifestations of SLE. The patient was treated with Methylprednisolone, which was followed by Prednisone and Mycophenolate Mofetil (MMF). On 6-month follow-up, there was improvement in C3 and C4, and 24-hour CrCl estimated the GFR of 35 ml/min; hence, hemodialysis was discontinued. On 6-month follow-up, serum creatinine 1 mg/dL, BUN 14 mg/dL, and GFR >60 ml/min. Our patient’s kidney function recovered; however, there is no definite prediction of RLLN prognosis due to limited data. 47% had a poor outcome with a permanent decrease of renal function and 62 % of patients with poor outcome had glomerular crescents involving 43–75% of the glomeruli.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Postpartum Thrombotic Microangiopathy of Unknown Etiology: Is It Too Late to Save the Kidneys?
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Introduction: Thrombotic microangiopathy (TMA) is a rare (0.004%) but life threatening complication in pregnancy. Differentials include uncontrolled hypertension, Hemolysis elevated liver enzymes low platelet count (HELLP) syndrome, atypical Hemolytic Uremic Syndrome (HUS), Thrombotic Thrombocytopenic Purpura (TTP) among others. Lack of randomized trials and absence of gold standard laboratory tests can make diagnosis and treatment challenging. We present a patient with post-partum TMA confirmed on renal biopsy with no conclusive etiology identified.

Case Description: A 36 years old African American patient, G7P5 with history of Hypertension (HTN) and preeclampsia was noted to have blood pressure elevated to 180/103 mmHg during an antenatal care visit at 36 weeks of gestation. Serum Creatinine (sCr) was 0.5mg/dl with urine protein/Cr ratio (UPCR) of 0.75 g/g. She had an induced labor with persistent HTN postpartum. She left against medical advice and was readmitted 10 days later with acute kidney injury (AKI) with sCr of 6 mg/dl and UPCR was 4g/g. urinalysis showed positive protein but no RBCs. BP was elevated to 143/97 mmHg. Laboratory data showed AST 33 U/L, ALT 24 U/L, Hb 9.5 g/dL, platelet counts 211 X10^9/L, C3 of 74 mg/dL, C4<2 mg/dL, negative ANA, ADAMTS 13 >94. Cryo results was inconclusive although RF was elevated at 160 IU/mL. Blood smear showed no schistocytes. She was started on pulse steroids for clinical suspicion of eclampsia. Her workup during his hospital admission revealed a normal ADAMTS13 activity, negative blood and urine cultures, negative 0157:H7 stool antigen, negative urinary streptococcal antigen, negative autoimmune screen, negative hepatitis and HIV serologies, normal vitamin B12 level, normal bone marrow and pan-imaging without malignancy. A renal biopsy revealed acute and chronic TMA in renal arterioles with fibrinoid necrosis, immunohistochemically-proven hemoglobin casts on kidney biopsy associated with intravascular hemolysis. Below is a case of Rifampin-induced hemolysis associated with acute kidney injury (AKI) by various mechanisms including hemoglobin cast nephropathy. This can resemble other causes of AKI such as acute tubular necrosis, acute interstitial nephritis (AIN) and thrombotic microangiopathy (TMA). Few studies have demonstrated immunohistochemically-proven hemoglobin casts on kidney biopsy associated with intravascular hemolysis. Below is a case of Rifampin-induced hemolysis associated with acute kidney injury (AKI).

Case Description: A 62-year-old man with recent diagnosis of Sweet’s syndrome was started on high dose prednisone and TMP-SMX for prophylaxis. He presented 4 days later with confusion, prolabous diaphoresis and “brown-colored” urine. He was normotensive on exam, without cardiac murmurs, clear lungs, soft non-tender abdomen and no skin rashes. Initial labs showed microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury with hyperkalemia. Blood smear showed schistocytes. He received emergent hemodialysis followed by plasma exchange for suspected TTP/HUS. Extensive workup during his hospital admission revealed a normal ADAMTS13 activity, negative blood and urine cultures, negative 0157:H7 stool antigen, negative urinary streptococcal antigen, negative autoimmune screen, negative hepatitis and HIV serologies, normal vitamin B12 level, normal bone marrow and pan-imaging without malignancy. A renal biopsy confirmed TMA. He remained anuric and dialysis dependent on discharge.

Discussion: Patients with TMA have symptoms arising from anemia, thrombocytopenia, renal failure, or from underlying diseases like systemic infections, malignancies or drug toxicities. Once TMA is confirmed, elucidating the cause of TMA is important because there are specific treatments available for primary TMA syndromes like TTP and complement-mediated TMA. High suspicion of TTP requires urgent plasma exchange until ADAMTS13 levels return, and if complement-mediated TMA is likely, the terminal-complement inhibitor eculizumab can be used. Drug-induced TMA require prompt discontinuation of the drug and supportive management. Trimethoprim-sulfamethoxazole is a rare cause of thrombotic microangiopathy, and the exact mechanism is not understood. Our case highlights the importance of considering TMP-SMX as a potential cause in patients presenting with TMA.

Hemoglobin Cast Nephropathy in Rifampin-Induced Hemolytic Anemia
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Introduction: Hemoglobin released after intravascular hemolysis causes acute kidney injury (AKI) by various mechanisms including hemoglobin cast nephropathy. This can resemble other causes of AKI such as acute tubular necrosis, acute interstitial nephritis (AIN) and thrombotic microangiopathy (TMA). Few studies have demonstrated immunohistochemically-proven hemoglobin casts on kidney biopsy associated with intravascular hemolysis. Below is a case of Rifampin-induced hemolysis associated with acute kidney injury (AKI).

Case Description: A 64-year-old female with recurrent pulmonary Mycobacterium Avium Complex (MAC) infection treated with Rifampin, Ethambutol and Azithromycin presented with nausea and vomiting two weeks after starting therapy. Physical exam was remarkable for small purpuric lesions on the back. Labs showed a serum creatinine of 0.66 mg/dL, BUN 66 mg/dL, hemoglobin 11.1 g/dL, and platelets 9,000/µL. Haptoglobin was normal. LDH was elevated at 507 units/L. A direct antibody test was negative. Urinalysis showed large blood and microscopy showed 2-5 RBCs per hpf and dark granular casts.

PO0182
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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Renal ultrasound was unremarkable. Plasma exchange was initiated for possible TMA but discontinued when ADAMTS13 level returned normal. On day four, serum creatinine was 8.1 mg/dL. She received methylprednisolone 120 mg daily for three days due to concern for possible Rifampin induced AIN. A kidney biopsy was planned and hemodialysis was performed to optimize platelet function. Kidney biopsy demonstrated intratubular pigmented casts that were strongly positive for hemoglobin A immunohistochemical stain confirming the diagnosis of hemoglobin cast nephropathy [Figure 1]. She received supportive care with kidney function gradually improving. Creatinine was 2.87 mg/dL on discharge and 1.18 mg/dL four weeks later.

**Discussion:** Hemoglobin cast nephropathy is a rare diagnosis and requires high index of suspicion in patients with hemolysis and AKI. Diagnosis is multifaceted requiring a clinical history, exam, lab workup and most importantly, a kidney biopsy.

**Case Description:** A 39-year-old woman who underwent laparoscopic hysterectomy presented to ED 4 days following surgery with abdominal pain. Her vitals revealed hypotension and tachycardia. Initial laboratory values were as follows: WBCs 18.0x10^9/L, Na 134 mmol/L, K 4.9 mmol/L, Cl 101 mmol/L, HCO3 17 mmol/L, BUN 45 mg/dL, serum Cr 7.4 mg/dL, lactate 2.4 mmol/L. UA was remarkable for hematuria with 25 RBCs/HPF. Abdominal US revealed moderate ascites. An indwelling bladder catheter was placed, and she underwent diagnostic paracentesis, with WBC noted at 1288/μL (35% neutrophils) and ascites-to-serum Cr ratio of 2.14. CT abdomen with IV contrast confirmed a full-thickness tear of the superior wall of the urinary bladder, with the bulk of the indwelling catheter extending beyond the bladder and an associated urinoma surrounding the catheter (Figure 1). She was diagnosed with bladder perforation and underwent open bladder repair emergently. Her serum Cr improved to 0.5 mg/dL in 24 hours.

**Discussion:** Uropertoneum can result in the reabsorption of urine into the systemic circulation, while sodium and chloride ions move in the opposite direction. This results in hyponatremia, metabolic acidosis, azotemia and rise in serum Cr. Uropertoneum should be expected when ascites to serum Cr ratio is >1.0. It is essential to recognize that the rise in serum BUN and Cr is due to pseudo-azotemia from the reabsorption of urine and not from true kidney dysfunction. Bladder injury is diagnosed by CT cystography, which was deferred in our patient giving the clear evidence of bladder injury in the CT abdomen. Complex extra-peritoneal and all intraperitoneal bladder injuries require surgical repair.

**PO0186**

**Recurrent Stage 3 AKI Resolves with Establishing the Diagnosis of TAFRO Syndrome and Treatment with Anti-IL-6 Antibody**

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**Introduction:** TAFRO syndrome, a unique variant of idiopathic multicentric Castleman’s disease (MCD), is a syndrome with a constellation of thrombocytopenia, anemia, fever, reticulin myelodysplasia/critical insufficiency, and organomegaly. Its pathogenesis is driven by excessive cytokine storm, most notably from IL-6, causing multiorgan failure. 30% of patients with TAFRO-MCD patients require dialysis. Glomerular thrombotic microangiopathy (TMA) and membranoproliferative glomerulonephritis are the most characteristic lesions. We present a challenging case of recurrent dialysis requiring AKI in whom recognition of TAFRO syndrome and glomerular TMA-like lesion led to successful treatment with anti-IL-6 therapy and subsequent definitive diagnosis of MCD.

**Case Description:** A 35-year-old Hispanic female presented in May 2019 with fever, hypotension, anemia, thrombocytopenia, anasarca, hepatosplenomegaly, generalized lymphadenopathy, and anuric AKI. She was admitted to the intensive care unit, required vasoressors, mechanical ventilation, and initiation of continuous renal replacement therapy (CRRT). A comprehensive workup for infectious and autoimmune etiologies was unrevealing. This puzzling presentation was presumed to be driven by an unidentified viral illness. She received an empiric course of IVIG and steroids with mild improvement in anemia, thrombocytopenia, and complete renal recovery. A month later, she was admitted with a similar presentation and proteinuria. She once again required CRRT. Lab work revealed elevated IL-6. Lymph node and bone marrow biopsy were non-contributory. A renal biopsy revealed glomerular capillary endotheliosis. This time it became clear that she had a TAFRO phenotype and decided to treat her with tocilizumab (anti-IL-6 antibody) every two weeks. She had complete recovery of AKI, anemia, and thrombocytopenia within four weeks. She has been on anti-IL-6 antibody for one year, and the disease is in remission. An excisional lymph node biopsy in May 2020 confirmed the diagnosis of Castleman’s disease.

**Discussion:** TAFRO syndrome-MCD related renal involvement has been reported from Japan and France. This case highlights that knowledge of TAFRO syndrome as a cause of AKI, its diagnostic approach, and renal history is valuable for Nephrologists.

**PO0188**

**Urine Proteomics Among Children Developing AKI After Hematopoietic Stem Cell Transplant (HCT): A Pilot Study**

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**Background:** AKI is common after HCT and contributes to high morbidity and mortality. Understanding the mechanisms of injury is essential to develop targeted therapies. Our objective was to examine urinary proteins among children after HCT to provide insights into the pathophysiology of AKI in a population whose immune system is newly developing.

**Methods:** Children (>2 years old) undergoing their first allogeneic HCT and enrolled in a prospective, observational cohort had urine collected at baseline and monthly for the 4 months post HCT. Six patients were selected for pilot proteomic analysis (age 7-19 years, median 10 years, 66% male, 3 with AKI, 3 without AKI). Stored urine samples were tested pre-HCT and at 1 and 4 months post-HCT. Samples were tested with liquid chromatography/tandem mass spectrometry with data-independent acquisition. Proteins were assigned and intensities compared between AKI and controls using t-tests at p<0.05. AKI was defined as a 1.5-fold increase in the monthly serum creatinine value compared to baseline.

**Results:** At 1 month post-HCT, 143 proteins were found distinct among the urine of children with AKI(n=3) compared to those without AKI (n=3). Pathway enrichment analysis linked these proteins to cell cycle and ubiquitous pathways. The 4 month time point resulted in identification of 67 proteins which were differentially expressed between AKI and control groups. These proteins were mostly involved in immune regulation. In both groups, unsupervised hierarchical clustering perfectly segregated the subjects based on AKI or control status (Figure). Protein analysis linked these proteins to cell cycle and ubiquitous pathways. The 4 month time point resulted in identification of 67 proteins which were differentially expressed between AKI and control groups.

**Conclusion:** The urinary proteomic fingerprint is distinct after AKI and are mostly cell cycle proteins in early AKI (first month) and immune mediated at 4 months, when most patients are fully engrafted. Additional studies are needed to define and understand the specific pathways.

**Funding:** Private Foundation Support

**PO0187**

**Apparent AKI in a Patient with Ascites Following Laparoscopic Hysterectomy**

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**Introduction:** Bladder injury occurs following blunt or penetrating trauma. Gynecological and colorectal surgeries are the most common surgeries associated with bladder injury. Bladder injury can be classified as intra versus extra-peritoneal. Clinical manifestations include gross or microscopic hematuria, ascites, and/or difficulty voiding. Peritonitis and sepsis are common complications.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline** represents presenting author.
glomerulosclerosis (FSGS). Anabolic steroids are directly toxic to renal glomeruli. Rates (GFR) and achieve greater muscle mass. However, steroids and high-protein supplements is widespread among athletes and bodybuilders seeking to enhance performance and renal function deteriorated. Renal biopsy showed global and segmental acute renal failure, rhabdomyolysis, and (8-25), Cr 13.4 mg/dL (.3-1.2), months ago. Labs were months. He...comes with a significant risk of renal failure. Unfortunately despite multiple hospitalizations, the patient repeatedly missed dialysis...tunneled dialysis catheter and was discharged with close outpatient follow up.

**PO0190**

Roid Renal Failure

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**Introduction:** Athletes and bodybuilders often utilize anabolic steroids and high-protein supplements to gain muscle mass, however the use of such performance enhancers comes with a significant risk of renal failure.

**Case Description:** A 34-year-old male weightlifter presented with worsening exertional dyspnea, hemoptysis, and bilateral leg swelling over 2-3 months. He admitted to weekly testosterone injections, testosterone-increasing supplements, and a high-protein diet for the past 5 years. To address his lower leg swelling, the patient started Expel, an over-the-counter potassium-sparing diuretic, 2 months ago. Labs were significant for bicarb 19 mmol/L (21-30), BUN 166 mg/dL (8-25), Cr 13.4 mg/dL (3.1-2), and CPK 2630 U/L (26-308). Chest X-ray showed right lower lobe pneumonia. Urinalysis showed proteinuria. Renal ultrasound revealed cortical echogenicity with no hydronephrosis. The patient was admitted for acute renal failure, rhabdomyolysis, and pneumonia. He was started on Ceftriaxone and Azithromycin and placed on IV fluids. During the hospitalization, the patient’s renal function deteriorated. Renal biopsy showed global and segmental glomerulosclerosis, tubular atrophy, severe interstitial fibrosis, arteriosclerosis, and arteriolar hyalinosis. The patient was counseled at length about long term renal replacement therapy and the gravity of his diagnosis. He underwent placement of a tunneled dialysis catheter and was discharged with close outpatient follow up.

Unfortunately despite multiple hospitalizations, the patient repeatedly missed dialysis treatments and continued to use anabolic steroids and high-protein supplements.

**Discussion:** The utilization of anabolic steroids and high-protein supplements is widespread among athletes and bodybuilders seeking to enhance performance and achieve greater muscle mass. However, steroids and high-protein supplements are not benign and their use comes at the risk of renal failure requiring possible long term renal replacement therapy. High-protein supplements increase glomerular filtration rates (GFR) and are associated with the development of focal segmental glomerulosclerosis (FSGS). Anabolic steroids are directly toxic to renal glomeruli. Anabolic steroids bind to podocyte androgen receptors resulting in the apoptotic destruction of podocytes. The patient’s clinic course highlighted the significant risk of renal failure in young athletes using anabolic steroids and high-protein supplements.

**PO0191**

Crystal Clear: A Case of Oxalate Nephropathy

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**Introduction:** Oxalate nephropathy is an uncommon and potentially devastating cause of acute kidney injury that can lead to end-stage kidney disease. Oxalate nephropathy can be hereditary (as in hereditary hyperoxaluria), related to toxins (such as ethylene glycol), medications, like high-dose vitamin C, or enteric malabsorption (such as gastric bypass surgery or malabsorptive disorders). Oxalate nephropathy occurs when calcium oxalate crystals form and deposit in the renal tubules and interstitium, leading to acute tubular necrosis.

**Case Description:** A 71-year-old female with a medical history of pulmonary adenocarcinoma s/p Whipple procedure seven months earlier and chronic kidney disease stage 3 (baseline creatinine 1.0 mg/dL) presented to the hospital with elevated serum creatinine found incidentally on outpatient labs. Initial evaluation was concerning for volume depletion, as she improved with intravenous fluids. Over the next several months, she had repeated hospital admissions with worsening non-oliguric renal failure that seemed to respond to intravenous fluids in the hospital but worsened at outpatient visits. Urinalysis repeatedly showed no microscopic hematuria and low-level proteinuria, and urine microscopy showed coarse granular casts, consistent with acute tubular necrosis. Kidney biopsy was consistent with acute tubular injury and extensive tubular calcium oxalate deposition concerning for oxalate nephropathy.

**Discussion:** Oxalate nephropathy is a rare complication of pancreatic surgery and ascorbic acid use. Vitamin C is metabolized to oxalate and then excreted in the urine. In malabsorptive disorders, a higher concentration of fatty acids are present in the gastrointestinal tract, which bind calcium, leaving less to bind oxalate, and thus more oxalate is absorbed. High urinary oxalate can cause crystallization in tubules, leading to acute renal failure. Treatment is supportive, with removal of offending agents, oral calcium supplementation, and adequate oral hydration. Despite this, our patient progressed to end-stage renal disease requiring dialysis.

**PO0192**

A Novel Flow Cytometry Approach Identifies Kidney Mononuclear Phagocyte Subsets Involved in Mouse Kidney Injury Models


**Background:** Mononuclear phagocytes (MNPs) are heterogeneous in phenotype and function, which reflects their double-edged role as drivers of inflammation and repair after kidney injury. Dissection of this complex network of cells into functional subunits has been challenging and more granular approaches could help to identify relevant subsets in preclinical kidney injury models. Here we used a novel flow cytometric approach to phenotypically and functionally dissect renal MNPs and perform a thorough comparison of MNP dynamics between two different kidney injury models.

**Methods:** The dynamic regulation of MNP subsets was monitored over 10d in two frequently used murine kidney injury models: ischemia reperfusion injury (IRI) and unilateral ureter obstruction (UUO). Using flow cytometric markers F4/80, CD11b and CD11c, kidney MNPs were phenotypically divided into five distinct subsets, which were further subdivided into functional subsets of proinflammatory M1-like (CD16+MHCI+CD206-) and regulatory M2-like (CD206+) cells.

**Results:** Three of the five renal MNP subsets were heavily contributing to both M1- and M2-like cell pools in both IRI and UUO, highlighting their functional multifinality in vivo. Phagocytosis. The F4/80pos MNP subset contributed most M2-like cells as from day 3 with a comparable MNP profile in both models. However, M1-like cells from two CD11b+ subsets spiked 24h after IRI, while this spike was shifted to day 3 in the UUO model, which had a temporary early influx of M1-like F4/80+ cells after 3h in turn. After 10d, total MNP numbers were decreasing in the UUO model, while M2-like F4/80+ cells persisted in IRI kidneys.
Conclusions: Our novel flow cytometric approach unravels functional multimodality among MP subpopulations for an earlier M1 response and a more persistent M2 response in IRI compared to UUO. These results might support preclinical model selection and disease understanding in kidney injury.

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PO0193
Microparticles Containing Monoocyte and Other Inflammatory Markers Are Released in AKI
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Background: Renal epithelial cell injury in AKI and induces a pleiotropic inflammatory cell response. Monoocyte phenotypes (M1 = CD14+/CD16–; M2 = CD14+ /CD16+), and subsequently derived tissue-resident macrophages play a critical role in inflammation and repair in acute kidney injury (AKI). It is accepted that M1 phenotype serves a pro-inflammatory/phagocytic role, whereas M2 phenotype influences tissue repair and remodeling. We have previously shown that microparticles (MP) derived from renal epithelial cells are released in the setting of kidney injury and can be detected in vitro as well as in human plasma, and can carry the biological activity.

Methods: In this study, we evaluated presence of MP expressing markers of inflammation in AKI (defined by standardized criteria). Human samples were derived from a prospectively collected repository (31 cases of AKI in critically ill patients compared to 22 living kidney donor healthy controls). Samples were prepared to measure MP (standard methods), and flow cytometric analysis was evaluated using antibodies against inflammatory proteins. FlowJo software was used for analysis. Mann-Whitney test was used for comparisons.

Results: The average age was 54 years; mean admission creatinine was 1.8 mg/dL and the time between admission and sample collection was 3-4 days. MP containing M2 Monoocyte markers were significantly higher in AKI patients compared to controls (347.03 vs 273.80 mL/ml; p=0.02). MP containing M1 markers were similar compared to control (177.85 vs 285.40 mL/ml; p=0.19). AKI cases also showed significantly higher levels of MP containing other inflammatory markers: Leukocytes (CD45, p=0.015), eosinophils (CD66b, p=0.001), and also in platelets (CD42b, p=0.05).

Conclusions: MP containing monocye/macrophage markers of M2 phenotype are released in the early phase of AKI, which can influence tissue modelling and repair. Moreover, a pattern of MP representing markers of M2 and other inflammatory cells may have prognostic significance to predict the severity of tissue injury or the prospect of recovery.
Conclusions: Activation of β-catenin signaling in tubular cells reduces apoptosis and necrosis in septic AKI. Tubular β-catenin might play a protective role in AKI by regulating cell death via modulating the p53/Akt signaling pathway. Funding: General Research Fund (HKU 171198/18), RGC Collaborative Research Fund (Ref: C7018-16G) and Hong Kong Society of Nephrology Research Grant (2019).

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PO0197
Pulsed Ultrasound Improves Dysregulated Oxygen Metabolism and Reduces Tissue Injury in Sepsis-Associated AKI
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Background: Sepsis associated-acute kidney injury (SA-AKI) results in part from oxidative stress in septic and non-septic AKI. Tubular β-catenin might play a protective role in AKI by regulating cell death via modulating the p53/Akt signaling pathway. We showed that pulsed US (PUS) reduces inflammatory conditions and kidney injury in sepsis (PMID: 25644106). Using multi-parametric photoacoustic microscopy (PAM) we demonstrated that the imbalance between oxygen supply and oxygen demand is one of the earliest (10 min) findings in the pathogenesis of SA-AKI. We tested the hypothesis that US attenuates kidney injury and improves early tissue oxygen metabolism and cellular bioenergetics.

Methods: We used PAM imaging to assay the change of renal blood oxygen saturation (sO2), peritubular capillary (PC) blood flow (BF) and the metabolic rate of oxygen (MRO) in saline- and LPS-treated mice and mice pretreated with US 24 hr before LPS (as described PMID: 25644106). Mice received a single injection of LPS (5 mg/kg, i.p.), and oxygen consumption and blood flow were measured 10-80 min later by PAM imaging with an image penetration depth of up to 200 μm, and MRO was calculated. Additional animals were treated with LPS and euthanized at increasing time intervals for measurement of blood creatinine and injury and inflammatory biochemical markers.

Results: PAM imaging revealed heterogeneous cortical regions of LPS-induced markedly enhanced oxygen consumption and MRO. Pretreatment with US reversed the early increase of sO2, decline observed 30-80 min after LPS and reversed the cortical regions of increased MRO. PUS prevented the overall reduction of PCBF. LPS-induced AKI, confirmed by increased plasma creatinine, mRNA expression of kidney injury marker Kim1 and Ngal 12-24 hr after LPS, and acute tubular necrosis (by H&E staining), was attenuated by US pretreatment. PUS reduced Kim1 expression in the brush border membrane of proximal tubules in cortex and medulla. PUS attenuated the increase in IL-6 and TNF-α, mRNA expression.

Conclusions: Our results demonstrate that PUS reverses kidney MRO, improves oxygen metabolism and reduces proinflammatory cytokines in SA-AKI. These results provide insight into the mechanisms of kidney tissue protection by US in AKI.

Funding: NIDDK Support

PO0198
Targeting Gadd34 Upstream Open Reading Frame to Treat Sepsis-Induced Kidney Injury
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Background: Sepsis-induced acute kidney injury remains a major clinical problem with no effective therapy to date. We have previously shown that bacterial sepsis causes global translation shutdown via phosphorylation of the eukaryotic translation initiation factor eIF2α (eIF2α2). Under physiological conditions, this eIF2α2 phosphorylation is counter-regulated by two eIF2α2 homolog phosphatases. Of the two homolog phosphatases, Growth Arrest DNA-inducible Gene 34 (Gadd34) is the only stress-inducible regulatory subunit. Using ribo-seq analysis of the kidney from septic mice revealed high ribosomal occupancy of the uORF, but not the main protein coding sequence (CDS), consistent with a model in which the uORF serves as a translational inhibitor of the downstream CDS. To investigate the inhibitory role of the Gadd34 uORF, we designed photosensitive Gadd34 5’UTR where a single nucleotide mutation was introduced to abolish the uORF start codon. We also designed antisense oligonucleotides (ASO) that are complementary to a specific portion of the uORF to modulate ribosomal scanning on the native Gadd34 mRNA.

Results: The uORF point mutation led to a two-fold increase in the readout luciferase signal compared with the wild-type control, confirming the inhibitory property of the Gadd34 uORF. We also found that masking of uORF by ASO resulted in sequence-specific increases in translation of the downstream CDS, possibly due to enhanced leaky ribosomal scanning. Finally, we tested the applicability of antisense approach in vivo using a mouse model of endotoxin-induced kidney injury. Despite late intervention (8 hrs post endotoxin challenge), the administration of uORF-targeted ASOs rescued translation and improved kidney injury.

Conclusions: These findings indicate that translational suppression of Gadd34 in late phase sepsis is a maladaptive response that could be therapeutically modulated by targeting its uORF.

Funding: NIDDK Support

PO0200
Lipopolysaccharide Induces NEAT 1 Expression in AKI via TLR4/NF-κB Signaling
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Background: Toll-like receptor 4 (TLR4) Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) have been implicated in the pathogenesis of acute kidney injury(AKI). Nuclear Paraspeckle Assembly Transcript 1 (NEAT1) is a long non-coding RNA that plays key roles in a variety of biological processes and is involved in many other diseases. Beyond its fundamental role of maintaining function of the nucleus, it remains unknown whether interaction between TLR4/NF-κB signaling and NEAT1 is involved in the process of the development of AKI.

Methods: Septic AKI model was established with injection of LPS into mice. Mouse tubular cells were stimulated with LPS for the study of tubular inflammation. The role and upstream regulatory mechanisms of NEAT1 in the inflammatory processes were studied by using signaling inhibitors.

Results: LPS caused elevation of Scr, BUN level, morphological injury and tubular apoptosis, enhanced NLRP3 and Col I expression, and increased expression of TGF β and STC 1 (P<0.05).

Conclusions: Our study reveals a novel TGF β-STC1 pathway that has homeostatic as well as LPS-induced cytoprotective functions in renal tubular epithelium. STC 1 has protective effects on LPS-induced acute renal tubular injury in mice, possibly by targeting TGF β, enhancing TLR4 expression, regulating the TGF β-STC1 signaling pathway, and inhibiting the expression of downstream inflammatory factors.

Funding: Government Support - Non-U.S.
cytokines including IL-6 and CCL-2, whereas treatment with an inhibitor of TLR4 or NF-κB signaling suppressed LPS-induced NEAT1 expression.

Conclusions: NEAT1 expression was induced in LPS-induced AKI model via TLR4-NF-κB signaling, suggesting its potential role in the inflammatory process. Our findings open the door to exploit NEAT1 expression as a potential novel therapeutic approach for AKI and other inflammatory-mediated renal diseases. 

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Background: Mitochondrial dysfunction in renal tubular epithelial cells (RTECs) is a hallmark of endotoxin-induced acute kidney injury (AKI). Forkhead box O1 (FOXO1) is responsible for regulating mitochondrial function and is involved in several kidney diseases. Herein, we investigated the effect of FOXO1 on endotoxin-induced AKI and related mechanisms.

Methods: In vivo, the mouse model of endotoxin-induced AKI was induced by intra-abdominal injection of LPS (10 mg/kg). The expression of FOXO1 and PGCI-α in mouse kidney were determined. Then we established a mouse model of renal overexpression of FOXO1 by in situ injection of FOXO1 adenovirus-related virus in renal cortex before intra-abdominal injection of LPS. In vitro, Human proximal tubular epithelial (HK-2) cells were stimulated with LPS (40μg/ml), then infected with FOXO1 overexpression adenovirus. The morphology changes of mitochondria were observed using mitotracker staining. Mitox-SOX was used to detect the changes of mitochondrial superoxide content and the expression of FOXO1.

Results: In vivo, FOXO-1 downregulation in mice RTECs and mitochondrial damage was found in endotoxin-induced AKI. Overexpression of FOXO1 could improve renal function and reduce mitochondrial damage. PGCI-α was reduced in endotoxin-induced AKI and reversed by FOXO-1 overexpression. In vitro, expression to LPS led to HK-2 cell viability decline, mitochondrial fragmentation, and mitochondrial superoxide accumulation, as well as downregulation of the FOXO1, PGCI-α and mitochondrial complex. Moreover, over-expression of FOXO1 in HK-2 cells could increase HK-2 cell viability and PGCI-α expression, and alleviated altered mitochondrial injury and superoxide accumulation induced by LPS. Meanwhile, inhibition of FOXO1 in HK-2 cells by siRNA decreased PGCI-α expression and HK-2 cell viability. Chromatin immunoprecipitation assays and PCR analysis confirmed FOXO1 binding to the PGCI-α promoter in HK-2 cells.

Conclusions: In conclusion, downregulation of RTECs FOXO1 mediated endotoxin-induced AKI and mitochondrial damage. Over-expression of FOXO1 could improve renal function and reduce mitochondrial damage. PGCI-α might be a potential target for the prevention and treatment of endotoxin-induced AKI.

Funding: Government Support - Non-U.S.

PO0203
Renal Angiotensin (Ang) Receptor Changes Following Cecal Ligation and Puncture (CLP)-Induced AKI
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Background: Angiotensin-II (Ang2) modulates renal function and thus may contribute to sepsis-induced acute kidney injury (SIAKI). We have shown that CLP reduced renal Ang2 type-1 receptors (AT1R), but effects on non-classical Ang receptors are unknown. We hypothesized that CLP altered renal abundance of Ang2 type-2 receptors (AT2R) and Ang-(1-7). Mas receptors (Ang-(1-7)R, Mas8), initiators of signaling axes that oppose AT1R.

Methods: C57BL6 mice were randomized to euthanasia at 6, 24, or 48hrs post-CLP (n=5/group). Unoperated mice (T0) served as controls. Mice were resuscitated (50mL/kg NS SQ) immediately and 25 hrs post-operatively. Prior to sacrifice we removed the kidneys under deep isoflurane anesthesia to minimize tissue ischemia. We obtained blood by cardiac puncture. Kidney Injury Molecule-1 (KIM-1) was measured in whole tissue homogenate (ELISA). AT1R, AT2R, and MasR were measured within specific regions of the kidney using immunofluorescence, (IF). We also used IF to compare kidney sections collected from sepsis patients within an hour of death (n=7) to sections from healthy controls (n=10).

Results: KIM-1 and BUN increased 6th post-CLP. Creatinine increased 48th post-CLP. AT1R and AT2R were both reduced AT1R in arteries, macula densa, and glomeruli. However, CLP did not alter MasR abundance in any region (p>0.05). The ratio of total renal MasR to AT1R more than doubled by 6hrs post-CLP (p<0.001 vs. T0). Renal AT2R intensity was increased in renal mesangium by 24h and in glomeruli by 48h (p<0.01 for both). We previously showed decreased AT1R IF in human sepsis kidney sections. In contrast, human sepsis kidneys did not show any decrease in MasR (p>0.05), again suggesting an increase in the MasR to AT1R ratio.

Conclusions: 1. Data on CLP-induced changes in KIM-1 in tissue and BUN in blood suggest that these are earlier markers of CLP-induced AKI than creatinine. 2. CLP and septic AKI may be associated with a shift from classical to non-classical angiotensin signaling in the kidney. Studies of non-classical angiotensin system modulation in septic AKI may enhance understanding of pathobiology and reveal therapeutic targets in septic AKI.

Funding: Government Support - Non-U.S.

PO0204
The Fibrogenic Response to Renal Injury Is Epigenetically Regulated Through the Activation of Bivalent Genes
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Background: Bivalent genes are regions of epigenetically modified nucleosomes that carry both enhancer and promoter activity. Bivalent genes are typically enriched for inflammatory, apoptotic and fibrogenic pathways is orchestrated through the epigenetic regulation of bivalent genes that are poised for response in the normal kidney.

Methods: Bivalent genes are regions of epigenetically modified nucleosomes that carry both enhancer and promoter activity. Bivalent genes are typically enriched for inflammatory, apoptotic and fibrogenic pathways is orchestrated through the epigenetic regulation of bivalent genes that are poised for response in the normal kidney.

Results: Through peak annotation of CUT&RUN results, 1546 bivalently marked genes were identified in the normal kidney. With the onset of UUO, 62% of these bivalent genes (951/1546, activated bivalent genes) are activated by the loss of the repressive Tgfbir2 (2.5 fold), Tgif (2.5 fold) and Tgfbir2 (2.5 fold). The activated bivalent genes are associated with upregulation of genes that drive the response to uninjured kidney obstruction (UO) in the mouse.

Methods: CUT&RUN ChIP-seq analysis using antibodies to H3K4me3 and H3K27me3 was carried out on normal kidneys and kidneys of mice 5 days after UUO.

Results: Enriched peaks were identified using SEACR, and HOMER was used to perform peak annotation. To determine fold change gene expression, RNA was collected and analyzed from samples 5 days after they were subjected to sham or UUO surgery.

Conclusions: We provide evidence to suggest that the response to renal injury via inflammatory, apoptotic and fibrogenic pathways is orchestrated through the epigenetic regulation of bivalent genes that are poised for response in the normal kidney.

Funding: NIDDK Support
Changes in NAD and Lipid Metabolism Drive Acidosis-Induced AKI

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Background: The kidney has an important role in maintaining normal blood pH. Mitochondria in the proximal tubule (PT) produce ammonia and bicarbonate from glutamine, and during metabolic acidosis (MA) this pathway (ammoniagenesis) is acutely upregulated. MA is frequently associated with acute kidney injury (AKI); however, to what extent the former causes the latter was unclear.

Methods: Multiphoton imaging of mitochondrial function in mouse kidney cortical slices and in vivo; oxygen consumption rate (OCR) in isolated PTs; histological analysis and electron microscopy (EM) in fixed tissue. MA was induced using an established protocol (gavage with 0.8 g/kg NHCl).

Results: Acutely lowering extracellular pH to 6.5 decreased mitochondrial NADH fluorescence signal specifically in PTs, without changing total NADH content, baseline OCR or mitochondrial membrane potential. However, maximal OCR was decreased and response to rotenone was exaggerated, suggesting a switch to complex I and increased oxidation of NADH to NAD+. This can prevent leakage of bacterial contents from the gut and result in improved renal function and decreased inflammation, as evidenced by decreased plasma cytokines, in IAPtg group.

Conclusions: Improved ZO-1 expression probably due to reduced apoptosis decreases intestinal permeability in transgenic mice subjected to endotoxemia. This can p<0.05 suggesting decreased inflammation in transgenic mice. Intestinal and colon Bax of IAPTG+LPS were lower and Bcl2 higher than C5+LPS suggesting improved intestinal integrity. Expression of tight junction protein (ZO-1), protein phosphatase 2A C (PP2Ac), and electron microscopy (EM) in fixed tissue. MA was induced using an established protocol. Partially reversing MA with intravenous injection of bicarbonate and electron microscopy (EM) in fixed tissue. MA was induced using an established protocol (gavage with 0.8 g/kg NHCl).

Results: Serum urea and creatinine of IAPtg mice were 0.6 mg/dl and 65 mg/dl respectively which were 70% lower suggesting low apoptosis in IAPTg. Plasma TNF α were 70% lower in IAPTg compared to C57Bl6 suggesting low inflammation in IAPTg mice. In IAPTg mice with MA, the expression of intestinal and colon caspase 3 in the IAPtg was 4 fold lower than C57Bl6 (p<0.01). Intestinal and renal Bax of IAPtg/LPS were lower and Bcl2 higher than C57Bl6 (p<0.05). Apoptotic markers of IAPtg/LPS were not significantly different from the control suggesting low inflammation in IAPtg. Plasma TNFα and IL-6 levels of IAPtg/LPS were 70±20 and 95±26 pg/ml respectively which were about 1.5 fold lower than C57Bl6 (p=0.05) suggesting decreased inflammation in transgenic mice.

Conclusions: Improved ZO-1 expression probably due to reduced apoptosis decreases intestinal permeability in transgenic mice subjected to endotoxemia. This can prevent leakage of bacterial contents from the gut and result in improved renal function and decreased inflammation, as evidenced by decreased plasma cytokines, in IAPtg group.

Funding: Private Foundation Support

Loss of HDAC8 Leads to hH2AX-Induced Cellular Repair and Decreased Epithelial-Mesenchymal Transition in Renal Tubule Epithelial Cells


Background: Acute kidney injury (AKI) remains a significant worldwide problem. Our previous work has shown that hdac8−/− larval zebrafish model of AKI improved survival and increased repair depleted in AKT3. More importantly, after AKI, some HDAC8 have not been elucidated. AKI is known to induce double stranded DNA breaks (DSB), activating factors including the phosphorylation of the histone variant H2AX producing γH2AX. Damaged cells undergo a complex multifactorial fate determination leading to either DNA repair and cell survival or apoptosis.

Methods: hdac8−/− and hdac8+/− mutant zebrafish were injected with gentamicin to induce AKI. Immunofluorescent microscopy, fluorescently activated cell sorting (FACS) of renal tubule epithelial cells (RTEC) were isolated for RNA-seq. We evaluated the expression of RTEC in wild type (WT) and hdac8−/− in RNA-seq. Following AKI, hH2AX at sites of DNA damage. hdac8−/− mutant zebrafish preferentially uses mechanism of DDR for repair and proliferation, as opposed to apoptosis. In the absence of apoptosis hH2AX tubules can prevent cell death and maintain membranes and maintain their epithelial gene signatures, whereas the WT zebrafish lose their polarization and begin EMT. These data support our hypothesis that the loss of HDAC8 allows cells to repair after injury from AKI.

Funding: NIDDK Support, Other U.S. Government Support

Protein Phosphatase 2A Ct Expressed in Tubular Cells Decrease Kidney Injury

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Background: Protein phosphatase 2A (PP2A), one of the primary serine-threonine phosphatases in mammalian cells, regulates various biological processes. The role and mechanisms for PP2A in kidney injury remains to be determined.

Methods: Generating the mice with Pp2aaca ablation with Cre-Loxp system. Mice were injected with cisplatin to induce AKI. UO was performed on the mice to induce kidney fibrosis.

Results: In this study, we found that the expression of protein phosphatase 2A Ct (Pp2aaca) in tubular cells could promote cell death and kidney injury. The organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1) regulate the renal secretion of drugs including metformin, norfloxacin, or toxins. In this study, we found that the expression of protein phosphatase 2A Ct (Pp2aaca) in tubular cells could promote cell death and kidney injury. The organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1) regulate the renal secretion of drugs including metformin, norfloxacin, or toxins. In this study, we found that the expression of protein phosphatase 2A Ct (Pp2aaca) in tubular cells could promote cell death and kidney injury. The organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1) regulate the renal secretion of drugs including metformin, norfloxacin, or toxins.

Conclusions: This study reveals the essential role for PP2A in regulating tubular cell energy metabolism and survival, which may shed light on treating patients with kidney injury.

In Vitro Inhibition of Renal OCT2 and MATE1 Secretion by Antiemetnic Drugs

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Background: The organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1) regulate the renal secretion of drugs including metformin, cisplatin, and etometein. Studies suggest that ondansetron, an antiemetetic drug and 5-HT3 antagonist, can inhibit OCT2- and MATE1-mediated transport. The purpose of this study was to test five structurally similar 5-HT3 antagonist, can inhibit OCT2- and MATE1-mediated transport.
Inhibiton of OCT2-MATE1 Secretion of ASP by Ondansetron in MDCK Cells

PO0211
supPAR Determines Outcomes in Septic AKI
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Background: Sepsis is the main contributor to the development of acute kidney injury (AKI) in critically ill patients. Plasma soluble urinokinase plasminogen activator receptor (supPAR) is a criculating risk factor for AKI and a prognostic marker for the need of renal replacement therapy (RRT). We analyzed the pathophysiologic role and kinetic properties of supPAR in septic AKI in critically ill patients and in a murine model of septic AKI.

Methods: 200 critically ill patients were enrolled prospectively after meeting Sepsis-3 criteria. Serum supPAR levels were measured at 0, 12, 24, 48, 72, 120 and 168-hour after enrollment and the need for RRT within 7 days was assessed as the primary outcome measure. Polybacterial sepsis was induced by cecal slurry injection in three mouse strains, respectively wild type (WT, N=9), supPAR-knockout (KO, N=13), and supPAR transgenic overexpression (OE, N=11).

Results: No or mild AKI occurred in 62 patients (31.0%), moderate or severe AKI without the need for RRT in 102 patients (51.0%), criteria for RRT were met in 36 patients (18.0%) and 7 patients (3.5%) died within the 7-day period. Compared to all other maximum AKI stages and AKI disease courses within 7 days, patients requiring RRT showed significantly higher supPAR levels at all time-points. Patients with supPAR levels ≥ 12.7 ng/ml (highest quartile) had an adjusted odds ratio of 5.22 (95% confidence interval [CI], 2.16-12.65) for the need for RRT, and 4.44 (95% CI, 1.98-9.97) for RRT or death within 7 days compared to patients with levels < 12.7 ng/ml. Compared to KO mice, WT and OE mice showed a significantly greater impairment of renal function and structure 24 hours after induction of sepsis. Kaplan-Meier analysis revealed a survival benefit of KO mice over OE mice within 24h (84.6% vs. 45.5%, p=0.041).

Conclusions: SupPAR distinguishes between divergent AKI stages/courses and the need for RRT at any time within 7 days after sepsis diagnosis. Our experimental data suggest that supPAR is a pathophysiologial driver of septic AKI and may serve as a target for future interventional strategies.

PO0212
Cardiovascular Effects of the American College of Radiology (ACR) Group II Agent Gadobutrol (Dotarem): Renal Proximal Tubular Mitochondrial Toxicity and Acute Tubular Damage
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Background: Patients are concerned about gadolinium (Gd) deposition from magnetic resonance contrast agents. Gd is the known cause of iatrogenic ‘nephrogenic’ systemic fibrosis and long-term gadolinium retention in every organ. Without prospective evidence, the ACR partitions brands of Gd-based contrast agents (GBCAs) into three groups: I, associated with the greatest number of systemic fibrosis cases; II, associated with few, if any, unconfounded cases of iatrogenic systemic fibrosis; and III, data are limited.

Methods: Male and female mice were randomized to GBCA treatment with an increasingly popular, ACR group II macrocyclic agent (Dotarem, 2.5 mmol/kg intraperitoneally, 20 doses over 4 weeks). Echocardiographic parameters were compared at the endpoint, tissues examined with transmission electron microscopy.

Results: Gd reduced cardiac systolic volume (29 ± 6 vs 34 ± 4 μL, mean ± SD, M-mode), increased fractional shortening (30 ± 4 vs 25 ± 2%, M-mode), and increased ejection fraction (57 ± 5 vs 50 ± 4%, M-mode). Renal tissue was characterized by tubular damage, pathologic lipid vacuolization, and diffuse mitochondrial toxicity (Figure). Conclusions: GBCA treatment leads to diffuse and long-term intracellular retention in every vital (and non-vital) organ. These studies demonstrate that the American College of Radiology group II agents are far from clinically inert. Consistent with the first element of the Nuremberg Code, voluntary consent for GBCA administration should be obtained from every patient.

Funding: NIDDK Support, Veterans Affairs Support, Commercial Support - DCI
Conclusion: We found that different biomarkers have variable kinetics after PTEC injury. As KIM-1 concentrations rose the earliest after antibiotic exposure. In RNAseq analyses, we found that pathways of metallothionein and cholesterol biosynthesis were dysregulated after colistin exposure. Finally, we found minimal PTEC injury with tobramycin, suggesting that this antibiotic may be less toxic than previously believed. Future work seeks to test these candidate biomarkers in human urine samples.

PO0214
GTS-21 Attenuates the Inflammation of AKI Independent of α7 Nicotinic Acetylcholine Receptor
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Background: Vagus nerve stimulation protects from kidney injury by activating the cholinergic inflammatory pathway (CAP). It is considered that α7 nicotinic acetylcholine receptor (α7nAChR) in splenich macrophages are important for CAP activation. To elucidate the mechanism of receptor signaling, we promoted further experiments using macrophage-specific α7nAChR knockout mice.

Methods: We generated macrophage-specific α7nAChR-deficient mice by crosses breeding LysM-Cre and α7nAChR flox mice. In vivo, GTS-21 (an α7nAChR specific agonist) was intraperitoneally injected to either wild type C57BL/6j mice (WT) or macrophage-specific α7nAChR-deficient mice prior to administration of lipopolysaccaride (LPS). 4 hours after LPS administration, the mice were euthanized and plasma TNF-α level, plasma creatinine, BUN were evaluated. In vitro, murine macrophage cell line RAW264.7 and primary peritoneal macrophages from either WT or α7nAChR-deficient mice were used. These cells were stimulated with LPS after nicotine (pan nicotinic acetylcholine receptor agonists) or GTS-21 was administrated, then TNF-α level was evaluated 4 hours later.

Results: GTS-21 protected the kidney and suppressed the increase of plasma TNF-α induced by LPS in WT mice. Surprisingly GTS-21 decreased plasma TNF-α level induced by LPS in not only WT mice but also macrophage-specific α7nAChR-deficient mice. In vitro experiments, GTS-21 or nicotine treatment suppressed TNF-α induction by LPS RAW264.7 cells or primary peritoneal macrophages from WT mice. Furthermore, nicotine also suppressed the induction of TNF-α by LPS even in peritoneal macrophages from α7nAChR-deficient mice.

Conclusions: These results suggest that nicotine or GTS-21 might suppress the inflammation independent of α7nAChR in macrophages in vivo and in vitro.

PO0215
Platelets vs. Neutrophils as Therapeutic Targets in Cholesterol Embolism-Related Arterial Occlusion, Kidney Infarction, and AKI

Background: Cholesterol crystal embolism (CCE), a life-threatening complication, is a consequence of the rupture of atheromatous plaques in patients with advanced atherosclerosis. CCE often mimics as a cause of AKI. We hypothesized that platelet contributes to CCE-related artery occlusion leading to AKI and kidney infarction.

Methods: C57/BL6 mice were injected with various doses of cholesterol crystals (CC) to induce CCE in kidney. Primary endpoint: GFR. Secondary endpoints: infarct size, vascular occlusions. 3D MRI and μCT were performed. In vitro studies CC with neutrophils, platelets, endothelial cells.

Results: At 24h, MRI and μCT showed perifocal edema around ischemic lesion and vascular rarefaction in CCE kidney. CC-induced clots causing a dose-dependent GFR loss and infarct size. Immunostaining revealed crystal clots contained fibrin, platelets, ecDNA, neutrophils. To study the role of platelets in this process, we treated mice with platelet antagonist clopidogrel. At 24h, clopidogrel completely protected mice from intravascular obstructions, GFR loss, and kidney infarction. In contrast, neutrophil depletion significantly decreased kidney infarction but not arterial obstructions or GFR loss. Maybe because mononuclear cells had partially replaced neutrophils within clots and ecDNA was still present. DNase I treatment also significantly reduced the percentage of ecDNA positive clots, occluded arterial, GFR loss, infarct size. In vitro studies show, CC-induced clot formation and enhanced fibrinogen release from platelet granules with promotes clot formation. DNase I can strongly inhibited clot formation, fibrin formation, also normalized collagen-driven platelet aggregation.

Conclusions: In summary, not CC itself but the CC-induced fibrin clots obstructed peripheral arteries causing tissue infarction and organ failure. Platelets and ecDNA are central for crystal clots formation. Hence, crystal clots represent the primary target for therapeutic interventions. Among the possible molecular targets in thrombosis, especially enhancing fibrinolysis or inhibiting platelet purinergic signaling could reduce arterial occlusions, infarction, and organ failure. DNase I could have a synergistic effect on CC-induced clot formation in mice and might be a prophylactic/therapeutic approach in human patients with a risk for procedure-related CC embolism.

Funding: Government Support - Non-U.S.
Characterizing De Novo Lymphangiogenesis During AKI Using 3D Imaging and Tissue Cytometry

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Background: The renal lymphatic system is essential for fluid and electrolyte homeostasis, lipid and cholesterol transport, and immune surveillance with lymphatic vessels (LV) primarily intertwined with the blood vasculature. LV development, or lymphangiogenesis (LA) is regulated by its master transcription factor, prospero-related homeobox-1 (Prox-1), which determines lymphatic cell fate. LA is accentuated during inflammation or injury states such as acute kidney injury (AKI), though mechanisms of LA in AKI remain unclear. Understanding the LA process is essential because it will elucidate potential therapeutic targets in AKI.

Methods: Using 10-week old male Prox1-tdTomato lymphatic reporter mice (ProxTom), we investigated the effect of AKI on the abundance and distribution of Prox-1+ cells at the mesoscale level using large scale three-dimensional (3D) imaging and tissue cytometry. ProxTom mice and their controls were subjected to ischemia-reperfusion (IR) or no surgery and kidneys were fixed on day 3. Large scale 3D imaging with confocal microscopy was done on 50µm thick sections spanning the entire cross section of the kidney, followed by tissue cytometry using the volumetric tissue exploration and analysis (VTEA) software tool.

Results: The average number of cells surveyed per specimen was 347,360 ± 36,647. Using VTEA, a gating strategy was devised to account for autofluorescence in the red channel, which was increased after IR due to cell debris and injury. IR samples displayed a significant increase in Prox-1+ cells compared to baseline controls: 717.2 ± 161.8 vs. 174.4 ± 62.1 Prox-1+ cells/mm², respectively (p=0.05). In baseline controls, Prox-1+ cells were well-organized and predominately localized around large vessels in the hilum. However, after injury, the distribution of Prox-1+ cells shifted to the hilar parenchyma and inner medulla in a consistent pattern. Few cells could also be detected in the outer medulla and cortex.

Conclusions: We demonstrate a scale of analytics that is amenable to characterizing de novo renal LA during AKI, which informs the origin and distribution of renal LVs and the dynamics of LA. Such findings will enhance our understanding of the functional role of LVs during injury and help identify novel therapeutics for intervention in AKI.

Funding: NIDDK Support, Other NIH Support - NIH-NRSA Training Grant Research Fellowship Interdisciplinary Training in Kidney Related Research, Veterans Affairs Support

Peritubular Transcytosis Enables Mesoscale Nanoparticle Treatment of AKI

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Background: In prior studies we demonstrated that mesoscale nanoparticles (MNP) localize to the kidneys up to 26-fold more than to any other organ and that they specifically target the renal tubular epithelium. In this study we investigated the mechanism of MNP localization to the renal tubules and evaluated this platform’s potential for therapeutic delivery in a model of cisplatin-induced acute kidney injury (AKI).

Methods: We synthesized ~400 nm diameter MNPs from the biocompatible polymers poly(lactic-co-glycolic acid) and polyethylene glycol (PLGA-PEG). MNPs were encapsulated with a fluorescent far-red dye or the reactive oxygen species scavenger edaravone. Male C57BL/6 mice, were sacrificed 30 minutes after injection for immune-efect microscope studies. We also performed intravital microscopy to visualize the transit of MNPs in Cx3cr1-/- C57BL/6 mice with GFP-expressing renal macrophages. We also evaluated their therapeutic potential in a cisplatin-induced AKI (25 mg/kg IP) model, 24 hours following cisplatin, mice received edaravone-loaded MNPs or appropriate controls. Serum creatinine and histology were analyzed 72 hours following cisplatin.

Results: We found that MNPs localize to the proximal tubular epithelium via transcytosis from the peritubular capillaries. We observed MNPs flowing in these capillaries and in transit across the tubular interstitium. We also found that transcytosis of MNPs was not facilitated by macrophage uptake. Finally, we found that therapeutic MNPs use this mechanism to localize to the proximal tubules of mice with cisplatin-induced AKI (Figure).

Conclusions: These studies characterized transcytosis from the peritubular capillaries as the mechanism of particle localization to the kidneys and portend the development of additional therapeutic targeting tools for renal diseases.

Funding: NIDDK Support

Role of the Exocyst, Cilia, and Mitochondria in AKI

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Background: AKI has high morbidity and mortality. Management consists of supportive care. Among the critical pathways in AKI are alterations of tubular mitochondrial metabolism, and, as recently suggested, disruption of primary ciliary homeostasis. Mitochondria are also involved in ciliopathies. Here we tested if cilia acting via mitochondria are involved in AKI.

Methods: We previously showed that the exocyst trafficking complex is necessary for ciliogenesis. Overexpression of Exoc5, a central exocyst component, protected renal tubule cells against H2O2-induced injury, whereas Exoc5 knockdown worsened it. In AKI, proximal tubules are most susceptible to injury. To determine the effect of Exoc5 loss, we crossed Exoc5fl/fl mice with mice expressing CreERT2 driven by the proximal tubule sodium-dependent inorganic phosphate transporter (SLC34A4-CreERT2). Proximal tubule-specific Exoc5 knockout (KO) mice and littermate controls were subjected to bilateral ischemia reperfusion (IR) injury by clamping the renal arteries. In order to gain mechanistic insight, we evaluated mitochondrial function in Exoc5 overexpressing (OE), Exoc5 knockdown (KD), Exoc5 ciliary targeting sequence point mutant (cts-mut), and control Madin-Darby canine kidney tubule (MDCK) cells.

Results: Proximal tubule-specific Exoc5 KO mice had worse renal injury, and higher serum creatinine following IR injury compared to control mice (p<0.005). Seahorse assays revealed diminished sparse respiratory capacity in Exoc5 KD and Exoc5 cts-mut cells, which was increased in Exoc5 OE cells, compared to control MDCK cells. Tetramethylrhodamine methyl ester was employed to measure mitochondrial membrane potential and we found mitochondrial uncoupling in Exoc5 KD and Exoc5 cts-mut cells as compared with control cells. Transmission electron microscopic imaging revealed healthy circular-shaped mitochondria with dense matrix in control and Exoc5 OE cells. Exoc5 KD cells exhibited mitochondrial damage and swelling consistent with the observed reduced respiration. Interestingly, Exoc5 cts-mut cells demonstrated formation of elongated mitochondria with pronounced cristae and large intracistal spaces, which could indicate less intensive bioenergetics, and would explain the reduced respiration.

Conclusions: For the first time we show that the exocyst and cilia are centrally involved in AKI and the effect may be mediated through mitochondria.

Funding: Veterans Affairs Support

Ascending Vasa Recta Responsible for Medullary Vascular Congestion

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Background: Vascular congestion of the renal medulla is common in acute kidney injury and has been shown to prolong ischemia and promote injury. We have reported that pretreatment with low dose lipopolysaccharide (LPS) attenuates ischemia reperfusion (IR) induced congestion. The temporal localization of congestion during IR and how LPS prevents congestion remains unknown. We hypothesized that vascular congestion

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
originates in the medullary vasa recta (VR) prior to the peritubular (PT) capillary plexus, and that pretreatment with low dose LPS aids in early VR reperfusion. 

Methods: To test this hypothesis, male WKY rats (100ks) were pretreated (I.p) with 1000ug/kg LPS or saline daily for 3 days and a 45-minute warm, bilateral ischemia was performed. Rats were randomized to 0, 1, 2, 6, 10, or 24 hours (n=4-6/group). Control of the medullary VR and PT capillaries was assessed in histological sections (scale: 0-5, 0=0%, 5=100% congestion).

Results: At time 0 (no reperfusion), congestion of the medullary VR averaged 80% in both saline and LPS treated rats. Following reperfusion for 1, 2, 6, and 10 hours, VR congestion in saline treated rats decreased (VR-[C5aR1]fl/fl mice and FoxD1-C5aR1 KO mice and performed qPCR and luminex analysis. Conclusions: Our findings demonstrate that pericytes and macrophages play important roles in the pathogenesis of renal scarring and implicate C5ar1 as a key mediator. Conditional deletion of C5ar1 in these two interstitial cell types reduces inflammation and extracellular matrix protein formation in pericytes as well as macrophage migration and profibrotic phenotype of kidney macrophages.

Funding: NIDDK Support, Veterans Affairs Support

PO0222

Selective Expansion of Kidney Double-Negative T Cells Is Driven by Renal Tubular Epithelial Cells Through Direct Cell-Contact and by Soluble Mediators

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Background: Kidney TCRβ+ +CD8+CD8+ double negative (DN) lymphocytes are a recently recognized unconventional T cell population with important roles in AKI and possibly other diseases like lupus. DN T cells expand after experimental AKI and confer improved renal recovery. However, mechanisms underlying their regeneration and expansion in the kidney are poorly understood. Here, we demonstrate a direct role for renal tubular epithelial cells (RTET) in regulating homeostasis of kidney DN T cells.

Methods: Age-matched B6 WT, MHC I KO, MHC II KO and DKO (MHC I and II KO) mice were studied. T FACS cell functional assays and an in-vitro co-culture system were used to investigate the functional relationship between RTET and DN T cells. RTETs were isolated, purified and cultured in collagen-coated plates. Lymphocytes from both kidney and periphery were isolated, co-cultured with RTET and analyzed by FACs.

Results: DN T cells were anergic when cultured alone, even after stimulation with anti-CD3/CD28, but spontaneously proliferated when co-cultured with RTET (DCN; 1.2 ± 0.6% vs RTET+DCN; 13.8 ± 3.5%, p≤0.0001). Expansion was due to increased proliferation and decreased apoptosis of DN T cells. RTET mediated expansion of DN T cells occurred by multiple mechanism including direct cell-contact and secretion of IL-7. Although activation of T cells required direct TCR crosslinking, activation of DN T cells were TCR-MHC independent as indicated by the ability of RTET from mice lacking MHC class-4, class-II or DKO mice to induce proliferation of DN T cells (21.2 ± 1.5%, vs RTET (MHC I KO)+DN; 17.1 ± 1.5%, vs RTET (MHC II KO)+DN; 17.9 ± 1.8%, vs RTET (DKO)+DN; 32.8 ± 0.3%, p≤0.0001). Reciprocally, DN T cells increased survival of RTET as demonstrated using in-vitro assays. Our ongoing experiments are focusing on identifying surface molecules involved in mediation interactions between DN T cells and RTET.

Funding: NIDDK Support

PO0223

TGF-β-Induced CD8+CD103+ Regulatory T Cells but Not Natural Regulatory T Cells Alleviates Acute Renal Injury Induced by Ischemia-Reperfusion

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Background: Acute kidney injury (AKI) is one of the most common complications in clinical practice, inflammatory response induced by hypoxia-reoxygenation is the key mechanism of ischemia-reperfusion acute kidney injury. Regulatory T cells (Treg) are crucial to maintain homeostasis in the main organs. Our previous studies show that the regulatory T cells (nTreg) tend to transfer into Th17 under conditions of inflammation and hypoxia. On the contrary, Treg-induced CD8+CD103+Treg (CD8+CD103+Treg), a new subgroup of Treg we have identified, maintains stable phenotype and immunomodulatory function. The instability of nTreg under conditions of inflammation and hypoxia suggests that Treg are not suitable for treatment of AKI. Accordingly, we studied the role of CD8+CD103+Treg in alleviating AKI.

Methods: In vitro study, we test the phenotype and immunomodulatory function of Treg-induced CD8+CD103+Treg, and expanded in the kidney, it is found that the efficiency of Treg-induced CD8+CD103+Treg with higher anti-inflammatory function and lower pro-inflammatory function. As a result, nTreg was preadministration into the mice and then transferred into the kidney to test its function, and then the kidney function was measured. The expression of CD103 was found to significantly reduce the expression of pro-inflammatory cytokines, such as TNF-α, IL-6, and IL-1β, and the expression of anti-inflammatory cytokines, such as IL-10, in the kidney. The results show that the expression of CD103 is stable in CD8+Treg in vitro under 1% O2 concentration (Fig 1). Treg transfer into Th17 under hypoxic condition. However, CD8+Treg+CD103+Treg seldom transfer into Th17, remain Foxp3 under hypoxic condition (Fig 2.3). In addition, the suppressive function of CD8+CD103+Treg over T cells proliferation under hypoxia remain steady. In vivo study, we found that CD8+CD103+Treg not only reduce the development of renal fibrosis in the mouse, alleviating acute tubular necrosis (ATN) and reducing the mortality of AKI mice. (Fig 4).
**PO0224**

A Novel Renoprotective Strategy: Upregulation of PD-L1 Expression Mitigates Cisplatin-Induced AKI

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**Background:** Cisplatin is an effective chemotherapeutic agent against various types of cancers; however, the use of cisplatin is associated with a major side-effect of nephrotoxicity, resulting in acute kidney injury (AKI). Growing evidence suggests that programmed death-1(PD-1)-programmed death ligand (PD-L1) immune checkpoint signaling plays a critical role in mediating inflammatory responses and immune homeostasis. While PD-L1 has emerged as a promising target for immunotherapy, little is known concerning how PD-L1 is regulated. In this study, we aimed to determine the expression and contribution of PD-L1 in cisplatin-induced AKI.

**Methods:** PD-L1 expression in kidney cells and tissues were determined by immunohistochemistry (IHC), real-time polymerase chain reaction and western blot assays. PD-L1-containing lentiviruses were subcapsularly injected into the kidneys of mice. 7 days after the injection, mice were intraperitoneally treated with cisplatin for 3 days and subjected to kidney function tests. High-dimensional single-cell mass spectrometry was used to reveal immune profiling and discover the underlying immunological mechanisms of PD-L1 in an AKI mouse model.

**Results:** IHC staining of PD-L1 shows a significantly lower intensity of staining and less stained proximal tubule epithelial cells in cisplatin-exposed mice tissues than that in the PBS controls. Next, we demonstrate that cisplatin exposure decreased mRNA expression and protein levels of PD-L1 in primary renal proximal tubular epithelial cells and mouse kidney tissues. Furthermore, we also find a decrease in PD-L1 expression with a concomitant increase in pro-inflammatory cytokines in response to cisplatin. Mass spectrometry analyses reveal cisplatin-induced multiple pro-inflammatory leukocytes infiltration in kidneys. Through genetically engineered kidney tissues in mice, ectopic expression PD-L1 in kidneys was able to suppress leukocytes infiltration and pro-inflammatory cytokines. In addition, both serum creatinine and blood urea nitrogen levels were significantly reduced in cisplatin-treated mice with PD-L1 overexpression.

**Conclusions:** Our data suggest a renoprotective effect of PD-L1 upregulation on cisplatin-induced AKI and also provide an alternative therapeutic strategy against nephrotoxicity.

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**PO025**

**Regulation of Renal Calbindin Expression During Cisplatin-Induced Kidney Injury**

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**Background:** Since the discovery of calbindin release into urine during renal injury, there has been growing interest in the utility of this calcium-binding protein as a biomarker of nephrotoxicity. However, little is known about the intrarenal regulation of calbindin during acute kidney injury. We sought to characterize the time-dependent expression and excitation of the renal proximal tubule protein calbindin in comparison to the proximal tubule protein Kim-1 in a mouse model of cisplatin nephrotoxicity.

**Methods:** Male C57BL/6 mice were administered saline vehicle or 20 mg/kg of cisplatin i.p. Urine was collected in metabolic cages for 24 h periods on days 0 – 4. Blood and kidneys were collected between days 2 and 4. Kim-1 and calbindin proteins were measured in urine, kidneys, and blood. Kim-1 and calbindin (Calb1) mRNAs were quantified in kidneys by qPCR.

**Results:** SCr and BUN levels increased in cisplatin-treated mice by day 3, confirming development of acute kidney injury. Urinary concentrations of calbindin and Kim-1 were elevated by 11.6-fold and 2.5-fold, respectively by day 2. Time-dependent decreases in intrarenal calbindin protein to levels 60% of control were observed on days 3 and 4. A 200-fold up-regulation of Calb1 and Kim-1 mRNAs was seen on day 3. These data suggest that early loss of calbindin protein into the urine along with declines in renal calbindin protein initiates a compensatory induction of mRNA expression at later time points (days 3 and 4).

**Conclusions:** Understanding the regulation of calbindin during cisplatin nephrotoxicity further enhances its utility as a urinary biomarker of kidney damage. The results of the current study support the combined use of a proximal (Kim-1) and distal tubule marker to phenotype acute kidney injury or AKI.

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**PO026**

**Neutral Ceramidase and Autophagy Play Diverse Roles in Cisplatin-Induced AKI and Fibrosis**

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**Background:** Cisplatin (CDDP) is a commonly used chemotherapeutic agent with a dose-limiting nephrotoxicity. 30% of patients given CDDP develop acute kidney injury (AKI), increasing risk of chronic kidney disease (CKD) development and mortality. Currently, there are no agents to treat or prevent CDDP-induced kidney injury. We believe this is due in part to a lack of clinically relevant animal models. In the past, only a single high-dose model has been used to study CDDP-induced AKI. Our lab and others have developed a repeated low dose model to also study CKD development following CDDP treatment. Acute and chronic injuries can both be affected by sphingolipids, a family of bioactive lipids. Metabolism of sphingolipids is carried out in part by neutral ceramidase (nCDase), which hydrolyzes ceramide into sphingosine that can then be phosphorylated to form sphingosine-1-phosphate. The regulation of these sphingolipids affects cellular processes implicated in the pathology of CDDP-induced kidney injury, including cell proliferation, autophagy, and apoptosis. Additionally, our lab has previously observed that nCDase knockout protected mouse embryonic fibroblasts from ER-stress induced apoptosis in vitro by upregulating autophagic flux. We hypothesized that loss of nCDase would confer protection from CDDP-induced kidney injury.

**Methods:** We assessed renal outcomes in nCDase knockout (KO) and wild type (WT) C57BL/6 mice in both the acute and chronic models of cisplatin treatment.

**Results:** We demonstrated that nCDase KO provides protection from AKI in the high-dose model of CDDP-induced kidney injury. This protection was reversed when the autophagy-inhibitor chloroquine was co-administered. In the repeated low dose CDDP model, however, we found nCDase KO does not protect against development of renal fibrosis. We also observed that nCDase KO reduces induction of ER stress in the single high-dose model but not in the repeated low dose model.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Cisplatin-Induced MARCKS Phosphorylation Activates NF-κB Signaling and Contributes to AKI

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Background: Cisplatin is widely used for cancer treatment but is known to induce nephrotoxicity with severe damage to the proximal tubules, leading to acute kidney injury (AKI). Although a major substrate of protein kinase C, MARCKS, was shown to be induced phosphorylation at Ser 159/163 (phospho-MARCKS) in response to cisplatin, the molecular mechanism underlying increased phosphorylation of MARCKS and its functional consequence in AKI remain to be established. Herein, we investigated how phospho-MARCKS is regulated in proximal tubular cells, and its role in the context of cisplatin exposure.

Methods: The clinical relevance of phospho-MARCKS was first confirmed using immunohistochemistry. Next, we examined the effect of cisplatin exposure on phospho-MARCKS levels in kidney tubular epithelium. The MARCKS-interactome was identified by mass spectrometry. We also used genetic and pharmacological approaches to verify the functionality and molecular mechanism of cisplatin-induced phospho-MARCKS.

Results: In a screen of 75 renal biopsies from patients, we found that strong phospho-MARCKS expression was observed in kidney specimens from patients with acute renal tubular necrosis and was positively correlated. Western blot analyses demonstrate that an elevated abundance of phospho-MARCKS in cisplatin-exposed tubular epithelial cells and this increase appeared to be concentration-dependent. Mechanistically, we show that MARCKS protein directly bound to nuclear factor-kappa-B-activating protein (NFKAP). Following cisplatin-induced phosphorylation at Ser159 and Ser163, the interaction of MARCKS with NFKAP was inhibited, contributing to NFκB phosphorylation and NF-κB activation. Surprisingly, an elevation of phospho-MARCKS by cisplatin occurred in parallel with upregulation of inflammatory cytokines and markers of nephrotoxicity. Conversely, targeting of MARCKS phosphorylation with the MPS peptide, a novel MARCKS inhibitor, downregulated NF-κB signaling as well as suppressed levels of serum creatinine and blood urea nitrogen in cisplatin-treated mice.

Conclusions: Our results suggest that MARCKS phosphorylation is a novel NF-κB activator in cisplatin-induced proximal tubule damage and also present a proof of concept for the use of MPS peptide as a renal protection agent for AKI.

Funding: Other U.S. Government Support, Commercial Support - Dialysis Clinic, Inc. (C-3917)

PO0230

Apobec1 Limits Cisplatin-Induced AKI by Regulating the Disposal of Pro-Ferroptotic Lipids

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Background: Cisplatin (CP) causes proximal tubules to undergo regulated necrosis. We previously reported that the RNA editing-specific cytosine deaminase Apobec1, which regulates mitochondrial metabolism, cell fate and proliferation pathways, plays a crucial role in recovery from this injury. Among the known RNA editing targets for Apobec1 is the lipid transport protein Apob and as the resultant smaller Apob48 is the preferred secretory route of potentially cytotoxic triglycerides (TG), we then ask if Apobec1 limits CP-induced AKI.

Methods: ApoBec1 knockout (ko) mice were given CP 15 mg/kg i.p. and renal function, histology, mRNA, protein and lipid content were analyzed and compared to wild type (WT) mice of similar genetic background. We overexpressed rat Apobec1 in PT cells and assessed cell viability histologically and by WST-1 assay after CP exposure. Apobec1 deletion resulted in more severe AKI, plasma creatinine 2.07 mg/dL vs. 0.59 (n=13) vs 0.23 mg/dL, p<0.01 in WT. Remarkably all Apobec1 ko mice died after 6 days, while WT animals all survived. ApoBec1 KO kidneys showed greater necrosis and neutrophil counts. mRNA and protein levels of RIPK3, MLKL, TLR2, TLR4, and ASC4 were markedly increased in ApoBec1-1 ko compared to WT kidneys (p<0.01). Overexpression of ApoBec1 in mouse PT reduced CP-induced cell death 2.35-fold versus cells transduced with vector alone (n = 4, p<0.05). Overexpression of ApoBec1 increased the activities of kinases associated with survival (ERK, STAT3, Akt) and inhibited those inducing cell death (IRF4, and JNK). Plasma TG increased 2-fold higher in CP-treated ApoBec1 ko mice compared to WT animals (104 ± 12.6 vs. 57.4 ± 9.1, n=4, p<0.05), while renal TG trended upward (437.1 ± 130.0 vs. 223.8 ± 121.7, n=5, p=0.27).

Conclusions: We have identified ApoBec1 as a crucial gene regulating the necrotic response to CP-induced nephrotoxicity. ApoBec1 limits lipid accumulation in the kidney following CP-induced AKI and limiting lipotoxicity. Increasing ApoBec1 activity could be an effective strategy to reduce or prevent CP-induced AKI.

Funding: NIDDK Support
Cisplatin is a chemotherapy drug, but it has notorious nephrotoxicity. Background: Salubrinal is a specific inhibitor of eIF2alpha phosphatase, it promotes eIF2alpha phosphorylation which blocks the formation of the pre-initiation complex and halts global protein translation and protein synthesis. In this study, we examined the effect of salubrinal on cisplatin-induced injury in kidney proximal tubular cells.

Methods: Rat proximal tubular cells (RPTC) were treated with cisplatin or cisplatin with salubrinal for 4, 8, and 24 hrs. Cell lysates were collected for immunoblot analysis to examine the expression of proteins. In addition, other signaling proteins implicated in cisplatin injury were examined, including p53, JNK, p38, and p32delta, and ERK. Apoptosis was determined at 24 hrs of treatment by phase contrast and fluorescence microscopy following nuclear staining with Hoechst. Caspase activities were measured enzymatically by using DEVD-AFC, a fluorogenic peptide substrate. To examine cell survival, the cells were changed to fresh medium for 48 hrs after 24 hrs of cisplatin treatments with or without Salubrinal.

Results: Salubrinal suppressed apoptosis and caspase activation in RPTC during cisplatin treatment. It also promoted long-term cell survival after cisplatin treatment. In immunoblot analysis, during cisplatin treatment salubrinal increased eIF2alpha phosphorylation. It also increased PERK phosphorylation and the expression of GRP78 and CHOP, indicative of ER stress or unfolded protein response. Signaling pathways including MAP kinases, PKCdelta, and p32 are involved in cisplatin-induced kidney injury. Our results indicate that inhibition of global protein synthesis may be a new therapeutic strategy for the side-effects of cisplatin chemotherapeutic drugs.

Funding: NIDDK Support, Veterans Affairs Support

PO0234
Quantitative Prediction of Cisplatin-Induced AKI Using RENAsym, a Mechanistic Quantitative Systems Toxicology Model, and Renal Proximal Tubule Epithelial Cell In Vitro Assays


Background: Nephrotoxic drugs like cisplatin cause acute kidney injury (AKI) through complex cellular mechanisms that include mitochondrial dysfunction, oxidative stress, and immune mediated injury pathways. However, quantitative prediction of the underlying toxicity mechanisms in a challenging system is not possible. Quantitative systems toxicology (QST) modeling offers a promise for quantitative description of toxicity mechanisms leading to drug-induced AKI. We developed a QST model of cisplatin induced AKI using in vitro assays to characterize kidney injury pathways.

Methods: RENAsym was used to quantify cisplatin induced AKI. The model represents aspects of renal proximal tubule epithelial cells (RPTC) including cell life cycle and death pathways, bioenergetics, immune signaling pathways and biomarker responses. In vitro data related to cisplatin mitochondrial toxicity and oxidative stress generation were measured using RPTEC assays incubated with cisplatin (Cyprotex Inc.). To quantify cisplatin-induced mitochondrial dysfunction, oxygen consumption rate (OCR) was measured using the Seahorse XF analyzer. Cisplatin-induced oxidative stress was measured using high content imaging (HCI).

Results: The Seahorse study shows that the OCR decline at 24 hours, suggesting cisplatin-induced electron transport chain (ETC) inhibition. Similarly, HCI reveals significant oxidative stress elevation after 9 days. Toxicity parameters for cisplatin-induced mitochondrial dysfunction and oxidative stress mechanisms were determined using the above data. Simulations predict dose-dependent cisplatin toxicity as quantified by elevations in cGST, a biomarker that marks RPTC death. A simulated single high dose of 533 mg/m2 i.v. cisplatin results in 14-fold change in cGST, while a simulated clinical dose of 100 mg/m2 shows 7-fold increase. The 100 mg/m2 result is in qualitative agreement with 3.4-fold change observed in a clinical study where patients administered 100 mg/m2 i.v. cisplatin exhibited 20% incidence of AKI (Ummar. 2012, IJBBB).

Conclusions: RENAsym simulations predicted dose-dependent cisplatin-induced AKI that is in qualitative agreement with clinical data. RENAsym shows promise in providing a unique tool for drug-induced AKI prediction.

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PO0235
Diuretic Resistance: When to Consider Hydralazine?
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Introduction: We present a case of acute cardiac failure complicating hydralazine resistance. Case Description: A 52-Year-old woman with a history of obesity, hypertension, congestive heart failure with New York Heart Association functional class IV (EF60-65%), and alcoholic liver disease presented with a 3-day history of mental status change. Her serum creatinine was 3.6mg/dL, compared to 0.8mg/dL a month prior. She was volume overloaded with distended jugular veins, pulmonary crackles, and 2+ edema to her lower abdomen; she had a 30Kg weight gain over 5 months. Her urine sodium and chloride were both <10mEq/L. Urine analysis had 1+ urine protein and 1+ blood. She was started on torsemide 80 mg twice daily and was escalation progressively to IV furosemide 20 mg/h with IV saline as needed. Diuretic resistance is observed in a subset of patients with congestive heart failure.
chlorothiazide 500 mg twice daily. However, these large doses of intravenous diuretics failed to increase daily urine output above 1000 mL. After 20 hours of stable diuretics, vasodilator therapy was initiated with low dose hydralazine 10 mg thrice daily. Within one day, her urine output more than doubled and, over the next 3 days of the stable therapy, it peaked at 4 liters. Her fraction Na excretion (FeNa) was initially 0.1%; it increased to a maximum of 0.8% on the high IV continuous diuretic therapy but increased further to 3.8%-6.2% over 9 days after hydralazine was added to the diuretic regimen. After addition of hydralazine, her congestion dissipated, she lost 23 Kg and the diuretic regimen was reduced eventually to furosemide 80 mg BID and spironolactone 200 mg daily prior to her discharge with a serum creatinine of 1.3 mg/dL. At follow up after 3 months, her symptoms remained well controlled, her weight was reduced by a further 10 kg and her serum creatinine was 0.9 mg/dL.

Discussion: Hydralazine has been recommended to treat diuretic resistance in HF by increasing cardiac output, renal blood flow and renal diuretic delivery. However, our case suggests that hydralazine greatly improves renal tubular diuretic responsiveness as her FeNa increased 3 fold. This is not likely due to better renal diuretic delivery since the patient received constant IV infusions of two diuretics at doses well above their ceiling. Further clinical trials and mechanistic studies of hydralazine-diuretic interaction are warranted.
how renal biopsy and social history remain vital diagnostic tools in patients presenting a pauci-immune or immune complex pattern as with our patient. The case demonstrates association reported with ANCAs, particularly anti-PR3, which can demonstrate either particularly in the absence of overt clinical endocarditis. There has been a crossover and multiple scratches. Treatment focus shifted from immunosuppression to antibiosis. Broader infectious workup was negative for ASO titters, Borrelia antibody, Quantiferon/ evidence of alveolar hemorrhage, immunosuppression and PLEX were discontinued. glomerulonephritis. With a biopsy suggesting an infectious process and BAL without few distinct subepithelial hump-like deposits by EM, suggestive of an infection related trace granular C1q. EM confirmed mixed mesangial (dominant), subendothelial, and a cultures, assays for hepatitis B/C, HIV and Respiratory panel were negative. Blood/urine ENA, anti-GBM, C-ANCA, P-ANCA, and MPO Ab were negative. However, PR3 Ab treated with immunosuppression and plasma exchange. Serologic tests including ANA/ hypoxia and blood-tinged sputum concerning for pulmonary/renal syndrome and was 120 glomeruli and 12 were sclerosed There was focal organizing arterial nephrostomy was place but creatinine rose to 5mg/dl so renal biopsy was done. The specimen had 2-3 schistocytes per high power field. Lactate dehydrogenase was 449 U/L, hemoglobin 6.7g/dl, platelets 228 K/mcl and Creatinine 2.3mg/dl (baseline 0.6 mg/dl). Renal function improved slightly after Foley placement for newly diagnosed BPH, but SCr remained elevated with negative initial AKI workup. Renal biopsy showed oxalate nephropathy. Further history revealed only occasional consumption of nuts with daily servings of tea and polyethylene glycol. Patient B’s genetic testing was also negative. He remains on hemodialysis and has been referred for transplant.

Discussion:
Oxalate nephropathy can result from primary (genetic) or secondary mechanisms. The most common secondary causes include increased intestinal oxalate availability (“enteric” hyperoxaluria) and increased dietary consumption. A basic medical history can reveal risk factors for enteric hyperoxaluria, while a thorough review of diet and supplements is often deferred, delaying the diagnosis. In some cases a single cause is not identified, and instead a combination of dietary and pharmacologic factors are to blame. We present 1 case of oxalate nephropathy most likely caused by high-dose Vitamin C, and another case with a less clear etiology aside from vague dietary and medication factors.

PO0240

Cat Scratch Kidney
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Introduction: Acase of amuric RPGN secondary to post infectious glomerulonephritis in setting of bartonella infection
Case Description: An 84-year-old female presented with creatinine of 7.85mg/dl (baseline 0.81mg/dl) during a workup for painful hematuria. She developed progressive hypoxia and blood-tinged sputum concerning for pulmonary/renal syndrome and was treated with immunosuppression and plasma exchange. Serologic tests including ANA/ENA, anti-GBM, C-ANCA, P-ANCA, and MPO Ab were negative. However, PR3 Ab was elevated at 29.3 Units. Complement C3 and C4 levels were normal. Blood/urine cultures, assays for hepatitis B/C, HIV and Respiratory panel were negative. Bartonella PCR was negative. Both TTE and TEE were negative for valvular lesions. Additional patient history elucidated recent acquisition of a pet cat and multiple scratches. Treatment focus shifted from immunosuppression to antibiotic.

Discussion: Our case highlights an underappreciated entity associated with GN, particularly in the absence of overt clinical endocarditis. There has been a crossover association reported with ANCAs, particularly anti-PR3, which can demonstrate either a pauci-immune or immune complex pattern as with our patient. The case demonstrates how renal biopsy and social history remain vital diagnostic tools in patients presenting with non-specific systemic illness.

PO0241

Two Cases of Oxalate Nephropathy: An Uncommon Disease, Often Missed
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Introduction: Oxalate nephropathy is a state of excess oxalate availability leading to damaging calcium oxalate crystal deposition in the renal tubules and interstitium. It is an uncommon but severe cause of renal damage and leads to dialysis dependence in the majority of patients; thus, diagnostic index of suspicion must be high.

Case Description: Patient A was a 58 year old male with 2 prior renal stones but no history of gastric bypass, IBD, or other malabsorptive state who presented with vomiting, metallic taste, and behavior changes. Serum creatinine (Scr) on admission was 10.2 mg/dL (baseline 1.1 mg/dL). Basic workup including ANCA, ANA, dsDNA, C3, C4, and Hepatitis B and C was unremarkable. A renal biopsy showed severe interstitial fibrosis and tubular atrophy with abundant calcium oxalate crystals, and dialysis was initiated. Dietary history revealed daily consumption of 1,000 mg Vitamin C, salads, and nuts. Genetic testing for primary hyperoxalosis was negative. After 1.5 months he was no longer dialysis-dependent but only attained partial renal recovery (Scr 2.67 mg/dL, eGFR 25).

Patient B was a 68 year old male with no history of renal or GI disease who presented with anemia, weakness, and urinary retention. Admission Scr was 7.7 mg/dL (baseline 1.4 mg/dL). Renal function improved slightly after Foley placement for newly diagnosed BPH, but Scr remained elevated with negative initial AKI workup. Renal biopsy showed oxalate nephropathy. Further history revealed only occasional consumption of nuts with daily servings of tea and polyethylene glycol. Patient B’s genetic testing was also negative. He remains on hemodialysis and has been referred for transplant.

Discussion: Oxalate nephropathy can result from primary (genetic) or secondary causes. The most common secondary causes include increased intestinal oxalate availability (“enteric” hyperoxaluria) and increased dietary consumption. A basic medical history can reveal risk factors for enteric hyperoxaluria, while a thorough review of diet and supplements is often deferred, delaying the diagnosis. In some cases a single cause is not identified, and instead a combination of dietary and pharmacologic factors are to blame. We present 1 case of oxalate nephropathy most likely caused by high-dose Vitamin C, and another case with a less clear etiology aside from vague dietary and medication factors.

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Underline represents presenting author.
P00243

Myeloid-Specific PKM2 Deletion Reduces Kidney Damage in Oxa-
late-Induced AKI

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Background: Reprogramming of immune cell metabolism have been associated with the development of kidney injury. The M2 isozyme of pyruvate kinase (PKM2) catalyzes a critical stage of glycolysis, which was shown to be a crucial metabolic pathway for pro-
flammatory processes in macrophages. The objective of this study was to investigate whether deletion of PKM2 in myeloid cells exerts renoprotection in calcium oxalate (CaOx)-crystal-induced acute kidney disease (AKI).

Methods: AKI was induced in myeloid-specific PKM2-knockout (PKM22/2+/LysM-Cre+) (p<0.05). FACS analysis indicated that the number of F4/80+ CD11b+ cells in kidneys were similarly elevated by CaOx in both PKM22/2+ and PKM2+LysM-
Crev+ mice with the pro-inflammatory phenotype LysM-Cre+ 2-copy mice were significantly reduced in PKM22/2+/LysM-Cre+ (p<0.05). In addition, PKM2 deletion also reduced renal levels of lactate (p<0.05).

Conclusions: The pro-inflammatory status of macrophages relays on glycolysis in CaOx nephropathy. Therefore, deletion of PKM2 in myeloid cells can reduce CaOx-induced renal inflammation and injury. FAPESP (19/02893-9 and 2017/05264-7), CNPq and CAPES.

Funding: Government Support - Non-U.S.

P00244

High-Content Imaging of Kidney Cell Function to Elucidate Mechanisms of Antiviral Drug Toxicity

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Background: Globally, millions of people live with HIV and hepatitis B virus (HBV). Toxicity from antiviral drugs is a major cause of kidney disease in these individuals. Tenovir disoproxil fumarate (TDF) is a first line therapy for HIV and HBV. TDF induces functional proximal tubule (PT) defects for reasons that are unknown, partly due to a lack of appropriate experimental models. Clinically, TDF toxicity is characterized by two major phenotypes: isolated defects in PT solute transport; and severe tubular damage (Fanconi syndrome/acute kidney injury) associated with grossly enlarged mitochondria. The aim of our study was to establish realistic in vitro models of TDF toxicity, to investigate the underlying mechanisms.

Methods: Experiments were performed on monolayers of differentiated human-derived PT cells (RPTEC/TERT1). A high-content image analysis pipeline was established, using automated microscopy and machine learning, to quantify transport function, using dome formation as a readout. Metabolism was evaluated by antibody staining for mitochondrial morphology and autophagy.

Results: We screened numerous treatment regimens and generated phenotypes matching those observed in patients, including transport inhibition and mitochondrial hypertrophy. Further experiments using these models revealed that TDF caused a dose dependent decrease in ATP content increased glycolysis and mtDNA content. Basal and ATP-linked respiration were decreased but maximal respiration was achieved, suggesting inhibition of complex V (ATP synthase). Metabolomic analysis confirmed that TDF was converted to the active antiviral metabolite Tenovir diphosphate (TFVpp), a structural analogue of ATP. Using an in vitro assay of complex V activity, we observed a dose dependent increase in ATP activity increased glycolysis and mitochondrial mass. Metabolomics revealed no major defects in the TCA cycle or beta-oxidation, but clear evidence of oxidative stress.

Conclusions: In summary, we have developed a high-content image analysis pipeline of human-derived PT cells to generate realistic in vitro models of functional TDF toxicity. Metabolic characterization of these revealed a clear phenotype consistent with ATP dependent inhibition with mitochondrial hypertrophy in patients, and the PT solute transport is highly dependent on aerobic respiration. ATP depletion might trigger compensatory mitochondrial biogenesis, leading to hypertrophy.

Funding: Government Support - Non-U.S.

P00245

Immunological Changes Following Cholineric Anti-Inflammatory Pathway Stimulation

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Background: The cholinergic anti-inflammatory pathway (CAP) protect mice from ischemia reperfusion injury (IRI). The interactions and mechanisms that regulate this effect are of great interest as targets for clinical intervention. Vagus nerve stimulation (VNS) induces neurotransmitter cascades that culminate in release of norepinephrine (NE) in the spleen. NE stimulates CD4+ T cells to produce acetylcholine via the choline acetyltransferase enzyme. Acetylcholine then stimulates anti-inflammatory via splenic immune cells that express the 67 nicotinic acetylcholine receptor (nAChR). Adaptive transfer of splenic cells from VNS-treated mice protects kidneys from IRI. However, the downstream effects on splenic structure and function that lead to protection are still not fully understood. The goal of this study is to profile immune cells following CAP stimulation and identify key downstream mechanisms.

Methods: VNS was performed on mice in vivo and nicotine stimulation on immune cells ex vivo. Vagus nerve stimulation was triggered optogenetically using blue light to target the vagus nerve of mice expressing channelrhodopsin-2 under control of the vasculature glutamate transporter 2 promoter. Cells were collected from the spleens between 24- and 48-hours post-stimulation. A concentration of 50 µM nicotine in culture media was used to stimulate α7nAChR-expressing immune cells collected from the peritoneum of mice. Analysis of immune cell populations was performed with flow cytometry and single cell RNA sequencing.

Results: Overall, optogenetic VNS led to a reduced number of CD4+ cells from the spleen. Within the CD4+ population, B1 cells and macrophages exhibited increased representations of ~30% and 60%, respectively. Monocyte and neutrophil representation remained relatively stable, but eosinophils displayed a marked reduction of ~60%. Single cell RNA sequencing showed increased novel gene expression in subpopulations of macrophages, including cell-cell adhesion genes (Sparc) and granule nitrreceptor exchange factors (Argef5) that could regulate function.

Conclusions: Cholinergic stimulation triggers reorganization of immune cell populations and alters gene expression patterns that are likely important for regulating the inflammatory environment. Additional characterization and functional studies are currently underway to fully identify the importance of observed changes.

Funding: NIDDK Support

P00246

Reduced Levels of Cyclic-GMP and Inhibition of cGMP-Dependent Protein Kinase Activate p21Waf1/Cip1 and p27Kip1 and Lead to Renal Fibrosis and Dysfunction

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Background: Targeted-deletion of Npr1 (coding for guanylyl cyclase/natriuretic peptide A, GC-ANP/NPR-A) extends hyperproliferative effects in target organs of Npr1 gene-knockout mice; however, the molecular mechanisms of these pathologies are poorly understood. Fibrosis and hypertrophy are regulated by p21Cip1 and p27Kip1, cell-cycle regulatory proteins that inhibit cyclin and cyclin-dependent kinase (cyclin-CDK) complex.

Methods: We examined the activation of CDK blocker (p21Waf1/Cip1 and p27Kip1) in Npr1 gene-knockout (0-copy); Npr1+/- mice and the GC inhibitor, A71915-treated and cGMP-dependent protein kinase (cGK) inhibitor, Rp-8-Br-cGMPS (Rp)-treated wild-type (Npr1)+/+(138.6 ± 3.1 mmHg; p<0.001) and gene-duplicated 4-copy (Npr1++/++) mice using Western blot and quantitative real-time PCR.

Results: Cyclic-GMP levels and cGK activity were significantly decreased in 0-copy mice compared with controls (138.6 ± 3.1 mmHg; p<0.001) and significantly lower BP in 4-copy mice (86.8 ± 2.8 mmHg; p<0.01) compared to 2-copy mice (102.2 ± 1.7 mmHg). Treatment with A71915 and Rp showed significant increase in BP in 2-copy mice but only a small increase in 4-copy mice compared with untreated control animals. Increased phosphorylation of e-erK1/2 (3-fold), p38MAPK (4-fold), p21Waf1/Cip1 (6-fold), and p27Kip1 (5-fold) occurred in 0-copy, A71915-treated and Rp-treated 2-copy mice, but less in A71915-treated 4-copy mice.

Conclusions: The present results suggest that Npr1 has a pivotal role in inhibiting the renal fibrosis and pathology and exerts renal protective effects through the cGK/cCIP1 axis by repressing the CDK inhibitors, p21Waf1/Cip1 and p27Kip1.

Funding: Other NIH Support - NHLBI

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

127
Inhibition of Acetyl-CoA Carboxylase in Acutely Injured Tubular Cells Exacerbates DNA Damage and Mitochondria Fission in Diabetic Nephropathy

Xiaohuan Liu,1,2 Jiahua Li,1 Shen-Yang Cheng,1 Guixia Li,1,3 Joseph V. Bonventre.1 Brigham and Women’s Hospital, Boston, MA; The Second Hospital, Chelou College of Medicine, Shandong University, Jinan, China; Shenzhen Third People’s Hospital, Shenzhen, China.

Background: Both diabetes and acute tubular injury (ATI) alter lipid metabolism of proximal tubules. Inhibiting lipogenesis causes G2M cell cycle arrest, which can cause maladaptive tubular repair. Acetyl-CoA carboxylase (ACC) stimulates lipogenesis and inhibits fatty acid oxidation (FAO). Phosphorylation (p-ACC) inhibits ACC, which inhibits lipogenesis and promotes FAO. We hypothesized that p-ACC exacerbates DNA damage and mitochondria dysfunction in diabetic nephropathy (DN) after ATI.

Methods: Human DN samples were co-stained for p-ACC, KiM-1, and a-SMA. ATI was introduced by a single diphtheria toxin (DT) injection in Akita mice in which the DT receptor (DTR) was introduced genetically into the kidney tubule (AkitaSIX2-DTR). The expression ratio of p-ACC/ACC was determined at 3 days after DT and markers for tubular injury and DNA damage (g-H2AX) were evaluated at 3 days and 4 months. Cisplatin-injured HK2 cells were treated with an ACC inhibitor, PF-05175157 (ACCi) or a carnitine palmitoyltransferase 1 inhibitor, etomoxir (CPT1i) and examined for DNA damage and mitochondria fission.

Results: P-ACC expression was increased and correlated with expression of tubular injury marker KiM-1 and myofibroblast marker a-SMA in human DN specimens. At day 3 after DT, ATI increased the p-ACC/ACC ratio in the Akita (60±20%) mice on HFD and resulted in enhanced expression of g-H2AX in KiM-1 positive tubules and kidney fibrosis at 4 months. When cisplatin-injured HK2 cells were treated with ACCi, which allowed b-oxidation of acyl-CoA, there was an increase in mitochondrial fission factor (MFF) without a further increase of g-H2AX. Etomoxir, which blocked acylcarnitine entry into mitochondria, reduced MFF and g-H2AX expression.

Conclusions: Increased levels of p-ACC were associated with increased tubular injury and fibrosis in human DN. P-ACC in injured renal epithelial cells permitted b-oxidation of acyl-CoA in damaged mitochondria and enhanced mitochondrial fission resulting in DNA damage plausibly from reactive oxygen species. Prevention of mitochondrial overload of acyl-CoA is a potential therapeutic target to mitigate mitochondria damage and DNA damage after ATI in DN.

Funding: NIDDK Support

The Effect of ANG-3777 on In Vitro Cell Proliferation

Background: Hepatocyte growth factor (HGF) regulates tissue growth and development by inducing cell motility, proliferation and morphogenesis in multiple cell types including endothelial and epithelial cells. However, it has no effect on proliferation in fibroblasts. ANG-3777 is a novel molecule that exerts similar cytoprotective and regenerative effects as HGF. This study compared the effect of ANG-3777 with that of HGF in stimulating cell proliferation.

Methods: In vitro cell proliferation assays were conducted in triplicate using human umbilical vein endothelial cells (HUVECs), rat neuronal Schwann cells, and mouse fibroblasts. HUVECs and fibroblasts were exposed to 5 μM ANG-3777 or 25 ng/mL HGF for up to 24 hours. Schwann cells were exposed to increasing doses of ANG-3777 (up to 10 μM) or HGF (up to 100 ng/mL) for 16 to 24 hours to evaluate the effective concentration at 50% proliferative activity (EC50). Radiolabeled [3H]-thymidine incorporation was used to quantify cell proliferation. For the cell-based proliferation assays confirmed that the activity of ANG-3777 and HGF compared with vehicle (p<0.01, Figure 1).

Results: A statistically significant increase in cell proliferation (~3-fold) was observed in HUVECs exposed to ANG-3777 and HGF compared with vehicle (p<0.01, Figure 1). Similarly, Schwann cell proliferation increased in a concentration-dependent manner following exposure to ANG-3777 (EC50 0.012 μM) and HGF (EC50 6.5 ng/mL). In mouse fibroblasts (negative control), neither ANG-3777 nor HGF exposure stimulated cell proliferation compared with vehicle.

Conclusions: In vitro cell-based proliferation assays confirmed that the activity of ANG-3777 is comparable to that of HGF in inducing cell proliferation in HUVECs and rat Schwann cells with neither agent stimulating proliferation in mouse fibroblasts.
was induced in mice after right kidney removal, then IRI mice were treated with 200 kIU for 24 h. We found that IRI resulted in a detectable rise in creatinine level.

Methods: Human kidney proximal tubule cells (PTCs; RPTEC cell line) were exposed to FLCs. Control/treated cells were harvested, and total RNA (mRNA+miRNA) was isolated following standard procedures for whole transcriptome sequencing (Agilent Bioanalyzer 2100). RNA sequencing for whole transcriptome was performed by using Illumina NextSeq 500 to generate ~600 paired-end 75bp reads per sample. After initial data quality checking by FastQC and RSeQC, bioinformatics analysis was performed using TopHat, Samtools, and Picard. Further classified, annotated, and visualized were facilitated by Partek and R statistical packages. RNA sequencing data were validated through qPCR.

Results: Whole transcriptome RNA-Seq data suggested role of several genes involved in innate immunity (VNN1, MX1, OAS2, TLRs, IFI6, IFI27, IFIT1, ISG15, BST2) and region-specific enrichment of FLCs. Control/treated cells were harvested, and total RNA (mRNA+miRNA) was isolated following standard procedures for whole transcriptome sequencing (Agilent Bioanalyzer 2100). RNA sequencing for whole transcriptome was performed by using Illumina NextSeq 500 to generate ~600 paired-end 75bp reads per sample. After initial data quality checking by FastQC and RSeQC, bioinformatics analysis was performed using TopHat, Samtools, and Picard. Further classified, annotated, and visualized were facilitated by Partek and R statistical packages. RNA sequencing data were validated through qPCR.

Conclusions: Our results show differentially expressed genes and a mechanism of injury involving cross-talk between innate immunity and inflammatory pathways in PTCs exposed to FLCs.

Funding: Private Foundation Support

PO0254 Long-Term Use of Ferric Citrate in the Treatment of Iron Deficiency Anemia in Patients with Non-Dialysis-Dependent CKD: The COMPASS Trial Pablo E. Pergola,1 Diogo S. Belo,3 Paul W. Crawford,6 Moustafa A. Moustafa,2 Wenli Luo,2 Alex Goldfarb,7 Renal Associates PA, San Antonio, TX, 1Cafeteria Research Institute of the University of Texas, El Paso, TX, 2South Carolina Nephrology & Hypertension Center, Inc, Orangeburg, SC, 3Akemia Therapeutics, Inc, Cambridge, MA, 4Research by Design, Chicago, IL.

Background: Ferric citrate (FC) is an FDA-approved oral iron replacement for adults with iron deficiency anemia (IDA) and non-dialysis-dependent (NDD) CKD and as a phosphate binder in adults with dialysis-dependent CKD. For IDA, the recommended FC starting dose is 1 tablet (1 g, contains 210 mg ferrous iron) 3 times daily (TID) titrated to maintain hemoglobin (Hb) goal. We studied the long-term efficacy and safety of various FC regimens for IDA treatment in adults with NDD-CKD (stages 3-5).

Methods: 48-wk, phase 4, randomized, open-label, multicenter study (NCT03236246). Patients received (1:1) FC 1 g tablet TID (3 g/day) or 2 tablets BID (4 g/day). At Wk 12, if Hb was <10 g/dL or changed <0.5 g/dL from baseline (BL), dose was increased to 2 tablets TID (from 1 TID) or 3 tablets BID (from 2 BID). Primary endpoint was change in Hb from BL to Wk 24. Secondary endpoints included change in transferrin saturation (TSAT), ferritin, and phosphate to Wk 48.

Results: This analysis included 183 of 206 randomised patients. Groups were well matched, with mean age 69±10.3 y and 54% with CKD due to diabetes. Mean BL eGFR was 33.6±10.9 mL/min/1.73 m², and Hb was 10.45±0.74 g/dL. Efficacy measures at 48 wks are presented in the Table. Adverse events (AEs) occurring in ≥5% included diarrhea (13.2%), constipation (12.7%), and constipation (12.2%). Incidence of serious AEs was 13.9% in BID and 17.3% in TID groups. Five deaths were reported, none deemed FC related by investigators.

Conclusions: Both FC regimens studied increased and maintained Hb through 48 wks in patients with NDD-CKD with IDA. Patients with lower baseline Hb and iron parameters had a higher increase in Hb with FC treatment. Serum phosphate remained within normal range over study duration. Mean changes in Hb, TSAT, ferritin, and phosphate were similar in the BID and TID and the 3 and 4 g/day dosing groups. These results support the potential for FC dosing flexibility in the long-term treatment of IDA.

Funding: Commercial Support - Akemia Therapeutics, Inc.

PO0255 Spatial Transcriptomic Signatures in Murine AKI Models Ricardo Melo ferreiro,1 Tarek M. El-Achkar, Kimberly S. Collins, Yinghua Cheng, Seth Winfree, Pierre C. Daghie, Michael T. Eadon. Indiana University School of Medicine, Indianapolis, IN.

Background: The localization of whole transcriptome differential expression in different forms of acute kidney injury (AKI) is incompletely understood. We investigated the distribution of expression across the entire kidney, mapping expression patterns to renal histology in the ischemia-reperfusion injury (IRI) and cecal ligation and puncture (CLP) murine models of AKI.

Results: Single cell RNA-seq analysis of kidney cells revealed differential gene expression that defined patterns of maladaptive proximal tubule repair and characterized important signatures in immune cell composition and activation in regenerating vs. fibrosing kidneys.

Funding: NIDDK Support, Private Foundation Support
Table 1. Risk of RBC transfusion in NDD-CKD and DD-CKD patients treated with roxadustat compared with placebo or epoetin alfa – FAS

<table>
<thead>
<tr>
<th>Study</th>
<th>Hb change (baseline to Week 52)</th>
<th>RBC transfusions</th>
<th>Risk reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1.9 vs 0.2 g/dL (P&lt;0.0001)</td>
<td>3.0 vs 2.1% (P=0.0001)</td>
<td>42% CI: -0.11 to 61%</td>
</tr>
<tr>
<td>Epoetin alfa (150,000 IU/week)</td>
<td>2.1 vs 1.5% (P=0.005)</td>
<td>2.1 vs 1.5% (P=0.005)</td>
<td>57% CI: -0.01 to 47%</td>
</tr>
</tbody>
</table>

aFull analysis set.
CI, confidence interval; CKD, chronic kidney disease; DD, dialysis-dependent; HR, hazard ratio; NDD, non-dialysis-dependent.
PO0258
Health-Related Quality of Life in Roxadustat-Treated Patients with Anemia and Non-Dialysis-Dependent CKD

Daniel W. Coyne,1 Roberto Manilo-Karin,2 Pablo E. Pergola,3 Carol A. Pollock,4 Roberto Pecetto-Filho,4,5 Tyson T. Lee,6 Elise Hardy,4,6 Kin-Hung P. Yu,4 Washington University in Saint Louis School of Medicine, Saint Louis, MO; 2South Texas Kidney Specialists, P.A., McAllen, TX; 3Renal Associates PA, San Antonio, TX; 4The University of Sydney, Sydney, NSW, Australia; 5Arbor Research Collaborative for Health, Ann Arbor, MI; 6Pontificia Universidade Catolica do Parana Departamento de Medicina, Curitiba, Brazil; 7 Fibrogen Inc, San Francisco, CA; 8AstraZeneca, Gaithersburg, MD.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Anemia in CKD impacts health-related quality of life (HRQL) by reducing physical capacity and energy levels. Studies have demonstrated a direct relationship between HRQL scores and hemoglobin (Hb) levels in non–dialysis-dependent (NDD) and dialysis-dependent patients with CKD. We assessed the impact of roxadustat on HRQL in patients with NDD-CKD.

Methods: Pooled data from three pivotal, phase 3, randomized, double-blind, placebo-controlled studies of roxadustat for the treatment of anemia in patients with NDD-CKD were assessed. Patients with data up to the time of dialysis treatment and who had pretreatment and a post-treatment HRQL measurement were included. Mean changes from baseline to Week 12 in HRQL scores were compared between the treatment groups.

Results: Least-squares mean treatment differences favored the roxadustat group at Week 12 in all p-values <0.05) in the majority of measures analyzed (Table). Between-group differences were larger in subgroups with lower (ie, worse) baseline scores.

Conclusions: Roxadustat demonstrated improvement in most HRQL measures vs. placebo in patients with NDD-CKD.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

Table: Mean CFB in HRQL scores vs. placebo (Weeks 28-52) in Patients with NDD-CKD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall</th>
<th>Females</th>
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<th>Region</th>
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</tr>
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<tbody>
<tr>
<td>SF-36 Physical Functioning Subscale</td>
<td>0.55 (0.25, 0.85)</td>
<td>0.70 (0.28, 1.21)</td>
<td>0.151</td>
<td>0.003</td>
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<td>0.008</td>
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</tr>
<tr>
<td>TAPA-Anemia Subscale Score</td>
<td>0.30 (0.16, 0.45)</td>
<td>0.49 (0.41, 0.57)</td>
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PO0259
Subgroup Analyses of Efficacy of Roxadustat for Treatment of Anemia in Patients with Incident Dialysis-Dependent CKD

Robert Provenzano,1 Jayant Kumar,2 Steven Fishbane,2 Anjay Rastogi,3 Lona Poole,4 Cameron S. Liu,5 Dustin J. Little,6 Kin-Hung P. Yu,7 Mohammad A. El-Shahawy,8 Roberto Pecetto-Filho,4,5 Hakim M. Gurcan,9 Cameron S. Liu,6 Elise Hardy,4,6 John Houghton,4 Kin-Hung P. Yu,7 Washington University School of Medicine, St. Louis, MO; 2Keck School of Medicine, University of Southern California, Los Angeles, CA; 3AstraZeneca Inc, San Francisco, CA; 4AstraZeneca, Gaithersburg, MD.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Anemia in CKD impacts health-related quality of life (HRQL) by reducing physical capacity and energy levels. Studies have demonstrated a direct relationship between HRQL scores and hemoglobin (Hb) levels in non–dialysis-dependent (NDD) and dialysis-dependent patients with CKD. We assessed the impact of roxadustat on HRQL in patients with NDD-CKD.

Methods: Pooled data from three pivotal, phase 3, randomized, double-blind, placebo-controlled studies of roxadustat for the treatment of anemia in patients with NDD-CKD were assessed. Patients with data up to the time of dialysis treatment and who had pretreatment and a post-treatment HRQL measurement were included. Mean changes from baseline to Week 12 in HRQL scores were compared between the treatment groups.

Results: Least-squares mean treatment differences favored the roxadustat group at Week 12 in all p-values <0.05) in the majority of measures analyzed (Table). Between-group differences were larger in subgroups with lower (ie, worse) baseline scores.

Conclusions: Roxadustat demonstrated improvement in most HRQL measures vs. placebo in patients with NDD-CKD.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

Table: Mean CFB in HRQL scores vs. placebo (Weeks 28-52) in Patients with NDD-CKD

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PO0260
Subgroup Analyses of Efficacy of Roxadustat for Treatment of Anemia in Patients with Non-Dialysis-Dependent CKD

Daniel W. Coyne,1 Mohamed A. El-Shahawy,2 Roberto Pecetto-Filho,4,5 Hakim M. Gurcan,9 Cameron S. Liu,6 Elise Hardy,4,6 John Houghton,4 Kin-Hung P. Yu,7 Washington University School of Medicine, St. Louis, MO; 2Keck School of Medicine, University of Southern California, Los Angeles, CA; 3AstraZeneca Inc, San Francisco, CA; 4AstraZeneca, Gaithersburg, MD.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Anemia in CKD impacts health-related quality of life (HRQL) by reducing physical capacity and energy levels. Studies have demonstrated a direct relationship between HRQL scores and hemoglobin (Hb) levels in non–dialysis-dependent (NDD) and dialysis-dependent patients with CKD. We assessed the impact of roxadustat on HRQL in patients with NDD-CKD.

Methods: Pooled data from three pivotal, phase 3, randomized, double-blind, placebo-controlled studies of roxadustat for the treatment of anemia in patients with non-dialysis-dependent (NDD) CKD were assessed. Data from prespecified, clinically relevant patient subgroups were analyzed for: mean change from baseline (CFB) in hemoglobin (Hb) averaged over weeks 28–52 regardless of rescue therapy (primary US efficacy endpoint) and patients (%) that received rescue therapy in the first 52 weeks.

Results: Roxadustat- (n=2391) vs. placebo-treated patients (n=1886) achieved a significantly larger mean (SD) CFB in Hb level (1.85 ± 0.94) vs. 0.13 ± 1.01 (p<0.0001). The effect was consistent in all subgroups and fewer patients that received rescue therapy was consistent across a wide range of prespecified subgroups in the overall population and by age group (18–64), gender (male), race (white), region (US, Europe), baseline iron status (ferritin ≥100 mg/dL & TSAT ≥20%), baseline Hb (<8.0 and ≥10.0 g/dL), and dialysis modality (hemodialysis). HR of MACE and MACE+ were lower in the roxadustat vs. epoetin alfa group: 0.70 (95% CI: 0.51, 0.96) (p=0.03) and 0.66 (95% CI: 0.50, 0.89) (p=0.005).

Conclusions: The efficacy of roxadustat vs. epoetin alfa for improving Hb level and reducing IV iron use was consistent across prespecified subgroups in the ID-DD population. Roxadustat reduced MACE and MACE+ vs. epoetin alfa.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

Table: Mean CFB in HRQL scores vs. placebo (Weeks 28-52) in Patients with NDD-CKD

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
PO0261
Risk of Transfusion in Patients with Non-Dialysis-Dependent CKD Increases with Hemoglobin Levels <10 g/dL vs. ≥10 g/dL: Pooled Results from Roxadustat Phase 3 Studies
Daniel W. Coyne, Roberto Pecotis-Filho, Anjay Rastogi, Lynda Szczech, Tyson T. Lee, Maksym Pola, Kin-Hung P. Yu. Washington University in Saint Louis School of Medicine, Saint Louis, MO; Arteriovascular Research Center for Health, Ann Arbor, MI; Pontificia Universidad Catolica de Parana Departamento de Medicina, Curitiba, Brazil; University of California Los Angeles, Los Angeles, CA; FibroGen Inc, San Francisco, CA; AstraZeneca, Warsaw, Poland.

Background: Roxadustat is a novel, orally bioavailable, heterocyclic small molecule that reversibly inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase enzymes and activates HIF and transcription of HIF-responsive genes, including erythropoietin. In patients with ESRD, the risk for blood/RBC transfusion is higher in patients with hemoglobin (Hb) levels <10 g/dL vs. those with Hb ≥10 g/dL. We evaluated the efficacy of roxadustat vs. placebo on blood/RBC transfusion by Hb level in US-based patients with non-dialysis-dependent (NDD) CKD.

Methods: Data from three pivotal phase 3 randomized, placebo-controlled studies of roxadustat for the treatment of anemia in NDD patients were assessed. Patients were randomized to receive roxadustat or placebo with periodic dose evaluation/titration. Transfusion was allowed at any time if it was deemed a medical necessity by the Investigator. The incidence rate of transfusion was calculated based on Hb level categories as: <9.0, 8.0 to <9.0, and ≥9.0 g/dL. Data were evaluated for the on-treatment period ≥28 days after the last dose of study drug.

Results: In the overall pooled population of patients with NDD-CKD, roxadustat reduced the risk of transfusion by 74% (HR, 0.26; 95% CI, 0.21, 0.32; p<0.0001) vs. placebo. When patient-exposure data were stratified by achieved Hb levels, the risk for transfusion increased as Hb levels decreased (Table). The incidence rate of transfusion increased approximately 4-fold in patients with Hb between 8.0 and <10.0 g/dL vs. those with Hb ≥10 g/dL regardless of treatment arm.

Conclusions: In US-based patients with NDD-CKD and anemia treated with roxadustat, the risk of transfusion was approximately 4 times higher in patients with Hb between 8.0 g/dL and <10.0 g/dL vs. those with Hb ≥10 g/dL.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

Table: Incidence rate of transfusion (events/100 PEY) based on Hb level and treatment group

PO0262
Roxadustat Favorably Modifies Iron Indices in Patients with Non-Dialysis-Dependent CKD-Related Anemia
Daniel W. Coyne, Simon D. Roger, Willis Chou, Anatole Besarab, Robert Leong, Tyson T. Lee, Lynda Szczech, Dustin J. Little, Kin-Hung P. Yu. Washington University in Saint Louis School of Medicine, Saint Louis, MO; Renal Research, Gosford, NSW, Australia; FibroGen Inc, San Francisco, CA; Stanford University School of Medicine Center for Neuroscience in Women’s Health, Palo Alto, CA.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis by increasing endogenous erythropoietin and improving iron metabolism.

Methods: We analyzed data from a Phase 3, randomized, double-blind study (ANDES) comparing roxadustat to placebo for the treatment of anemia in NDD-CKD patients. 922 patients were randomized (2:1) to receive roxadustat (n=616) or placebo (n=306) thrice weekly with monthly dose titrations. Patients were encouraged to receive oral iron daily unless not tolerated. Change in Hb was compared to changes in key iron and red blood cell (RBC) parameters.

Results: All baseline (BL) parameters were comparable between the study arms. Roxadustat was superior to placebo in increasing mean Hb from BL over weeks (wks) 28-52: +2.00 vs. +0.16 g/dL (p<0.0001), respectively. Iron parameters were unchanged over time in the placebo arm. In the roxadustat arm, significant erythropoiesis was noted with mean Hb increases of 1.52 and 1.89 g/dL at wks 4 and 24; mean decrease in hepcidin was 54.6 μg/L at wk 4 and DTBIC was +0.3 μg/dL at wk 4. An initial decline in mean ferritin and TSAT was noted primarily in the higher BL quartiles, with little change in the 2 lower BL quartiles. Serum iron increased by 13.6 μg/mL at wk 20 from baseline. All initial changes in iron parameters plateaued by wks 16-20, and remained unchanged thereafter. Reticulocyte Hb content at wk 20 were at baseline level, and it was slightly increased by 1-4 fL at wk 4 before plateauing and stabilizing, while mean MCHC was unchanged.

Conclusions: Roxadustat lowered serum hepcidin, accompanied with initial decline in ferritin and TSAT in patients with high BL levels but little change in ferritin and TSAT in patients with low-normal BL levels despite active erythropoiesis. Maintenance of reticulocyte Hb content level during treatment reassures sufficient iron availability during erythropoiesis with roxadustat. These findings in iron parameters suggest that iron is efficiently absorbed and mobilized for erythropoiesis during anemia correction and Hb maintenance with roxadustat in NDD-CKD patients.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

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Underline represents presenting author.
similar across all hsCRP quintiles in roxadustat-treated patients (Figure). Mean weekly roxadustat doses at Week 24 for baseline hsCRP quintiles 1 through to 5 were comparable at 3.2, 2.9, 2.5, 3.0, and 3.0 mg/kg, respectively.

Conclusions: Roxadustat increased Hb in anemic NDD-CKD patients independent of inflammation.

Funding: Commercial Support - AstraZeneca

PO0265
Roxadustat Increases Hemoglobin in Anemic Dialysis-Dependent (DD) CKD Patients Independent of Inflammation
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Background: Inflammation is a common cause of decreased responsiveness to erythropoiesis-stimulating agents. Roxadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, treats anemia by inducing endogenous erythropoietin production and increasing iron utilization via reducing hepcidin. Roxadustat efficacy has been shown in those with inflammation, as defined by baseline (BL) elevation of high sensitivity C-reactive protein (hsCRP). This pooled analysis explored the efficacy of roxadustat in correcting Hb in DD-CKD patients across the spectrum of baseline hsCRP values.

Methods: Data from three randomized Phase 3 pivotal trials in anemic patients with DD-CKD were pooled, and the efficacy of roxadustat in increasing hemoglobin (Hb) from BL was assessed. hsCRP concentration was used as a marker of inflammation; patients with hsCRP >5 mg/L were considered to have inflammation at BL. Mean Hb change from BL (CBF) to Weeks 28–52 was summarized by BL hsCRP quintiles 1 through to 5.

Results: Over all, 1538 roxadustat-treated DD-CKD patients were assessed and had a mean BL hsCRP of 10.5 mg/L. Mean BL Hb measures were similar across the hsCRP quintiles (range 9.5–9.7 g/dL). In patients with BL inflammation (n=723), mean Hb CFB to Weeks 28–52 was 1.29 g/dL with roxadustat. Mean Hb CBF to Weeks 28–52 was similar across all hsCRP quintiles in roxadustat-treated patients (Figure). Mean weekly roxadustat doses at Week 24 for BL hsCRP quintiles 1 through to 5 were comparable at 3.9, 3.4, 3.5, 3.3, and 3.6 mg/kg, respectively.

Conclusions: Roxadustat increased Hb in anemic DD-CKD patients independent of inflammation.

Funding: Commercial Support - AstraZeneca

PO0266
Effects of Roxadustat Treatment on Serum Parathyroid Hormone (PTH) in Hemodialysis Patients with Erythropoiesis-Stimulating Agent (ESA) Resistant Anemia
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Background: Roxadustat, an oral HIF-prolyl hydroxylase inhibitor, is shown to stimulate erythropoiesis thereby improving iron metabolism. Of note, recent research suggests that iron utilization plays an important role in bone turnover in hemodialysis patients.

Methods: A total of 64 hemodialysis patients with ESA-resistant anemia despite high-dose epoetin α (3000 units 3 times weekly) therapy participated in the study after giving informed consent. Patients were switched from intravenous epoetin α to oral roxadustat therapy (100 mg 3 times weekly), with no dose change in any of the iron supplements, calcimimetics or vitamin D formulations being used, and were assessed after 8 weeks of roxadustat therapy for improvements in anemia, as well as for changes in parameters related to iron metabolism and bone turnover.

Results: The study included 39 men and 25 women (age, 70.8 ± 11.8 years; Hb concentration, 10.3 ± 1.2 g/dL). After 8 weeks, the Hb concentration tended to be increased (P = 0.06). As shown in Figure, the serum iron, ferritin concentration and TSAT significantly decreased (P < 0.05), suggesting increased iron utilization. Again, the serum calcium concentration was significantly decreased from 8.54 to 8.36 mg/dL, while the intact-PTH (i-PTH) concentration was significantly decreased from 98.6 to 75.80 pg/mL (P < 0.001).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: Switching hemodialysis patients with ESA-resistant anemia from intravenous ESA to oral roxadustat therapy may result in a decrease in their serum PTH concentrations presumably through improved iron utilization, thus potentially improving their bone mineral metabolism.

Funding: Private Foundation Support

Effects of Roxadustat Treatment on HD Patients with ESA-resistant Anemia

PO0267

Ophthalmological Effects of Roxadustat in the Treatment of Anemia in Dialysis-Dependent and Non-Dialysis-Dependent CKD Patients: Findings from Two Phase 3 Studies

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Background: Roxadustat is an orally active hypoxia-inducible factor prolyl hydroxylase inhibitor in late-stage development for the treatment of chronic kidney disease (CKD) anemia. Nonclinical data had suggested that hypoxia-inducible factor stabilization promotes angiogenesis, increasing the risk of retinal pathologies. We herein report the 24-week ophthalmological findings from two phase 3 studies of roxadustat in Japan.

Methods: Dialysis-dependent (DD) and non-dialysis-dependent (NDD) CKD patients (pts) with anemia were randomized to roxadustat (three times weekly) or darbeopoeitin alfa (DA; once weekly [DD]; once every two weeks [NDD]). Darbeopoeitin levels were titrated to maintain target hemoglobin. Ophthalmological assessments (funduscopic photograph, optical coherence tomography) were performed by centralized grading; visit-specific data were presented.

Results: A total of 302 DD pts (150, roxadustat; 152, DA) and 262 NDD pts (131, roxadustat; 131, DA) were randomized and received at least one dose of study drug. Results from the ophthalmological funduscopic photograph assessments are reported in Table 1. No meaningful changes occurred in visual acuity or retinal thickness in the treatment groups of either study.

Conclusions: In DD and NDD CKD pts with anemia, the risk of developing ophthalmic abnormalities was comparable between roxadustat and DA.

Funding: Commercial Support - Astellas Pharma, Inc.

Table: Incidence rate of transfusion (events/100 PEY) based on Hb level and treatment group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dialysis-Dependent</th>
<th>Non-Dialysis-Dependent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb &lt; 8.0 g/dL</td>
<td>14.8</td>
<td>14.6</td>
</tr>
<tr>
<td>8.0 ≤ Hb ≤ 10.0 g/dL</td>
<td>9.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Hb &gt; 10.0 g/dL</td>
<td>6.7</td>
<td>6.6</td>
</tr>
</tbody>
</table>

* Any evidence of retinal hemorrhage, from “No” at baseline to “Yes,” and/or an increase in hemoglobin (Hb) levels >10 g/dL vs. those with Hb >10 g/dL. We evaluated the efficacy of roxadustat vs. epoetin alfa on blood/RBC transfusion by Hb level in US-based patients with dialysis-dependent (DD) CKD.

Methods: Data from three pivotal phase 3, randomized, active-controlled studies of roxadustat for the treatment of anemia in DD patients were assessed. Patients were randomized to receive roxadustat or epoetin alfa with periodic dose evaluation/titration. Transfusion was allowed at any time if it was deemed a medical necessity by the Investigator. The incidence rate of transfusion was calculated based on Hb level categorized as: <8.0, 8 to <10, and ≥10 g/dL. Data were evaluated for the on-treatment period + 28 days after the last dose of study drug.

Results: In the overall pooled population of patients with DD-CKD, roxadustat vs. epoetin alfa reduced the risk for transfusion by 18% (HR, 0.82 [95% CI: 0.68, 1.00]; p=0.046). Among patients who were patient-exposed for ≥1 dose of study drug were stratified by achieved Hb level, the risk for transfusion increased as Hb levels decreased (Table). The incidence rate of transfusion increased approximately 5-fold in patients with Hb <10 g/dL vs. those with Hb ≥10 g/dL.

Conclusions: In US-based patients with DD-CKD and anemia treated with roxadustat, the risk for transfusion was approximately 5 times higher in patients with Hb <10 g/dL vs. those with Hb ≥10 g/dL, regardless of treatment arm.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

PO0269

A Phase 3, Multicenter, Randomized, Open-Label, Active Comparator Conversion Study of Roxadustat in Non-Dialysis-Dependent (NDD) Patients with Anemia in CKD

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Background: Roxadustat is an orally active hypoxia-inducible factor-prolyl hydroxylase inhibitor for the treatment of anemia in CKD. Efficacy and long-term safety of roxadustat was assessed, following conversion from darbepoeitin alfa (DA), recombinant human erythropoietin (rHuEPO), or epoetin beta pegol (EBP) to roxadustat, in NDD-CKD patients (pts) with anemia. Noninferiority of roxadustat efficacy against DA was evaluated.

Methods: This study enrolled adult Japanese NDD-CKD pts receiving DA, rHuEPO, or EBP for ≥8 weeks before prescreening. Patients who had used rHuEPO or DA were randomized to receive roxadustat or DA (comparative group [CG]). EBP-using pts were allocated to receive roxadustat (referential group [RG]). The primary endpoint was change in average hemoglobin (Hb) from baseline (BL) at Weeks 18-24. Roxadustat efficacy was confirmed if the 95% CI of average Hb at Weeks 18-24 was within 10-12 g/dL; noninferiority of roxadustat efficacy against DA was evaluated.

Results: This study enrolled 134 JAPANAKI patients (n=131) or DA (n=131); 70 pts were allocated to RG and received ≥1 dose of study drug (n=69). The mean (95% CI) of average Hb at Weeks 18-24 in roxadustat was 11.14 (11.01, 11.28) g/dL, confirming the noninferiority of roxadustat. The difference between roxadustat and DA (CGs) in the change in average Hb from BL at Weeks 18-24 was -0.75 g/dL. Treatment-emergent adverse events (TEAEs) were assessed.

Results: A total of 262 pts were randomized to CGs and received at least one dose of roxadustat (n=131) or DA (n=131); 70 pts were allocated to RG and received at least one dose. The mean (95% CI) of average Hb at Weeks 18-24 in roxadustat (CG) was 11.14 (11.01, 11.27) g/dL, confirming the noninferiority of roxadustat. The difference between roxadustat and DA (CGs) in the change in average Hb from BL at Weeks 18-24 was -0.75 g/dL. Treatment-emergent adverse events (TEAEs) were assessed.

Conclusions: This study confirmed the efficacy of roxadustat after conversion from DA, rHuEPO, or EBP, as well as its noninferiority to DA, in NDD-CKD pts with anemia. The safety profile of roxadustat was consistent with previous reports. A final analysis of this study (including 52-week data) will be presented at the congress.

Funding: Commercial Support - Astellas Pharma, Inc.

PO0270

HIF Prolyl Hydroxylase Inhibitor Improves Exercise Endurance and Hardly Affects Instantaneous Force in Mice


Background: Erythropoietin (EPO) and hypoxia-inducible factor (HIF) stabilizers (PH inhibitors) are efficient therapeutic modalities against anemia in CKD. Compared to EPO and EPO receptor system, extra-renal action of PH inhibitors has still been subtly unclear. Previous reports caution us about the actual misuse of PH inhibitors in doped athletes, but nonhematopoietic effects of PH inhibitors on skeletal muscles remain controversial. Metabolic shift from oxidative phosphorylation toward glycolysis in myotubes in vitro was previously reported. Direct pharmacological effects of PH inhibitors on skeletal muscles and exercise performance were assessed in vivo.

Methods: Roxadustat, one of PH inhibitors, was administered via oral gavage to 8-week-old C57BL6 mice. Plasma EPO levels and HIF-targeted gene expression were measured.
Temporal Trends in Anemia Management and Major Clinical Outcomes in Incident Dialysis Patients in Canada

Methods: The Canadian Organ Replacement Register was used to identify 35,945 adult patients who initiated hemodialysis or peritoneal dialysis from Jan 1 2007 to Dec 31 2015. Time at risk started on day 90 of dialysis and continued for a minimum of 12 months to capture outcomes via data linkage with hospital discharge diagnoses. Patients were categorized into 3 time periods anchored to landmark target hemoglobin trials and publications of anemia guidelines: Era 1 (Jan 2007-Dec 2009); Era 2 (Jan 2010-Dec 2012); Era 3 (Jan 2013-Dec 2015). Cox proportional hazards regression models were used to investigate the association between era and the primary composite outcome (acute myocardial infarction (AMI), stroke or mortality).

Results: The mean hemoglobin at dialysis initiation decreased from 102.9g/L in 2007 to 95.5g/L in 2015, corresponding with a doubling in the prevalence of hemoglobin <80g/L, which represents a substantial shift in practice and merits further investigation in terms of patient-centered outcomes.

Conclusions: There have been modest declines in average hemoglobin values and ESA use among incident dialysis patients in Canada. Unlike the US, there has been no temporal reduction in stroke. Patient survival has improved over time, likely for reasons other than anemia management. An increasing number of patients are starting dialysis with a hemoglobin <90g/L, which represents a substantial shift in practice and merits further investigation in terms of patient-centered outcomes.

Reported Caregiver Burden in CKD with and Without Anemia: A US-Based Survey

Methods: The survey was administered in January-February 2020 to adult participants recruited from the American Association of Kidney Patients (AAKP) and a third-party recruitment firm. Eligible participants provided care to an adult with CKD within the last 4 weeks. The 15-20 minute survey included questions related to caregiver and patient demographics, clinical characteristics, preferences on anemia treatment, caregiver quality of life (Burden Scale for Family Caregivers [BSFC-S]), and work productivity (Work Productivity Activity Impairment-Caregiver). Outcome was summarized descriptively for caregivers of patients with anemia (A+) and without anemia (A-).

Results: Among 258 caregivers who completed the survey, 42.6% cared for a patient with anemia (A+); non-dialysis dependent (NDD), 38.2%, dialysis dependent (DD), 61.8%). Male caregivers were older (A+: 64 years, A-: 54 years) and more likely to report a high burden (BSFC-S:A+: 69.1%, A-: 58.8%) and work impairment (absenteeism: A+, 19.0%; A-, 14.8%; presenteeism: A+, 37.9%; A-, 32.3%). In the A+ group, >75% of caregivers described anemia as being moderate or severe, and >90% of caregivers had received anemia treatment in the past month (oral iron, 45.5%; intravenous iron, 33.6%; erythropoiesis-stimulating agents, 22.7%; red blood cell transfusion, 20.9%). If a patient was to initiate a new anemia treatment, 46.4% of caregivers would prefer an oral agent, of which 41.2% prefer a once daily formulation.

Conclusions: There is significant caregiver experience by caregivers of patients with CKD, especially when anemia is present. Further studies are needed to better understand its full extent and explore support strategies for caregivers.

Cost and Healthcare Resource Use in Patients with Anemia in CKD

Methods: This retrospective analysis of the integrated Limited Claims and Electronic Health Record (IBM Health, Armonk, NY) spanned Jan 1, 2012 to Sept 30, 2018. Patients were aged ≥18 years with a eGFR measures <60 mL/min/1.73 m² ≥90 days apart. Anemia was defined as any hemoglobin (Hb) value <10 g/dL observed within 6 months of a confirmatory eGFR (baseline period). Total and site-specific costs and selected healthcare resource utilization were analyzed and stratified by presence of baseline anemia, Hb range, CKD stage, sex, and insurance type.

Results: 21.7% of patients (mean age, 72% in the 12 months post-index period.

Conclusions: This descriptive examination of treatment by CKD stage for NDD patients with anemia found that anemia was oftentimes left untreated, especially in the stage 3-4 CKD patients. After NDD CKD patients were diagnosed with anemia, it was almost 1.5 months before treatment was initiated. In NDD CKD patients with anemia, as stage increased, HCRU increased, highlighting the importance of care coordination as CKD progresses.
Anemia and Iron Management
Poster

PO0275
Modelling the Clinical and Economic Burden of Anemia in Patients with CKD
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Background: Chronic Kidney Disease (CKD) imposes a significant societal burden. Anemia is a common complication of CKD and is independently associated with poorer patient outcomes, including CKD progression, cardiovascular (CV) events and death. The objective of this study was to develop a natural history model to characterize the consequences of anemia in patients with CKD.

Methods: A lifetime Markov model was developed to estimate the economic impact of anemia. Two cohorts aged 58 years with CKD stage 3b were modelled with and without anemia (Hb 9-10 g/dL and Hb > 12 g/dL) to estimate differences in life expectancy (LE) and quality-adjusted life expectancy (QALYs), and event incidence. Hb level was linked to CKD progression, CV hospitalization and mortality using published data. Published direct costs and utility estimates associated with CKD and event incidence were incorporated, and costs were inflated to 2019 US dollars. Costs associated with anemia treatment such as erythropoiesis-stimulating agents or supplemental iron were not considered. Future costs and benefits were discounted at 3.0% per annum.

Results: Predicted LE was 10.21 years in patients with anemia compared to 12.16 years in patients without anemia, or a reduction of 2.15 years. Decreased patient LE and reduced quality of life with anemia resulted in 2.18 fewer QALYs. Time to end stage renal disease was 10.4 years with anemia and 12.5 years without anemia. Patients with anemia experienced 25 additional CV-related hospitalizations per 1,000 patients. Total lifetime costs were higher in the non-anemic cohort due to improved LE ($342,867 vs. $316,510), however annual costs were lower in anemic patients with an undisclosed loss of $2,628 per year due to reduced CV event incidence and CKD management costs.

Conclusions: This analysis supports that those without anemia have increased LE and QALYs, and account for less costs to the healthcare system. Therefore, anemia management, aligned with clinical guidelines, has the potential for better outcomes for both the patient and the healthcare system.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc. & Akebia Therapeutics, Inc.

PO0276
Prevalence of Severe Anemia and Transfusion Risk in Medicare and Non-Medicare Populations with CKD Stages 3 and 4
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Background: While 30 million people in the United States have chronic kidney disease (CKD), real-world clinical burden of anemia in non-dialysis dependent (NDD) CKD patients is poorly documented, which we seek to address.

Methods: A retrospective cohort analysis was conducted using the 100% sample of Medicare Fee-For-Service (FFS) beneficiaries (parts A/B/D) and a convenience sample of Commercial (Com), Medicare Advantage (MA), and Managed Medicaid (MM) lives of Commercial (Com), Medicare Advantage (MA), and Managed Medicaid (MM) lives (136,163 from MORE 1999-2016) was conducted. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula. Participants were classified as no CKD, CKD stage 1-2, and CKD stage 3-5 using KDIGO criteria. Anemia was defined as WHO criteria. ADL impairments were defined as “some difficulty” or “a lot of difficulty” in activities. Results: Mean age of participants was 46.7 years; 51.0% were female. The percentage of participants with no CKD, CKD stage 1-2, and CKD stage 3-5 was 86.4%, 7.6%, and 6.0%, respectively. Anemia prevalence in each CKD category was 4.9%, 8.7%, and 18.6%, respectively. Multivariable-adjusted prevalence of impairment in ≥1 ADL, by CKD and anemia status, is presented along with covariates in the Table. Compared to participants with no anemia, the adjusted prevalence ratio for impairment in ≥1 ADL was 1.06 (95% CI: 0.98-1.14; p = 0.13) in no CKD, 1.14 (0.99-1.28; p = 0.06) in CKD stage 1-2, and 1.20 (1.05-1.35; p = 0.01) in CKD stage 3-5. The clinical implications of this association should be investigated further.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc. & Akebia Therapeutics, Inc.

PO0277
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Background: Anemia is a major contributor to clinical burden and may negatively impact patient outcomes in chronic kidney disease (CKD). We assessed the impact of anemia on activities of daily living (ADLs) among participants with CKD in the US population.

Methods: A cross-sectional study (n=13,300; aged ≥20 years) using NHANES data (1999-2016) was conducted. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula. Participants were classified as no CKD, CKD stage 1-2, and CKD stage 3-5 using KDIGO criteria. Anemia was defined as WHO criteria. ADL impairments were defined as “some difficulty” or “a lot of difficulty” in activities. Results: Mean age of participants was 46.7 years; 51.0% were female. The percentage of participants with no CKD, CKD stage 1-2, and CKD stage 3-5 was 86.4%, 7.6%, and 6.0%, respectively. Anemia prevalence in each CKD category was 4.9%, 8.7%, and 18.6%, respectively. Multivariable-adjusted prevalence of impairment in ≥1 ADL, by CKD and anemia status, is presented along with covariates in the Table. Compared to participants with no anemia, the adjusted prevalence ratio for impairment in ≥1 ADL was 1.06 (95% CI: 0.98-1.14; p = 0.13) in no CKD, 1.14 (0.99-1.28; p = 0.06) in CKD stage 1-2, and 1.20 (1.05-1.35; p = 0.01) in CKD stage 3-5. The clinical implications of this association should be investigated further.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc. & Akebia Therapeutics, Inc.

Adjusted prevalence (95%CI) of impairment in ≥1 ADL by CKD and anemia category

Table reports percentages. Marginally-adjusted prevalence derived using logistic regression models (age, sex, race, education, marital status, income, health insurance, employment, smoking, alcohol use, comorbidities, heart failure, coronary heart disease, angina pectoris, heart attack, stroke, arthritis, chronic obstructive pulmonary disease, body mass index, hypertension, diabetes, and hyperlipidemia).

P-values compare anemia vs. no anemia.

PO0278
Clinical Outcomes in Patients with Anemia in CKD Using Linked US Claims and Electronic Health Records
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Background: Anemia is common in pts with CKD, yet contemporary outcome data to understand the long-term clinical burden are scarce. This analysis describes selected cardiovascular and renal outcomes in non-dialysis CKD pts with and without anemia at baseline (BL) in US real-world practice.

Methods: This retrospective observational study evaluated the integrated Limited Claims and Electronic Health Record data (IBM Health, Armonk, NY). Pts were aged ≥18 y with ≥2 eGFR measures <60 mL/min/1.73 m2 ≥90 days apart. A total of 13,692 pts with available BL ≥1 eGFR measures were included. BL pt characteristics and clinical outcomes during follow-up were analyzed for the period from Jan 1, 2012 to Sep 30, 2017. Descriptive data were summarized; no inferential statistics were performed.

Results: A total of 1,305,354 patients were identified from Medicare FFS and 154,163 from MORE. Prevalence of severe anemia in the Medicare FFS cohort was 3.1% and 3.3% in the MORE cohort (Table 1). Severe anemia was highest among stage 4 CKD patients at 11.3% in the FFS cohort and 15.4% in MORE cohort, with prevalence among Medicare FFS beneficiaries at 17.1%. High value, cancer, diabetes, liver disease, and hospitalizations were risk factors for RBCT. Within the MORE cohort, the odds of receiving RBCT increased by 47% for each 1 g/dL decrease in hemoglobin.

Conclusions: The proportion of severe anemia increases with worsening CKD stage in US pts primarily in Medicare FFS. Many clinical factors influence the odds of severely anemic NDD CKD patients receiving RBCT.

Funding: Commercial Support - AstraZeneca

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: Of the total study cohort (N=22,720), 23% (n=5,283) had BL Hb <10 g/dL. The following results are for pts with and without anemia at BL, respectively. Females accounted for 60% and 57% and mean ages (± SD) were 70 (±14) and 71 (±12) y. Proportions by BL CKD stage were: 3a, 50% and 68%; 3b, 27% and 24%; 4, 15% and 7%; 5, 9% and 1%. Median follow-up times were 2.9 and 3.8 y. Acute coronary syndrome (ACS) events during follow-up occurred in 2.2% of pts with BL anemia and 2.3% of pts without BL anemia, heart failure hospitalizations (HFH) occurred in 5.9% and 3.7%, and stroke hospitalizations and emergency visits (S) occurred in 2.8% and 3.0% of pts. Incidence rates/100 pt-yr were 0.8 and 0.7 for ACS, 1.6 and 0.8 for HFH, respectively, and 0.7 in both groups for S. ESRD occurred in 4% and 1%, 40% eGFR decrease in 44% and 25%, and CKD stage progression in 67% and 59% of pts. Median change in eGFR slope was −0.6 and −0.3 mL/min/1.73 m².

Conclusions: This analysis highlights worsened outcomes associated with anemia in CKD, particularly ifH and eGFR decline, in pts of a large US cohort.

Funding: Commercial Support - AstraZeneca

PO0279
Prevalence of Anemia and Associated Erythropoiesis-Stimulating Agent Use in 5.9 Million Non-Dialysis CKD Patients
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Background: Chronic kidney disease (CKD) leads to anemia through erythropoietin deficiency and resistance, and a heightened inflammatory state. Characterizing the burden and factors associated with severe anemia (hemoglobin <9 g/dL) is of particular interest since treatment with erythropoiesis-stimulating agents (ESAs) or other therapies is often considered at this level.

Methods: We analyzed patients in the OptumLabs® Data Warehouse, which contains de-identified claims and electronic health record data, with a complete blood count and serum creatinine measured within 30 days of each other in 2016. Patients requiring dialysis were excluded. We examined the association between low hemoglobin (Hb) categories (<9 g/dL, 9-10 g/dL, 10-11 g/dL) and age, sex, diabetes, history of cardiovascular disease (CVD), and categories of eGFR using polychotomous logistic regression to estimate adjusted relative risk ratios (RRR). Results: Among 5,875,383 patients in 52 centers, mean age was 56 years (SD 17), and 42% were male. The prevalence of Hb <10 g/dL in CKD stages G1-G2, G3a, G3b, G4 and G5 was 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were strongly associated with increased risk of anemia, even after adjustment for female sex (RRR 2.6-3.9), diabetes (RRR 1.4-1.8), history of CVD (RRR 1.7-1.9), and age (RRR 2.2-2.4 for age 75+). The frequency of ESA use in patients with hemoglobin <10 g/dL was 0.2%-4%, 0.4%-1.0% and 1.0% in CKD stage G3a, 3b, 4, and 5.

Conclusions: Severe anemia is common and strongly associated with low GFR, female sex, older age, diabetes and history of CVD in a wide range of health care systems. ESA use in non-dialysis CKD patients was very uncommon.

Funding: Private Foundation Support

PO0280
Lower Transferrin Saturation (TSAT) Index Is Associated with Anemia-Independent Risk of Increased Mortality in Non-Dialysis (ND) CKD Patients
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Background: Iron Deficiency (ID), defined by a TSAT index <20%, is present in approximately half of ND-CKD patients, varying little by CKD stage. Distinct from approaches in conditions such as heart failure, the importance of iron reserves and the basis for iron therapy in CKD has focused primarily on supporting effective erythropoiesis. A comprehensive approach and design to estimate the impact of ID, independently from hemoglobin (Hb) levels, on mortality risk has not been explored in ND-CKD until the present.

Methods: 5144 patients from Brazil (N=294), France (N=2227), the US (N=494), and Germany (N=2129) enrolled in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps) from 2013-2019 with available TSAT were included in the analysis. We categorized patients by first available TSAT at enrollment. Hb measurements at same time as TSAT were used. Cox models were used to estimate hazard ratios (HR) of TSAT on mortality, censored at start of dialysis or kidney transplantation. Models were progressively adjusted including demographics, comorbidities, inflammation surrogates, treatment with erythropoietin stimulating-agents and Hb.

Results: Sample characteristics were: 59% male; 45% diabetes; and mean (SD) age 69 (13) years, eGFR 28 (11) mL/min, Hb 12 (2) g/dL, TSAT 24 (2) %, ferritin 196 (214) ng/dL. TSAT levels below 25% were progressively associated with higher mortality risk, while patients with TSAT greater than 45% tended to have higher risks for mortality (Figure).

Conclusions: ID, as measured by the TSAT index, is associated with higher risk of all-cause mortality in ND-CKD patients, even after extensive adjustments for clinical, demographic and biochemical confounders, including Hb levels. Interventional studies evaluating the impact of iron supplementation and alternative targets on clinical outcomes in ND-CKD patients are needed to better inform ID management strategies.

Funding: Commercial Support - Vifor Pharma

PO0281
Lower Transferrin Saturation (TSAT) Index Is Associated with Worse Health-Related Quality of Life (HRQOL) in Non-Dialysis CKD (ND-CKD) Patients Independently from Hemoglobin (Hb) Levels
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Background: Iron Deficiency (ID) is a common condition in NDD-CKD patients that is associated with poorer outcomes. However, the effect of ID on HRQOL in this population is unknown. We analyzed real world data from a multinational cohort of ND-CKD stage 3 to 5 patients to test the association between TSAT and ferritin with HRQOL.

Methods: Patients from Brazil (N=205), France (N=2,015), the US (N=494), and Germany (N=2129) enrolled in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps) from 2013-2019 with available TSAT were included. We grouped patients according to TSAT and ferritin levels closest to the HRQOL measurement. Our primary analyses evaluated the associations of TSAT and ferritin with mean differences in physical component summary (PCS) and mental component summary (MCS). Secondary analyses evaluated joint TSAT and ferritin categories, as well as additional pre-specified HRQOL measures. Linear mixed models were adjusted for potential confounders including Hb level.
Results: 2313 patients were included. In the primary analyses, TSAT ≤15% and both ferritin >300 ng/mL and <300 ng/mL were associated with worse PCS scores, while M-CSF was not directionally associated with iron parameters (Figure). Patients with the composite TSAT ≤15%/ferritin ≥300 ng/mL had lower functionality scores and worse PCS, compared to those with TSAT between 20-30% and ferritin 50-299 ng/mL. Adjustment for Hb only slightly attenuated the effects, and the results were similar for subgroups of patients with Hb <11.5 vs ≥11.5 g/dL.

Conclusions: Low TSAT levels, and both low and high ferritin levels, are associated with poorer physical HRQOL in ND-CKD patients, even after adjustment or stratification by Hb level. Intervention studies of iron therapy on HRQOL among ND-CKD individuals are needed to confirm these findings.

Funding: Commercial Support - Vifor Pharma

PO0283
A Novel, Fast-Acting Iron Sucrose Formulation for CKD Patients with Iron Deficiency Anemia
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Background: Intravenous (IV) iron is commonly used to treat iron deficiency anemia in patients with chronic kidney disease (CKD). However, the report of the physicochemical and safety profile of RBT-3, a novel iron sucrose formulation, which was assessed in a Phase 1b study conducted in healthy volunteers and subjects with chronic kidney disease (CKD) Stage 3 or 4.

Methods: Analytical testing was conducted to examine the physicochemical profile of RBT-3. Safety of RBT-3 was assessed in a Phase 1b study in healthy volunteers and subjects with CKD. RBT-3 was administered IV as a single dose of 120, 240, or 360 mg. Plasma and urine ferritin were measured at baseline, then 2 h (plasma) or 24 h (urine) through 168 h post-treatment to assess clinical response.

Results: RBT-3 particle size is similar to commercially available iron sucrose. However, RBT-3 has a lower molecular weight and higher water content than similar IV iron formulations, suggesting faster uptake and greater solubility, respectively. RBT-3 also has a negative Zeta potential, demonstrating low cytotoxic potential. The quantity of labile iron in RBT-3 is 1.48%, suggesting very low availability of free inorganic iron hydroxide, with a low cytotoxic potential. Furthermore, Fe2+, which is associated with oxidative stress, is present in much lower quantities in RBT-3 (3.4%) compared to commercially available iron sucrose (15.8%). In this Phase 1b study of RBT-3, 18 subjects were enrolled; 6 subjects (3 healthy volunteers and 3 subjects with CKD) randomized to 3 cohorts received a single dose of RBT-3 at 120, 240, or 360 mg. Mean age was 60.3 years; 66.7% of the subjects were female. Dose-dependent increases in plasma ferritin were observed in all subjects within 2 h of treatment and reached statistical significance by 8-12 h. Urine levels were increased at 24 h. Both plasma and urine ferritin levels remained elevated through 168 h (7 days). No treatment-related adverse events (AEs) were observed, and no serious AEs (SAEs) were reported.

Conclusions: RBT-3 represents a novel iron sucrose formulation with desirable physicochemical characteristics that makes it a fast-acting mediator of iron hemodynamics. This is the first report of ferritin level increases within only 2 h by an iron formulation. RBT-3 is safe and well tolerated in healthy volunteers and subjects with CKD at a single dose up to 360 mg.

Funding: Commercial Support - Renibus Therapeutics

PO0284
Response to Oral Iron Therapy in Children with Anemia of CKD
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Background: Anemia is a common complication of chronic kidney disease (CKD). Current guidelines recommend oral iron therapy as the initial treatment of anemia in CKD. However, the efficacy of iron therapy in children with pre-dialysis CKD has not been evaluated. Factors determining the response to oral iron in pediatric CKD remain poorly understood.

Methods: An ongoing retrospective observational study. Data were abstracted from health records of children with pre-dialysis CKD at the time of iron therapy initiation and at the next clinic visit and compared using paired T-test. Children receiving receiving hypoxia-stimulating agents were excluded. Response to iron therapy was defined as improvement in both hemoglobin and hematocrit after iron therapy. Changes of serum ferritin and TSAT levels remained elevated through 168 h (7 days). No treatment-related adverse events (AEs) were observed, and no serious AEs (SAEs) were reported.

Conclusions: RBT-3 represents a novel iron sucrose formulation with desirable physicochemical characteristics that makes it a fast-acting mediator of iron hemodynamics. This is the first report of ferritin level increases within only 2 h by an iron formulation. RBT-3 is safe and well tolerated in healthy volunteers and subjects with CKD at a single dose up to 360 mg.

Funding: Commercial Support - Renibus Therapeutics

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0285
Improving Knowledge of Nephrologists Regarding an Emerging Class to Treat Anemia Associated with CKD

Background: As emerging therapies hold promise to improve treatment of anemia in patients with CKD, clinicians need to understand mechanisms of action in order to understand the potential place in therapy when available. We sought to determine if online, continuing medical education (CME) could improve the clinical knowledge of nephrologist related to emerging Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors (HIF-PHIs).

Methods: The effect of 2 online, 30-minute, CME-certified activities were analyzed. Multiple-choice knowledge and self-efficacy confidence questions were presented both before and immediately after each activity. A repeated pairs pre-/post-assessment study design was used and chi-square test (5% significance level, P < 0.05) assessed educational effect. Cramer’s V was used to calculate the effect size (0.06–0.15 is a noticeable effect, 0.16–0.26 considerable, and >0.26 extensive). The activity launched June 20, 2019 and data were collected through July 11, 2019.

Results: In total, 167 nephrologists were included in the study. Overall improvements were seen for both activities after participation: Activity 1: N=75, P=0.01, V=0.16; Activity 2: N=93, P=0.01, V=0.162. Individual question-level improvement was also demonstrated: 21% of nephrologists (N=75, P<0.05; V=0.169) improved at correctly identifying the mechanism of action of HIF-PHIs 20% of nephrologists (N=75, P<0.05; V=0.197) improved at recognizing clinical trial data for HIF-PHIs 33% of nephrologists (N=92, P<0.05; V=0.315) improved at recognizing clinical trial data for HIF-PHIs 21% of nephrologists (N=93, P<0.05; V=0.103) improved at recognizing CVOTs for HIF-PHIs 45% (N=75) and 47% (N=92) reported increased confidence in understanding HIF PHI clinical trial data Continued educational gaps: 55% (activity 2) and 59% (activity 1) of nephrologists did not recognize the mechanism of action of emerging HIF-PHIs 46% of nephrologists did not recognize clinical trial data for emerging HIF-PHIs 62% of nephrologists did not recognize CVOT data for emerging HIF-PHIs

Conclusions: This study demonstrates the success of online, video-based CME on improving knowledge of nephrologists related to emerging treatments for anemia associated with CKD. Continued knowledge gaps were identified for future educational targets.

Funding: Commercial Support - AstraZeneca ad Fibrogen

PO0287
Treatment Pathways of Non-Dialysis-Dependent CKD Patients with Anemia: A Report from the DISCOVER CKD Posters
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Background: Anemia is a frequent complication of chronic kidney disease (CKD), yet most patients experiencing this problem remain untreated until the initiation of renal replacement therapy. We describe treatment pathways of key medications prescribed to non-dialysis dependent (NDD) CKD patients with anemia in DISCOVER CKD.

Methods: Patients included in this analysis were extracted from the Limited Claims and EHR (LCED) data. The study cohort included patients aged ≥18 years with 2 estimate glomerular filtration rate (eGFR) measures ≤60 mL/min/1.73m2 >90 days apart between January 2008 and September 2018. The index date was the first Hb measure <12 g/dL (females), <13 g/dL [males] per WHO criteria), or an anemia therapy (iron, ESA or blood transfusion) prescription after the 2nd eGFR measure. Exclusion criteria were: <1-year registration/medical history prior to index, active bleeding in the 30 days preceding and inclusive of index, an Hb value (only) within 30 days from transfusion or bleeding and no Hb measure within a year after CKD diagnosis. Oral iron was incompletely captured in LCED. Sankey Plots were used to visualize chronological treatment pathways (1st to 3rd line) post-index of key medications commonly prescribed to CKD patients with anemia including: oral iron, IV Iron, ESA and blood transfusion.

Results: Preliminarily, 1446 (2.6% of anemia base cohort) patients were prescribed anemia therapies during follow-up, with IV iron (32.5%), transfusions (30.5%), ESA (21.6%), oral iron (12.2%) and ESA-IV Iron (2.7%) used as 1st-line therapies, Figure 1. Median times to 1st-line therapy initiation after index were: 108 days for oral iron, 194 days for ESA, 197 days for IV iron, and 244 days for blood transfusion.

Conclusions: In routine clinical care, anemia in NDD CKD is under treated and rescue therapies are used for anemia more often than preventive therapies.

PO0286
Online CME Successful at Improving Nephrologist Understanding of Emerging Class to Treat Anemia Associated with CKD

Background: As emerging therapies hold promise to improve treatment of anemia in patients with CKD, clinicians need to understand mechanisms of action in order to understand the potential place in therapy when available. We sought to determine if online continuing medical education (CME) could improve the clinical knowledge of nephrologist related to emerging Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors (HIF-PHIs).

Methods: The effect of an online, CME-certified, roundtable video discussion was analyzed to determine efficacy of online education. Three multiple-choice knowledge/competence questions and 1 self-efficacy confidence question were presented both before and immediately after each activity. A repeated pairs pre-/post-assessment study design was used and McNemar’s chi-squared test (5% significance level, P < 0.05) assessed educational effect. Cramer’s V was used to calculate the effect size (0.00-0.05 is a noticeable effect, 0.06-0.15 is a noticeable effect, 0.16-0.26 considerable, and >0.26 extensive). The activity launched June 27, 2019 and data were collected through August 27, 2019.

Results: In total, 62 nephrologists answered all pre-/post-assessment questions and were included in the study. Overall improvements were seen after participation in both CME activities: 24% of nephrologists (P<0.05; V=0.216) improved at correctly identifying the mechanism of action of HIF-PHIs 11% of nephrologists (P=0.72; V=0.032) demonstrated improvement at selecting the recommended use of erythropoiesis stimulating agents (ESAs) in the treatment of anemia 21% of nephrologists (P<0.05; V=0.181) improved at recognizing clinical trial data of HIF-PHIs 47% reported increased confidence in understanding HIF PHI clinical trial data Continued educational gaps: 55% of nephrologists did not recognize the mechanism of action of emerging HIF-PHIs 46% of nephrologists did not recognize clinical trial data for emerging HIF-PHIs

Conclusions: This study demonstrates the success of online, video-based roundtable discussion on improving knowledge of nephrologists related to emerging treatments for anemia associated with CKD. Continued knowledge gaps were identified for future educational targets.

Funding: Commercial Support - independent educational grant from AstraZeneca and Fibrogen

PO0288
Physician Attitudes Toward Diagnosis, Treatment Initiation, and Unmet Needs in the Management of Anemia due to CKD: Results from a Real-World Survey in Germany, Italy, and the United Kingdom
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Background: Anemia, a complication of chronic kidney disease (CKD), is often defined as serum hemoglobin (Hb) levels of <12 g/dL in women and <13 g/dL in men. Traditionally, primary care physicians (PCPs) have less involvement managing and treating patients with anemia due to CKD while nephrologists play a greater role in treatment decisions. We describe current physician perceptions towards the diagnosis and treatment of anemia due to CKD and unmet needs in anemia management, in a real-world setting

Methods: Data were drawn from the Adelphi CKD Disease Specific Programme, a point-in-time study conducted between November 2019 and April 2020 with nephrologists and PCPs from Germany, Italy, and the United Kingdom. Physicians completed an online survey providing information on their demographics, perceptions on the diagnosis and treatment of anemia, and the current unmet needs they believe exist in the management and treatment of anemia. Results were descriptively analyzed.

Results: A total of 200 physicians (n=140 nephrologists; n=60 PCPs) were included in the analysis. Among those who responded, the majority (98% nephrologists; 80% PCPs) used Hb levels to diagnose anemia in CKD patients. Over two thirds of physicians mentioned using ferritin to diagnose anemia and over half reported using transferrin saturation (TSAT) levels. Approximately 4 in 5 nephrologists and PCPs (78%
PO0291

Amelioration of CKD-Associated Anemia by Vadadustat in Mice Is Not Dependent on Erythropoferone

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Background: Vadadustat is an investigational hypoxia inducible factor prolyl hydroxylase inhibitor that increases endogenous erythropoietin (EPO) production, and has been shown to decrease increased hepcidin levels, improve iron status, and increase hemoglobin concentrations in anemic chronic kidney disease (CKD) patients. Increased EPO induces erythropoietin secretion of erythropoferone (ERFE), which acts on the liver to suppress serum hepcidin production. To determine whether vadadustat mechanisms of action are dependent on ERFE, we treated wild type (WT) and ERFE knockout (EKO) mice, with and without adenine diet-induced CKD, with vadadustat.

Methods: 6-week-old male C57BL/6 WT and EKO mice were placed on 8-week diets that did or did not contain 0.2% adenine. For the last 3 weeks of the diets, the mice were treated with vadadustat (75 mg/kg/day via oral gavage) or vehicle solution. Mice were euthanized at 14 weeks of age (n=8 mice per group).

Results: Unlike the WT mice, EKO mice had undetectable spleen Erfe mRNA, minimal marrow Erfe mRNA, and no increase in ERFE mRNA or protein in response to vadadustat. However, in both WT and EKO CKD models, vadadustat normalized hemoglobin concentrations (Fig 1a), increased expression of duodenal iron transporters, tended to lower serum hepcidin, and decreased tissue iron concentrations (consistent with increased iron mobilization), suggesting ERFE-independent pro-erythropoietic effects. Vadadustat treatment was also associated with improved kidney function (Fig 1b) and decreased expression of renal fibrosis markers. Lastly, vadadustat affected FGF23 profiles: In non-CKD mice, vadadustat increased plasma total FGF23 out of proportion to intact FGF23, consistent with the known effects of Hf on EPO on FGF23 production and metabolism. However, in the CKD mice, vadadustat markedly decreased both total and intact FGF23 (Fig 1e), effects likely contributed to by improved kidney function.

Conclusions: Vadadustat ameliorates CKD-associated anemia independently of ERFE, and also improves kidney function and lowers FGF23 in this CKD model. How vadadustat affects CKD progression in humans may warrant future studies.

Funding: Commercial Support - Aketiba Therapeutics, Inc.

PO0292

Oxidative Stress and Heme Metabolism in Red Blood Cells of Hemodialysis Patients

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Background: We have previously described that indoxyl sulfate promotes red blood cells (RBC) ROS generation in humans (OLM.2018). However, there is little information regarding pathways of antioxidant balance to protect RBC from oxidative stress that occurs during hemodialysis (HD). Intracellular free heme is degraded by Heme Oxygenase (HO-1), which is regarded as the major cytoprotective enzyme (Maines, 1988; Gozzelino et al., 2010). In the current study, we assessed HO-1 activity and ROS production in RBC from healthy subjects and hemodialysis (HD) patients before and after HD.

Conclusions: Blood was drawn from 6 healthy individuals (CON-RBC) and 6 HD patients (HD-RBC) before (pre-HD-RBC) and after high flux HD (post-HD-RBC). Isolated RBC were stained with DCFH-DA (Abcam) for ROS measurements. To quantify HO-1, RBC were incubated with anti-HO-1 antibody (Abcam) and m-IgG BP-CEL 488 (Santa Cruz Biotechnology) as a secondary antibody. Samples were analyzed by flow cytometry.

Results: Our results show a 4-fold increase in ROS levels in pre-HD-RBC compared to CON-RBC. ROS levels were even further increased by 1.65-fold after HD treatment in post-HD-RBC (Figure 1). Both pre-HD-RBC and post-HD-RBC showed a similarly significant increase of 3.36-fold compared to CON-RBC (Figure 1).

Conclusions: High levels of HO-1 may represent a defense against oxidative stress that occurs in ESKD and particularly during the HD session. Further research is needed to evaluate whether HO-1 overexpression could accelerate heme degradation and contribute to renal anemia.

Funding: Private Foundation Support, Government Support - Non-U.S.
Daprodustat Interaction with Phosphate Binders Has Minimal Impact on Hemoglobin Values in Hemodialysis Population

Background: Daprodustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor (PHI) in phase 3 development for the treatment of anemia of chronic kidney disease. Phosphate binders (PB) are widely prescribed for patients on hemodialysis (HD) to control hyperphosphatemia. PB may interfere with medication absorption; thus, coadministration with a PHI may potentially impact the latter’s efficacy on hemoglobin (Hgb). The purpose of this analysis was to determine whether administration of daprodustat in subjects receiving PB has an impact on Hgb values in the HD population.

Methods: The 24-week GSK PHI11033 study (NCT01977482) included 216 subjects on maintenance HD previously treated with recombinant human erythropoietin (Clin Kidney J 2019;12:139–148). Target Hgb range was 10.0 g/dL to 11.5 g/dL. Baseline PB users were defined as a prespecified study subgroup. The difference in mean Hgb values at Week 24 between treatment groups was summarized overall and by subgroup. Comparisons were performed for the Week 24 Hgb (post hoc), as well as the final dose of daprodustat, for those receiving/not receiving PB.

Results: The majority of HD subjects received PB at baseline; 136/177 (77%) of daprodustat and 33/39 (85%) of control subjects were taking PB, with comparable phosphate control at baseline (mean ± SD: phosphate; daprodustat 1.76 mmol/L ± 0.56; control 1.67 mmol/L ± 0.44]). All subjects receiving PB at baseline, except two, continued throughout the study. No meaningful difference in Hgb change from baseline (CFB) at Week 24 was noted between treatment groups. The final median dose for subjects on maintenance HD previously treated with recombinant human erythropoietin was 10 mg (6 mg), with no meaningful difference in the Hgb at Week 24 (mean ± SD: PB use=Yes 10.40 g/dL ± 0.95; PB use=No 10.79 g/dL ± 0.95).

Conclusions: These results suggest that PB use does not have a major impact on Hgb values during the 24-week study. Results of an ongoing, phase 3 dialysis study of daprodustat compared with conventional treatment are awaited to confirm these initial observations.

Funding: Commercial Support - GlaxoSmithKline

Prevalence and Severity of Anemia Between Non-Dialysis and Dialysis Outpatients referred to Nephrology Consultation: Epidemiologic Data from 1568 Mexican Patients at a National Reference Hospital L. M. Perez-Navarro1, Samantha Escorza Valdivia1, Alberto Sigfrido Benitez Renteria1, Rafael Valdez-Oroz1, 'Hospital General de Mexico De Eduardo Liceaga, Ciudad de Mexico, Mexico; 2AstraZeneca, Ciudad de Mexico, Mexico.

Background: Anemia is a frequent complication in chronic kidney disease (CKD), and is frequently associated with symptoms such as physical disability, decreased neurocognitive function, and poor quality of life. Our objective is to know the prevalence and severity of anemia between stages of CKD in patients who attended a nephrology clinic for the first time.

Methods: Transversal, descriptive, observational study. Records of adult patients who attended an outpatient nephrology clinic in the period from February 2019 to February 2020 were included. Anemia staging was performed according to the world health organization. Descriptive statistics were performed, with a 95% CI and a p-value ≤0.05.

Results: 1568 patient records were included. Mean age was 56.01 ± 16 years and 51% (804) were women. Distribution of patients by CKD stage: 9% stage 1, 11% stage 2, 12% stage 3a, 16% stage 3b, 23% stage 4, and 27% stage 5. 12% were undergoing renal replacement therapy. 53% of the population had anemia at the cut-off point of Hb<13 for men and <12 for women; stratification of anemia severity between stages of CKD is presented in figure 1. The main comorbidities and risk factors in the subjects with anemia were type 2 diabetes mellitus and hypertension (55%), proteinuria (38%), hypoalbuminemia (34%), hyperkalemia (37%) overweight or obesity (58%), hyperglycemia (45%) hypertriglyceridemia (35%) and hypercholesterolemia (31%).

Conclusions: In patients who attended for the first time an outpatient nephrology clinic, a high prevalence of anemia was found in CKD patients, being more frequent and more severe from stage 3b to stage 5. Identifying these findings will allow establishing public health policies and models of care for patients with CKD.

Funding: Commercial Support - AstraZeneca


Background: Anemia is a common complication in patients with chronic kidney disease (CKD), contributing to reduced quality of life and increased risk of morbidity and mortality. Erythropoiesis-stimulating agents (ESAs) are the established standard of care for anemia management in CKD patients. This review examines hemoglobin (Hb) requirements in randomized controlled trials (RCTs) of ESAs as treatment of anemia in CKD.

Methods: Embase, Medline, and Cochrane Library were searched from 1946 to November 2019 for RCTs evaluating the safety and efficacy of ESAs as treatment for adults with anemia and CKD. Descriptive analyses were performed to assess between-trial differences with respect to baseline Hb and Hb target ranges. Studies were classified by dialysis status (non-dialysis-dependent [NDD] vs dialysis-dependent [DD]) vs renal transplant recipient (RTR), and by treatment goal (correction vs conversion).

Results: Searches retrieved 3,482 records, from which 57 trials met the inclusion criteria. Thirty-seven studies reported a Hb target, including 15 correction studies (NDD, 11; DD, 3; RTR, 1), 19 conversion studies (NDD, 2; DD, 16; RTR, 1) and 3 that were mixed/unclear (DD, 2; NDD/DD, 1). The unweighted means (range) of the mean baseline Hb in correction and conversion studies were 10.1 g/dL (7.0-11.7) and 11.2 g/dL (9.1-13.1), respectively. There were 20 different Hb target ranges used to assess efficacy; 10-12 g/dL was utilized most often (n=8). Three of 37 RCTs used a singular Hb target threshold, whilst the remaining studies used a Hb target range, which varied from narrow (0.5 g/dL) to wide (5.0 g/dL) between the lower and upper limits. Target Hb ranges used an upper limit of >12 g/dL in 21/37 RCTs (correction, 13/15; conversion, 10/19); however, only 3/21 RCTs were published after 2012 (the last update of KDIGO Clinical Practice Guideline).

Conclusions: This systematic review shows that changing Hb requirements over time are a source of difference in RCTs of ESAs for treatment of anemia in CKD. Such differences may introduce bias when using quantitative synthesis methods (e.g. network meta-analysis) to assess the comparative efficacy and safety of ESAs relative to new treatment options.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc. & Akebia Therapeutics, Inc.

Excessive Decrease of Hematocrit After Discontinuation of Dapagliflozin Yoshihara Wada1, Yoshiyuki Hamamoto,2 Yoshishia Nakatani,3 Sachiko Honjo,1 Yamato Keida1, Yohei Seno1, Kanako Iwasaki,1 Yorihito Iwasaki,1 Jun Fujikawa,1 Hiroko Nakata,1 Akihiro Hamasaki,1,2 Izuku Kofukai Medical Research Institute Kitano Hospital, Osaka, Japan; 2Kansai Electric Power Hospital, Osaka, Japan; 3Kindai University, Osaka, Japan.

Background: Recently, sodium-glucose cotransporter 2 (SGLT-2) inhibitors were indicated to have hematopoietic effect, but it is still unclear how the effect continues after discontinuation. In this study, we investigated changes in hematocrit, urinary gravity and HbA1c after discontinuation of SGLT-2 inhibitor in patients with type 2 diabetes.
Methods: A total of 8 patients (male: n=4, age: 54.4±11.9 [mean±SD] years, BMI: 27.1±4.4 kg/m², HbA1c: 9.2±1.2 %) with type 2 diabetes who were newly administered 5mg per day of dapagliflozin from March 2015 to September 2019 and discontinued the drug due to adverse events or side effects which did not require admission were retrospectively identified. Changes in HbA1c, hematocrit and urine specific gravity levels before the administration and after the discontinuation of the drugs were evaluated.

Results: The drug was discontinued 8.4±6.6 months after administration due to non-benefit on glycemic control (n=4), polyuria (n=2), weight loss (n=1) and genital infections (n=1). HbA1c was not changed (-0.3±1.1 %; p=0.45) whereas urine specific gravity (0.014±0.009 g/mL; p=0.001) and hematocrit (1.63±1.99 %; p=0.04) were significantly increased at the time of discontinuation. Urine specific gravity (0.005±0.009 g/mL; p=0.12) and hematocrit (0.15±0.14 %; p=0.84) levels were returned to the levels of before drug administration 60 days after the discontinuation. After the 120 days of discontinuation, hematocrit was still decreased during the level of baseline (-1.29±1.70 %; p=0.05) whereas urine specific gravity was not.

Conclusions: Our data demonstrate that the increased urine specific gravity and hematocrit return to original levels within 60 days after the discontinuation of dapagliflozin, and that hematocrit may continue to decrease below the level original even after.

PO0297

Human Mesenchymal Stem Cells Cultured in a Hollow Fiber Bioreactor Maintain Constant Levels of Exosomes in the Perfusion Medium: Relevance to the Simultaneous Production of Two Biotherapeutic Agents

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Background: We have shown that the administration of allogeneic Mesenchymal Stem Cells (MSC) to patients at high risk for Acute Kidney Injury (AKI) following on-pump cardiac surgery prevents AKI and progression to Chronic Kidney Disease (CKD). Treatment of rats with severe, progressive IRI AKI with MSC-derived exosomes affords significant survival benefits and rescues their renal function (see abstract this meeting). The current study examined the possibility to simultaneously collect MSC-derived exosomes while culturing human MSCs, both used for various therapies in renal and other diseases. This approach, if successful, would be cost saving, efficient and facilitate up-scaling of the production of both MSCs and their exosomes.

Methods: Human MSCs (20x10⁶) were loaded into a hollow fiber Cell Expansion System (Quantum®, TERUMOHeart, pre-conditioned for cell adhesion with Fibronectin) and expanded using cMEM with 5% human Platelet Lysate (hPL). The number of exosomes in aliquots of the perfusion medium were monitored (NanoSight instrument) throughout the course of cell expansion.

Results: MSCs reached ~90% confluence within 12 days, yielding 500x10⁶ MSCs. The number of exosomes/nanoparticles derived from the 5% hPL per se was 4x1x10⁶/ml. Post seeding of MSCs in the bioreactor, exosome numbers in the perfusate decreased and stabilized at 1.1x10⁶/ml. The size of collected exosomes was between 60 and 100 nm.

Conclusions: The data from this pilot study demonstrate that hPL-derived exosomes or nanoparticles are taken up by the expanding MSCs, which lowers their total number in the perfusion medium. However, exosome numbers stabilized during the subsequent cell expansion, indicating that growing MSCs release high numbers of exosomes. This conclusion will be confirmed by quantifying hPL- and MSC-derived exosomes, using specific markers for each type of nanoparticle. Together, these observations show promise for the efficient generation of MSCs and their exosomes to be used for various clinical applications.

Funding: Commercial Support - SymbioCellTech, LLC

PO0298

Clinical Study Results Confirming a Novel Fluorescent Compound Is a Glomerular Filtration Rate (GFR) Tracer Agent in Humans


Background: A fluorescent GFR tracer agent for use in the clinic would enable a noninvasive transdermal continuous GFR detection method. This would make possible the initial compartment being the vascular to tissue equilibrium, and the terminal compartment (i.e., plasma GFR measurement). The terminal compartment yielded a single GFR value and was unperturbed over the approximate 10 hour time span for which the subjects were eating and taking their usual medications. The comparison of GFR from the MB-102 data to that of GFR from the iohexol data is shown in Figure 1.

Conclusions: The correlation of GFR from plasma MB-102 to that of plasma iohexol is excellent (r-squared = 0.99). Thus MB-102 is a fluorescent GFR tracer agent in humans. This result is the first step in the development of a noninvasive transdermal GFR measurement at the point-of-care.

Funding: Commercial Support - MediBeacon Inc.

PO0299

Dialysate Exposure Does Not Compromise the Function of Bioengineered Proximal Tubules for Bioartificial Kidney

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Background: Protein-bound uremic toxins (PBUTs) accumulate in plasma of end-stage kidney disease patients and are associated with a wide range of comorbidities. Their removal by conventional hemodialysis is severely limited, warranting the development of novel renal replacement therapies such as the bioartificial kidney (BAK). Recently, we developed bioengineered kidney tubules as functional BAK units capable of active PBUTs secretion via organic anion transporter-1 (OAT1). To accelerate their application, a comprehensive assessment under clinical-like conditions is essential. Here, we assessed the extent to which exposure to dialysate and uremic plasma would affect the viability and function of the kidney tubules.

Methods: Human conditionally immortalized proximal tubule epithelial cells equipped with OAT1 (cPTEC-OAT1) exposed to plasma (30min) and assessed for PBUTs clearance (indoxyl sulfate (IS), kynurenic acid (KA), L-kynurenine (L-Kyn), hippuric acid (HA) and indole-3-acetic acid (IAA)), determined by LC-MS/MS (n=7). Membrane integrity was evaluated by paracellular FITC-inulin leakage.

Results: Prolonged exposure (240min) of flat monolayers of cPTEC-OAT1 to dialysate slightly reduced the metabolic activity to 80±4% (p=0.001) and OAT1 function to 81±5% (p=0.001) and an increased LDL release (from 10±2% in controls to 15±3%, p=0.05), without inducing the release of IL-6 or IL-8. After 30min, a 3.6±0.1 fold increase in ROS production was noticed. Still, exposure of cPTEC-OAT1-containing hollow fiber membranes to dialysate enabled the concomitant clearance of five PBUTs (IS = 2980±1438; KA = 223±120; L-Kyn = 32±400; HA = 6547±1478 and IAA = 88±1±30 nmol/cm², n=6-7) without compromising the membrane integrity as observed by FITC-inulin leakage (20±4 % vs 25±5%).

Conclusions: The demonstrated functionality of bioengineered kidney tubules in PBUT clearance under clinical-like conditions advances the development of a BAK.

Funding: Government Support - Non-U.S.
PO0300

May the (Mechanical) Force Be with You: Modeling Shear Stress on the Glomerulus-On-a-Chip
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Background: In the glomerulus, mechanical forces generated on glomerular endothelial cells (GEC) by the passage of blood in capillaries and by the flow of ultrafiltrate between adjacent podocytes play a critical role in regulating glomerular filtration. In vivo modeling of shear stress is difficult and traditional in vitro 2D systems are unable to faithfully replicate shear and tensile stress. We have recently developed a barrier-free glomerulus-on-a-chip (GOAC) system that closely mimics architecture, physiology and function of the GFB. In this work we have further modeled shear stress on the chip and assessed how changes in mechanical forces affect the barrier formation and function.

Methods: Mathematical modeling of the shear stress on the GOAC was performed and shear stress was calculated for standard GOAC culture conditions. Using model simulations, angle of inclination and rocking frequency of the GOAC were changed to modify shear stress, and results were assessed after 5 days. Phenotypological analysis by IF were performed and function was measured by albumin-leakage assay. Podocytes and GEC were separated by FACS and transcriptomics and proteomics analysis performed.

Results: Under standard culture conditions, time-averaged shear stress generated by rocking the GOAC is equal to 0.1Pa. By changing angle of the rocking platform, shear stress could be modulated from 0 to ~4Pa exerted on the GEC with each rocking motion. Permeability was not significantly affected by different rocking angles (but was impaired under static conditions) after 5 days. Importantly, Gene and protein expression analysis on podocytes and GEC have identified important changes in cytokines regulation, ECM-cell interaction, proliferation and transcription factors, suggesting that longer-term modification of the shear stress might significantly impact phenotypical and functional cell activity.

Conclusions: The glomerulus-on-a-chip is an ideal system to model architecture and function of the glomerular filtration barrier, including mechanical forces. Changes in shear stress affect cellular gene and protein expression in the GFB and can have long-term effects on phenotype and function. The glomerulus-on-a-chip system can provide an important in vitro tool to study the role of shear stress in physiological and pathologic conditions.

Funding: NIDDK Support, Private Foundation Support

PO0301

Chronic AMPK Activation Repprograms Glucose Metabolism and Oxygen Respiration in Renal Tubule Epithelial Cells
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Background: In vitro human renal tubule epithelial cells (HREC) exhibit a glycolytic, de-differentiated phenotype that limits their use in bioartificial kidney development. We have identified AMP-activated protein kinase (AMPK) and Transforming Growth Factor-β (TGFβ) as critical modulators of HREC differentiation. Here we show that inhibition of TGFβ signaling enhances increased respiration induced by activation of AMPK.

Methods: Primary HREC were seeded on polystyrene tissue culture plates (100,000 cells cm⁻²). After one week, cells were supplemented with AMPK activator Metformin (200μM), TGFβ receptor 1 inhibitor SB431542 (10μM), or both. After five weeks, cell oxygen consumption (OCR) and extracellular acidification rates (ECAR) were assessed using a Seahorse XF96 Analyzer and respiratory inhibitors oligomycin (2μM), CCCP (2μM), Rotenone (0.5μM), Antimycin A (0.5μM) and 2-deoxyglucose (50mM). Statistical differences were estimated by paired, two-tailed Student’s t-test in MatLab.

Results: Metformin and Combination treatments increased cell glycolytic capacity as shown in Fig 1A. Metformin and Combination treatments significantly decreased ATP-coupled respiration, while increasing maximal oxidative phosphorylation capacity and non-mitochondrial respiration capacity as shown by elevated OCR following injections of Oligomycin, CCCP, and Rotenone/Antimycin A, respectively, as shown in Fig 1B.

Conclusions: Concurrent increases in both glycolytic and oxidative phosphorylation capacity suggest AMPK activation and TGFβ inhibition modulate cell mitochondrial and non-mitochondrial metabolic activity.

Funding: Private Foundation Support

PO0302

An In Vitro Model of the Glomerular Filtration Barrier Using Tissue-Derived Glomerular Basement Membrane
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Background: The glomerular filtration barrier consists of the glomerular basement membrane (GBM), podocytes and endothelial cells that regulate kidney permeability to macromolecules. Damage to podocytes increases albumin permeability, resulting in proteinuria. Interactions between podocytes and the GBM are important for regulating glomerular permeability and are not captured in standard in vitro cell culture systems. This work aims to investigate molecular permeability of the GBM and podocytes using a novel in vitro model that incorporates decellularized GBM.

Methods: GBM substrates were made by pressure compacting decellularized glomeruli from porcine kidneys against a Transwell membrane in a stirred cell. GBM alone provided a stringent barrier to diffusion of both albumin and Ficoll. Podocytes were plated on the GBM at low and high concentrations. Transepithelial electrical resistance (TEER) was measured before molecular permeability measurements. Podocytes on GBM were imaged by staining with phalloidin and DAPI. Permeability of the GBM with and without podocytes were analyzed by measuring FITC-BSA and FITC-Ficoll diffusion through the filtration barrier.

Results: GBM characterization showed that cells are efficiently removed from the glomeruli, and the GBM retains laminin and collagen IV after decellularization. GBM alone provided a stringent barrier to diffusion of both albumin and Ficoll. Podocytes attached and spread on the GBM to further restricted albumin diffusion. TEER showed an increased resistance of GBM with podocyte compared to GBM alone. Podocytes resulted in slightly lower permeability at high seeding concentration than low concentration. Conclusions: Interactions between the GBM and podocytes are important for regulating the permeability of the glomerulus. We developed a new in vitro model of the glomerular filtration barrier that incorporates tissue derived GBM to support podocyte culture. GBM alone restricted albumin and Ficoll diffusion and incorporation of podocytes further restricted albumin diffusion. Future work will focus on the co-culture of podocytes and endothelial cells on both sides of the GBM for evaluating the permeability of the filtration barrier and evaluate how podocyte and endothelial injury regulate permeability.

Funding: NIDDK Support, Private Foundation Support
PO0303

**Extraction of Escherichia coli in Urine by New Static Electricity Technique In Vitro**

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**Background:** The treatment results for sepsis are poor due to infectious diseases, and the mortality rate is over 25%. It is clinically significant that the detection identifies patient specimen primary causative organisms as promptly as possible to give appropriate antimicrobial treatment, and to save patients with serious infectious disease. However, it usually takes 2-3 days from the submission of the sample to the identification of the primary causative organism. We newly developed the device (PixeeMoTM approved by AOAC® Performance Tested Certificate No. 012002 in January 14, 2020.) with quick extraction of bacteria in drinking water by static electricity technique. In this report, we evaluated the ability of PixeeMoTM to extract E. coli from urine.

**Methods:** Samples were prepared by adding Ecoli to artificial urine. 27 mL of a dedicated buffer was added to 3 mL of the sample, and after centrifugation (8000 xg, 20 min), 27 mL of the supernatant was removed. This operation was performed 3 times. After the preparation, E. coli was extracted from each sample using PixeeMoTM less than 0.5 hour. The number of bacteria in the sample prepared on the standard agar medium was measured by colony count.

**Results:** The table shows results of the experiments. The components of artificial urine and E. coli were separable and the extraction results by PixeeMo were consistent with the culture method. It was also suggested that the detection limit concentration is 10cells / mL (Table)

**Conclusions:** The new technique could detect clinical pathological conc. of E. coli in short time less than 2.0 hour. Extremely useful possibility is suggested as the new measurement technology of sepsis to reflect a diagnosis and evaluation of treatment, curative effect, very quickly.

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PO0304

**Kidney Segmentation with Deep Learning in MRI of 40,000 UK Biobank Subjects**

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**Background:** Kidney volume and its association to several demographic and physiological parameters are subject of ongoing research. The UK Biobank (UKB) studies over half a million volunteers, examining blood samples, lifestyle, genetics, and body composition, including medical imaging for 100,000 participants, and 10,000 repeat scans. We have developed a system for automated kidney segmentation in 40,000 currently available MRI scans for image-based measurements of parenchymal kidney volume.

**Methods:** UKB neck-to-knee body MRI has been released for 40,264 participants (52% women), aged 44-82 (mean 64) years, with BMI 14-62 (mean 27). The kidneys are imaged in two 17s breath-hold stations with a Siemens 1.5T Aera device at (224 x 174 x 44) voxels of (2.23 x 2.23 x 4.5) mm. In this work, three operators marked cortex and medulla, excluding cysts, in 122 subjects (Fig a, b) for training and validation of a 2.5D U-Net with short skip connections. This neural network learned to segment axial slices.

**Results:** The network predictions matched the references in total kidney volume for a mean error below 4% (or 10 cm³, Dice score 0.956), whereas human repeat segmentation yielded 3% (or 6 cm³, Dice score 0.962). While imaging limitations such as motion may compound this error, similar performance is expected for future UKB releases. After 30 minutes of training, the network can process all scans within two days. Exclusion of anomalies, such as 40 cases of renal fusion, left 37,468 subjects with median voxel count volumes of 277 cm³ for men and 220 cm³ for women.

**Conclusion:** The proposed system may ultimately provide measurements of left and right kidney volume for all imaged UKB subjects which can be analyzed and shared for further large-scale investigation of associations and longitudinal changes in kidney volume.

**Funding:** Other NIH Support - The Swedish Heart-Lung Foundation and Swedish Research Council (2016-01040, 2019-04756) supported this work, which used the UKB, application no. 14237., Government Support - Non-U.S.
Results: KT exposed to CM showed increased OAT1 levels (protein: 2.0±0.3-fold and mRNA: 2.8±0.5-fold). Moreover, EVs mimicked CM effects (2.6±0.4-fold), while CM EV depleted didn’t induce OAT1. EVs were shown to contain OAT1 protein and mRNA as cargo. Visual observations of KT seeded on hollow fibers with CM containing EVs, presented slightly improvement in 3D tubular structure organization with the expression of tight junction protein (ZO-1) and cell polarity (apical cell formation and Na+/K+-ATPase presence at the basolateral side) when compared with the control condition.

Conclusions: KT phenotype can be directed by renal EVs obtained from ciPTEC-OAT1. In addition, renal EVs can support KT to form tight monolayers on hollow fiber membranes. Further research is aimed at a full functional characterization of these bioengineered proximal tubules for application in BAK. ACKNOWLEDGEMENTS Work supported by Regenerative Medicine Crossing Borders (www.regmedxb.com).

Funding: Government Support - Non-U.S.

PO0308

Nitric Oxide (NO) Based Urinary Catheter Balloon Inflation Solution to Prevent Urinary Tract Infection

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Background: UTI is the most common hospital acquired infection with indwelling catheters being a major risk factor and are difficult to treat due to the formation of bacterial biofilms which are resistant to systemic antibiotics. NO is an endogenously formed gas molecule known to play a key role in preventing infection by dispersing biofilm formed by a variety of bacterial strains. In this abstract, we describe the effectiveness of a novel urinary catheter balloon inflation fluid to effectively reduce catheter associated urinary tract infections (CAUTI) by providing up to 7 days of bactericidal effect via NO release.

Methods: Our innovative approach to prevent CAUTI involves employing a balloon inflation fluid by using novel NO secreting materials based on using S-nitrosothiol type NO donors like S-nitrosoglutathione (GSNO) within the balloon of urinary catheters that slowly releases NO over a period of up to one week. The advantages of the use of NO in CAUTI prevention is its short half-life with a very low steady-state level immediately adjacent to the surface of the device required to achieve the desired anti-microbial effect with no risk of systemic effects when using NO secreting materials with fluxes that are near physiological levels.

Results: We performed in vitro studies using a Foley catheter placed in a long-necked flask with a shape resembling the urinary bladder and the urethra. (Fig 1) The Foley catheter retention balloon was filled with GSNO solution and the balloon was used to seal the neck of the flask. Then the flask was filled with synthetic urine inoculated with E. coli and incubated for seven days at 37 °C with horizontal shaking at 80 rpm. The results showed a 7-log reduction in planktonic bacterial growth (Fig 2) and a 3-log reduction in biofilm (Fig 3) of the GSNO Foley balloon solution compared to the control.

Conclusions: These data suggest that NO-based urinary catheter balloon fluid results in significant anti-microbial effects in our in vitro model of CAUTI.
dyes for proteins and aldehyde-reactive dyes for carbohydrates. We term this approach FLARE.”

Results: We first showed FLARE’s utilities in freshly fixed mouse kidney tissues (~100 μm) using super-resolution fluorescence microscopy. Within glomeruli, the carbohydrate stain specifically labeled the basement membranes of the capillary loops and the mesangial matrix, while the amine stain revealed interdigitated podocyte epithelial cells that are a major component of the glomerular filtration barrier (Fig. A). In proximal convoluted tubule, the basement membrane was also labeled by the carbohydrate stain, and the amine stain revealed mitochondria and brush border microvilli (Fig. B). Then we stained optically cleared FFPE human kidney tissues (~50 μm) without performing antigen retrieval (Fig C), revealing more general features. Furthermore, FLARE does not perturb antigenicity, where immunolabeling of proteins can be easily integrated afterwards (data not shown).

Conclusions: We have shown that FLARE reveals abundant details in a wide range of kidney tissue processing methods using super-resolution and cleared-tissue microscopy, and is compatible with other staining modalities.

Funding: NIDDK Support, Other NIH Support - R01

PO0310
Ex Vivo Perfusion and Initial Function of a Recellularized Human-Scale Bioengineered Kidney
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Background: The need for more transplantable kidneys is greater than ever, with nearly 100,000 patients actively waiting for a kidney. To meet this growing demand, our team is developing a fully transplantable bioengineered kidney (BEK) by seeding cells into perfusion-decellularized porcine kidney scaffolds. Previously, orthotopic transplantation of HUVEC-only BEKs in pigs resulted in 83.3% (n=5/6 pigs) renal perfusion at 7 days post in vivo implantation. Building on these results, the focus of the current study was to recellularize the glomerulus of a clinically relevant whole kidney matrix and then assess the preliminary filtration function.

Methods: Adult porcine kidneys were decellularized via detergent perfusion through the vasculature. Primary glomerular cells were isolated from fresh porcine kidneys or rejected human kidneys. The porcine matrix was then seeded with either human umbilical vein endothelial cells (HUVECs), HUVECs and porcine glomerular cells as a model system, or HUVECs and human glomerular cells. Recellularized tissues were then cultured using a custom perfusion recellularization bioreactor until sufficient cellular coverage of the vasculature was obtained through nondestructive metabolic markers. Both HUVEC-only and co-culture BEKs were then implanted in an ex vivo blood loop for 30 minutes, where urine effluent was collected and analyzed for filtration function.

Results: Sufficient histological vascular coverage with endothelial cells and thrombore sistance with vascular patency was found for grafts with a minimum glucose consumption rate of 20 mg/hr. From the ex vivo blood loop test, the ureter effluent hematocrit concentration in the co-culture BEK was found to be undetectable. In comparison, the endothelial-only BEK and the pig’s blood hematocrit levels were both 22%. The addition of glomerular cells in the BEK restored physiological flow rates of ureter effluent.

Conclusions: These results demonstrated human cellular engraftment and growth, long-term vascular patency, sustained hemoperfusion, removal of processed filtrate, and early signs of filtration and waste clearance in BEKs, which moves the field closer to an alternative for kidney transplantation.

Funding: Commercial Support - Miromatrix Medical

PO0311
Stiffening of Decellularized Tubular Basement Membrane Regulates Renal Tubular Epithelial Cell Function
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Background: Damage to renal proximal tubule epithelial cells (RPTEC) plays an important role in chronic kidney disease. Epithelial cells are supported by a specialized extracellular matrix called the basement membrane (BM). The structure of the BM is altered in various kidney diseases such as diabetic nephropathy and may result in increased BM stiffness. We have developed a novel cell culture model that utilizes tissue derived tubular basement membrane (TBM) with tunable stiffness as a culture substrate for RPTEC. The aim of this study was to determine if TBM stiffening promotes activation of pro-fibrotic signaling pathways and/or regulates RPTEC differentiation.

Methods: TBM was isolated from decellularized porcine kidneys. TBM cell culture substrates were made by pressure compacting the TBM on Transwell inserts. Conditionally immortalized mouse RPTEC were grown on TBM substrates. To induce stiffening, TBM was treated with the chemical crosslinker genipin. Decellularized TBM was characterized by western blot and immunofluorescence staining. Viability and morphology of RPTEC were evaluated by MTT assay. Real-time PCR was performed on RPTEC to evaluate the effect of stiffness on multiple genes related to kidney fibrosis and RPTEC differentiation.

Results: Western blot analysis of decellularized TBM showed the presence of laminin and collagen IV and absence of lamin B1 showing proper decellularization of TBM. Genipin treatments (0.05% and 0.5%) resulted in average stiffness of 2 kPa and 3.2 kPa respectively, compared to 0.5 kPa for untreated TBM. Neither decellularization nor genipin modification had a significant effect on cell viability. Pro-fibrotic downstream targets of YAP activation (CTGF, AREG, and ANKRDI) were upregulated on stiff TBM substrates. Additionally, stiffness regulated expression of cell-cell junction markers E-cadherin and N-cadherin.

Conclusions: A new cell culture model was developed using tissue derived TBM as a substrate for tubular epithelial cells. Stiffness of the TBM was tuned using genipin. Increased TBM stiffness upregulated pro-fibrotic targets of YAP activation and altered RPTEC cell differentiation. These data show that stiffness significantly affects renal tubal cell function and suggest that TBM stiffening in chronic kidney disease may play a role in disease progression.

Funding: NIDDK Support, Private Foundation Support

PO0312
HIF-PHI Improves Anemia and Controls Circulating FGF-23 in a CKD Model
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Background: The phosphatase hormone FGF23 is a critical factor in chronic kidney disease-mineral and bone disorder (CKD-MBD), with elevated levels in blood associated with increased odds for patient mortality (>6-fold). Anemia is a potent driver of FGF23 expression, and patients with CKD ultimately develop anemia as the kidneys lose the ability to produce erythropoietin (EPO), in concert with FGF23-mediated alterations in mineral metabolism. Our goal was to investigate a HIF-PHI (hypoxia-inducible factor prolyl hydroxylase inhibitor) for effects on anemia-dependent FGF23 levels and key outcomes in a mouse model of CKD.

Methods: Female C57BL6 mice were fed a casein control or adenine-containing diet to induce CKD, which resulted in markedly elevated iFGF23 and BUN, hyperphosphatemia, and anemia. After 12 weeks of CKD induction, mice were treated with the HIF-PHI Bay 85-3934 (‘Bay’; Molsidurnat) at a human equivalent dose over every other day for 3 weeks.

Results: Compared to saline controls, BAY elevated serum EPO and restored CBCs to normal levels in CKD mice. iFGF23 was significantly elevated in saline-treated CKD mice (120-fold; p<0.01). Importantly, circulating iFGF23 was significantly attenuated (>60%; p=0.05) in BAY-treated mice with CKD, coinciding with downregulated renal Egr-1 expression (p<0.01). Renal 1,25dihydroxyvitamin D3 (1,25D3) was significantly reduced in BAY-treated mice with CKD (p<0.01). The basal activity of bone marker alkaline phosphatase was also reduced (p<0.01). BAY treatment significantly reduced circulating osteocalcin (p<0.01). HIF activation in osteoblasts/osteocytes is associated with increased bone mass, therefore we investigated femur trabecular parameters and cortical porosity, however saw no effect with BAY over this time course. Serum alkaline phosphatase was significantly elevated in CKD-BAY mice compared to CKD controls (p=0.01), suggesting increased osteoblast activity.

Conclusions: Collectively, these results support that resolving anemia using a HIF-PHI may improve kidney function and lower FGF23 during CKD, potentially providing modifiable outcomes beyond improving iron utilization for this patient population.

Funding: NIDDK Support, Other NIH Support - NHLBI, NIAMS

PO0313
Second Harmonic Generation and Fluorescence Imaging Reveal Collagen Fibris and Cell Nuclei in Mature Randall Plaque
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Background: The formation of calcium oxalate (CaOx) stones on Randall’s plaque (RP) is a common phenomenon (perhaps 25% of CaOx stones), yet this mechanism of stones formation is still poorly understood. The objective of the study was to devise novel techniques to study RP structure.

Methods: Micro CT was used to orient RP stones for decalcification and sectioning. Sections were examined for collagen using Second Harmonic Generation (SHG)
signals with multiphoton excitation. Other sections were stained with the DNA marker 7-aminomethylcoumarin D (7-AAD).

**Results:** SHG showed collagen fibrils in the plaque but not in the CaOx overgrowth region. Demineralized RP displayed autofluorescence in the far-blue region, as we have previously described in mineralized RP. Staining of plaque sections with the DNA marker, 7-AAD, confirmed the presence of cell nuclei within mature RP.

**Conclusions:** Our results show that collagen fibrils and cell nuclei are present in RP. The nature of cells and their role in plaque formation are yet to be determined. Our data suggest that these cells contain ordinary nuclear morphology and were well-preserved within the mature plaque. The presence of cell nuclei in the plaque raises critical questions about the role of apoptosis/necrosis and survival in this mineralized environment. Future studies exploring organization of collagen and the nature of cells in plaque will be invaluable in understanding plaque and stone pathogenesis.

**Funding:** NIDDK Support

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**PO0315**

**Treatment with β,γ-Methylenedehydrogeno 5'-Triphosphate Prevents Arterial Media Calcification in a Warfarin Rat Model**

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**Background:** Arterial media calcification (AMC) is a severe complication in patients with chronic kidney disease, diabetes and osteoporosis. In vitro studies showed that the synthetic P2X receptor agonist β,γ-meATP is a potent inhibitor of vascular smooth muscle cell calcification. We aimed to evaluate whether β,γ-meATP prevents the development of AMC in a rat model of warfarin-induced AMC.

**Methods:** To induce AMC, rats received a diet containing 0.30% warfarin + 0.15% vitK1 throughout the entire study and were subjected to daily i.p. treatments with vehicle (n=10) or 2 mg/kg/day β,γ-meATP (n=10) from start of the study until sacrifice at wk 7. Four rats on a standard chow diet were included as a control group. Serum calcium (Ca) and phosphorus (P) levels were analyzed at sacrifice. To evaluate the bone-like switch of VSMCs, aortic mRNA expression of TNAP and SOX9 were analyzed by qPCR. AMC was evaluated by analysis of total Ca content in the arteries and quantification of the area % calcification on Von Kossa stained aortic sections. To determine arterial stiffness, ultrasound-based pulse wave velocity (PWV) was evaluated in the abdominal aorta.

**Results:** Serum P levels were unchanged in all groups while serum Ca was significantly lower in rats treated with β,γ-meATP vs vehicle group. Exposure to warfarin induced distinct calcification in the aorta and peripheral arteries in vehicle treated rats which led to an increase in PWV score. Interestingly, daily treatment with β,γ-meATP significantly reduced the Ca content in the aorta (mean ± SEM; vehicle 1.49 ± 1.5 mg Ca/g wet tissue vs β,γ-meATP 0.38 ± 0.20 mg Ca/g wet tissue; p<0.05) and peripheral vessels which was further reinforced by a significant (p<0.01) reduction in aortic Von Kossa positive area % vs vehicle group. However, β,γ-meATP did not significantly affect PWV scores. Treatment with β,γ-meATP also did not alter the mRNA expression of bone-like marker genes.

**Conclusions:** β,γ-meATP significantly decreased AMC in the aorta and peripheral vessels of warfarin exposed rats, however, without affecting the bone-like switch of VSMCs suggesting that β,γ-meATP mediates its inhibitory effects on AMC probably by interfering with the formation of Ca-P crystals via its breakdown product methylene β,γ-meATP.

**Funding:** Government Support - Non-U.S.

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**PO0316**

**Efficacy of Oxidative Stress Inhibitor Alone or Combined Therapy with a Calcimimetic in a Rat Model of CKD-MBD**

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**Background:** We previously demonstrated the role of NADPH oxidase (NOX 1 & 4) and hyperparathyroidism in the pathogenesis of arterial calcification, a component of CKD-MBD. We hypothesized that the combination of reduced NOX activity and lower PTH would have additive benefit on CKD-MBD. To test this hypothesis, we evaluated the efficacy of the NOX 1/4 inhibitor GKT137831 (GKT) alone or combination with the PTH-lowering calcimimetic KP-2326 (KP) on CKD-MBD in a slowly progressing rat model of CKD-MBD, the CP-1 rat.

**Methods:** We compared five groups of animals: 1: Normal (NL); 2: CKD; 3: CKD+GKT (60mg/kg s.q. daily); 4: CKD+ KP (0.6mg/kg i.p., 3x/wk) and 5: CKD+GKT+KP. Treatment began at 18 weeks of age (~60% NL kidney function) and ended at 28 weeks (~25% NL function). Serum biochemistries, aortic calcification and bone architecture were assessed. One Way ANOVA was used for statistical analysis.

**Results:** As expected, there was a decline in kidney function in all CKD groups compared to NL. There was no difference in serum phosphorus or calcium levels between NL and any of the CKD groups. PTH and FGF23 serum levels were elevated by 5 and 2.3 fold, respectively, in CKD rats; only KP treatment reduced PTH levels (p<0.003). Interestingly, GKT alone or combined with KP increased FGF23 levels by 2-fold in

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

Underline represents presenting author.
CKD rats (p<0.002). Serum 8-OHdG (marker of DNA oxidation) was higher in all CKD animals (p<0.01) and unaffected by treatment. There was increased aorta calcification (by 45%) and heart calcification (by 32%) in all of the CKD animal groups (p<0.01) and only GKT treatment reduced aorta calcification (p<0.03). Compared to NL, trabecular bone volume (BV/TV%) and trabecular number were lower and trabecular separation was higher in all CKD rats (p<0.001). GKT also increased trabecular separation in CKD rats (p<0.04).

Conclusions: In a progressive rat model of CKD-MBD, treatment with a NOX1/4 inhibitor (GTK) early in the course of CKD reduced aorta calcification but did not decrease oxidative stress or increased FGF23 in CKD rats. KP treatment decreased serum PTH levels in CKD, but had no effect on aorta calcification or bone architecture. There were no additive beneficial or adverse effects with the combination of KP and GKT.

Funding: Veterans Affairs Support

PQ0317
Comparison of the Effects of Ferric Citrate and Intravenous Iron on Markers of Mineral and Bone Disorder and Oxidative Stress in a Rat Model of CKD

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Background: Anemia and chronic kidney disease-mineral and bone disorder (CKD-MBD) are common in CKD. Ferric citrate is an oral therapy approved as an oral iron replacement product in non-dialysis dependent CKD and as a phosphate binder for dialysis dependent CKD patients. However, studies comparing the effects of ferric citrate vs. IV iron on markers of CKD-MBD and oxidative stress in moderate CKD are limited.

Methods: We compared four groups of male rats (n=11-14 rats/group): 1) Rats with normal kidney function (NL); 2) CKD rats without iron treatment (CKD); 3) CKD rats treated with 35% ferric citrate (FCD); 4) CKD rats treated with 30mg/kg IV ferric iron sucrose (CKD + IV iron). Treatments started at 18 weeks of age (mild CKD) until euthanized at 28 weeks of age (moderate-to-advanced CKD). We determined biochemical markers of CKD-MBD, oxidative stress, bone morphology (by CT), and bone formation rate at 28 weeks. One-way ANOVA was performed with Tukey’s post hoc comparisons.

Results: Untreated and iron-treated CKD rats had higher concentrations of BUN and creatinine than NL rats. Untreated CKD rats had elevated plasma phosphorus and intact FGF23 when compared to NL. CKD+FC rats had lower plasma phosphorus and intact FGF23 while CKD+IV iron rats had lower intact FGF23 compared to CKD rats. However, the C-terminal FGF23 remained high in the untreated CKD and the CKD+IV iron rats compared to NL, but CKD+FC rats tended to be lower than the untreated CKD rats (p<0.07). PTH was elevated in the untreated and iron-treated CKD rats compared to NL. A marker of oxidative stress, 8OHdG, was increased in the untreated and iron-treated CKD rats compared to NL and was not different between iron treatments. At this stage of CKD, there was no cortical porosity in all the CKD rats compared to NL. CKD-induced alterations in trabecular and cortical bone properties and bone formation rate were not changed compared to untreated CKD rats in the iron-treated rats.

Conclusions: Ferric citrate led to more robust reductions in plasma phosphorus and FGF23 than IV iron, while neither source of iron had adverse effects on oxidative stress or bone architecture in a rat model with moderate CKD-MBD.

Funding: Other NIH Support - T32 AR065971-04, Commercial Support - Keryx Pharmaceuticals

PQ0318
Upacicalcet, a Novel Non-Peptide Calcimimetic for the Treatment of Secondary Hyperparathyroidism, Has a Low Risk of Hypocalcemia

Upacicalcet also significantly decreased the serum Ca level dose-dependently at 24h and 48h after administration. However, interestingly, it bottomed out without getting too low even with 30 mg/kg of upacicalcet, 100-fold higher than the efficacious dose (0.3 mg/kg) (Table 1).

Conclusions: These findings suggest upacicalcet is a novel non-peptide positive allosteric modulator on human CaSR with a low risk of hypocalcemia for the patients with SHPT.

Funding: Other NIH Support - NIGMS

PQ0319
Influence of Vitamin D and Uremia on Functional Expression of Drug Transporters in Human Proximal Tubule Cells

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Background: Vitamin D (ViD) deficiency is common in patients with chronic kidney disease (CKD), with prevalence rates as high as 90%. CKD and ViD have independently been shown to modulate the function and expression of various drug transporters, including drug-transport drug interactions and pharmacokinetic alterations. However, the mechanisms remain unclear how the combination of CKD and ViD alters drug transporters. The purpose of this study was to evaluate the function and expression of drug transporters in human proximal tubule cells (hPtCs) following treatment with ViD analogues under in vitro conditions employing human healthy serum (HS) and uremic serum (US) to mimic the CKD environment.

Methods: hPtCs were exposed to 10% HS or 10% US for 24 h, followed by treatment with cholecalciferol (D3) or the active form, calcitriol (1,25D3), at 100 or 440 nM concentrations or 2% ethanol vehicle control (VEH) for 5 days. RT-qPCR and immunoblotting were used to assess effects on gene and protein expression, respectively of P-gp (efflux) and OATP4C1 (uptake) transporters. Apical to basolateral (A>B) and basolateral to apical (B>A) transport was assessed in hPtCs using tranwell inserts and the reporter probe [3H]Doxorubicin (DIO).

Results: Data are shown in the Table. Compared to VEH, 1,25D3 increased P-gp gene expression under HS and US (with exception of the 240 nM concentration). 1,25D3 also increased SLC04C1 protein in HS, but no increase was demonstrated in US. B>A transport was enhanced in HS under treatment with 1,25D3.

Conclusions: These data suggest that uremia decreases OATP4C1 expression and prevents an induction of OATP4C1 expression and function by 1,25D3. Enhanced B>A transport in HS under treatment with 1,25D3, was consistent with the up-regulation of P-gp and SLC04C1. These alterations may help to inform disposition of transporter substrates under ViD treatments.

Funding: Other NIH Support - NIGMS

PQ0320
SNF472 Inhibits Heart Valve Calcification in a Novel In Vitro Method Using Porcine Whole Leaflets

SFN472 inhibits heart valve calcification in a novel in vitro method using porcine whole leaflets.


Aortic valve leaflets from commercial pig hearts were dissected free and randomly assigned to experimental groups. Valve leaflets were cultured in individual wells. Two growth media were used for cultivation: standard growth medium and an antimitroblastic growth medium. The latter was employed to inhibit contraction of the leaflet into a ball-like structure. Calcification was induced in the growth medium by supplementation with 100 μM b-glycerophosphate (control 1) but not CKD media. Leaflets were cultivated for four weeks and medium was changed every third day. To block calcification, SNF472 was used at concentrations between 1 and 100 μM. Calcium amount in leaflets after four weeks was measured by inductively coupled plasma optical emission spectroscopy.

Results: Osteoheterfermentation and calcification accumulation was in principle absent when standard medium was used. However, when the antimitroblastic medium was used, a strong calcium accumulation was induced (p=0.006 compared to controls), and this was blocked in a dose-dependent manner by the calcification inhibitor SNF472 (p<0.001 with EC50 of 3.3 μM).

Conclusions: Cultured whole leaflets of porcine aortic valves are a new in vitro model to study calcification of heart valves. This model will be useful for studying the basic mechanisms of valve calcification and to test pharmacological approaches to inhibit calcification. The latter was shown by SNF472, which strongly inhibited calcification in this model of aortic valve disease.

Funding: Commercial Support - SaniTherapics, Government Support - Non-U.S.

Anamolization of Uremic Vascular Calcification After Experimental Aortic Transplantation

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Background: CKD causes a shift in phenotype of the vascular smooth muscle cell (VSMC) to a bone-like secretory cell and promotes vascular calcification (VC). Our aim was to study whether VC is reversed by transplantation of a uremic calcified aorta into a healthy recipient.

Methods: A novel model of isogenic aorta transplantation in the rat was used (ATx). VC was induced in inbred Dark Agouti rats by 5/6 nephrectomy, high phosphate diet and alfloxurin treatment. The abdominal aorta of the uremic rat was transplanted into a normal rat (uremic ATx, n=16). Control groups: ATx between normal rats (normal ATx, n=9) and age-matched rats (control, n=6). Four weeks after ATx, the aorta was analyzed for genes related to the osteochondrogenic transition by RT-qPCR. Data are presented as mean±SD. mRNA levels are normalized to stabile housekeeping genes and expressed as the ratio to controls.

Results: The uremic donor rat had severe CKD with disturbed mineral and bone metabolism as well as severe aorta calcification with altered expression of genes related to the osteochondrogenic phenotype: ATx mitigated some of these genetic changes as indicated by a significant downregulation of the expression level of mineralization inhibitors and fibrosis matrix proteins. More specifically, mRNA levels of MGP (control 1.0±1.8 vs. uremic ATx 1.74±0.18, p=0.01), Spro (control 1.0±0.2 vs. uremic ATx 13.69±0.47 vs. uremic ATx 2.62±0.84), ANKH (control 1.0±0.15 vs. uremic 10.43±6.90 vs. uremic ATx 4.49±1.72), Postn (control 1.0±0.34 vs. uremic 3.39±0.77 vs. uremic ATx 1.74±0.85), Fntl (control 1.0±0.25 vs. uremic 7.26±2.49 vs. 3.02±1.45), all p<0.01. No difference in expression of these genes between control and normal ATx was noticed. The VSMC markers ACTA2 & Eln were downregulated in uremic VC with no recovery through ATx. The Wnt inhibitor sclerostin showed a trend towards downregulation by ATx. Activin A & TGF-beta were highly upregulated in uremic VC with no reversibility. Plasma biochemistry did not differ between control, normal ATx and uremic ATx.

Conclusions: Our results for the first time show downregulation of genes related to mineralization and fibrosis, indicating amelioration of uremic vasculopathy after experimental aorta transplantation.

Funding: Government Support - Non-U.S.
effects of Pi versus FGFR23 to determine their contributions towards these CKD-associated pathological phenotypes in vitro models.

Methods: We subject mice with global FGFR4 deletion & wild-type littermates to an increasing dietary Pi load (0.7%, 2.0%, or 3.0%) or an adenine-rich diet (CKD model) to examine systemic inflammation, iron metabolism and skeletal muscle function. Furthermore, mice on a high Pi diet were treated with FGFR23 or Pi to examine activation of downstream signaling events & expression levels of specific target genes. We determine if co-treatment with inhibitors of Pi uptake & of downstream mediators block these observed effects.

Results: A 3% Pi diet as well as an adenine-rich diet promote inflammation, iron dysregulation & skeletal muscle wasting in mice. Outcomes are not alleviated in FGFR4 knockout mice. Furthermore, liver Pi accumulation occurs before hyperphosphatemia, as shown by 2% Pi diet. In cultured hepatocytes, inflammatory cytokine and hepcidin expression are induced by Pi in a dose-dependent manner. Moreover, Pi activates NFκB signaling. Blocking Pi uptake & NFκB attenuates the observed Pi-induced effects.

Conclusions: We postulate in CKD, gradual elevations in serum Pi as well as tissue Pi accumulation, which may occur before detectable changes in systemic Pi, promotes inflammation & anemia by targeting the liver to induce gene programs that regulate inflammation, erythropoiesis & iron metabolism. Our study indicates these Pi effects may be FGFR4-independent. Pharmacological approaches targeting Pi uptake and excretion or Pi’s direct hepatic actions may alleviate various CKD-associated pathologies.

Funding: NIDDK Support

P00325

Extrarenal Expression of the Kidney-Related Longevity Gene, α-Klotho, in the Long-Lived Naked Mole Rat (Heterocephalus glaber): A Comparative Biology Study

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Background: The naked mole-rat (NMR) is expanding in popularity as a model for studying biomarkers of aging and mineral metabolism. NMR has a lifespan of 30 years, almost ten times longer than the mouse and rat (app. 3-4 years). α-klotho (Kl) is an aging-suppressor gene. Knockout of Kl is associated with decreased lifespan, and overexpression of this gene is linked to extended lifespan in mice. Kl is predominantly expressed in the kidney. We speculated that the expression level of this gene might play a role in the longevity of NMR. The present comparative study aimed to establish the expression level of Kl in long-living NMR vs. normal rats, Rattus norvegicus (RN).

The naked mole-rats (NMR) of Ten NMR's kindly provided by Randers Regnskov (Danish Zoo) (N=5) and Gorburnova and Selavanov laboratory (Aging Research Center, University of Rochester, USA) (N=5) were used and compared to corresponding tissues from RN (N=9).

Methods used were: qPCR, standard PCR, and Sanger sequencing.

Results: In the kidney, similar levels of Kl mRNA were observed between those two species by qPCR (RN: 0.9 ± 0.1 vs. NMR: 1.2 ± 0.2; n.s.). The expression of Kl was further examined in the lung, skin, and liver of NMR, compared to RN. There was no expression of Kl in the lung and skin of NMR. In the liver of NMR, a high expression of Kl mRNA was observed (Cy: 25) by qPCR in contrast to RN, where no expression was detected. Sanger sequencing was performed to confirm that the gene expressed in the liver was Kl. In order to ensure that this was not a truncated form of Kl, which could be a target for mRNA decay, the predicted region for alternative splicing sites for Kl was sequenced in both RN and NMR. These results indicated that this was not the case, neither in the kidney nor in the liver.

Conclusions: This comparative study showed for the first time that α-klotho is significantly expressed in the liver of NMR, while the gene is absent in the liver of RN. Thus, the expression levels of Kl in the kidney are similar in kidneys of NMR and RN. Further downstream experiments are required to clarify whether the hepatic expression of α-klotho might contribute to the longevity of the NMR.

Funding: Government Support - Non-U.S.

P00326

Increased Urinary Leukocyte Esterase Distinguishes Brushite Stone Formers from Patients with Other Stone Types


Background: Compared with calcium oxalate (CaOx) stone formers (SF), patients with brushite (Br) stones have elevated neutrophil infiltration in their renal papillae which may be associated with the observed marked increase in papillary scarring and inflammation. We investigated whether a signal of neutrophil elevation in the kidney could be detected in the urine when not associated with infection.

Methods: We performed urine dipstick analyses for leukocyte esterase (LEU), an enzyme produced by neutrophils and many various forms of infection including nitric (NIT), blood (BLO) and protein (PRO). 24-hr urine specimens were tested using the Siemens Multistix 10SG dipstick read on a Clinitek Status analyzer. We measured urinary ammonia on a Beckman DxC600. We retrospectively analyzed 812 urines from 215 patients; stone type of patients was determined by stone analysis containing >50% apatite (Ap), Br CaOx or uric acid (UA), respectively. BLO, PRO and LEU measurements were on a 5 point scale (negative=0, trace=0.5, small=1, moderate=2, large=3); NIT was yes or no.

Results: In a fully adjusted ANOVA model by stone type and sex with LEU as the dependent variable, crude and BLO, PRO, NIT, sex were independent predictors of urine CaOx vs CaP urine. In turn, these events indicate patients’ urinary chemistry. Brushite SF had significantly higher LEU than CaOx or UA (Table). By chi-square, NIT was not different between the stone types (p = 0.25). Ammonia excretion was not different between stone types. Adjusting for other indicators of infection, such as ammonia, BLO, and PRO as well as the number of stone removal procedures did not abolish this difference. Dipstick LEU may serve as a urine biomarker of the inflammatory activity and neutrophil infiltration that we have observed in the kidneys of Br SF and may improve the papillary histopathology.

Funding: NIDDK Support

Table. Dipstick LEU by Sex and Stone Type

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<th>Stone Type</th>
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<td>CaOx SF</td>
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<td>CaP SF</td>
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Mean(SE) *p<0.0001 vs CaOx or UA; Sp<0.001 vs Ap; p<.0001 vs UA; p<0.05 vs CaOx

P00327

Heterogeneity of Mechanisms for Idiopathic Hypercalciuria in Calcium Stone Formers

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Background: In past research, we have found evidence that patterns of segmental nephron tubule calcium reabsorption differ between the sexes in calcium (Ca) stone formers (SF) demonstrating a different underlying mechanism of their hypercalciuria. Whether or not these mechanisms differ between calcium oxalate (CaOx) and calcium phosphates (CaP) SF is not known.

Methods: We studied 18 CaOx SF subjects (12 male), 17 CaP SF subjects (9 male), and 25 normal (N) subjects (13 male) in both the fasted and fed state. Subjects ate a diet consisting of three isocaloric meals with hourly blood and urine samples for 14 hours. We measured endogenous and an exogenous allowance of urinary Ca to determine the calcium (Ca) reabsorption. To account for within-subject correlation due to repeated measures, generalized estimating equations (GEE) were used to estimate and test mean laboratory values between groups. Linear mixed effects models were used to model urine Ca, distally delivered Ca, absolute reabsorption of distally delivered urine Ca and urinary CaOx.

Results: In SF women, distal Ca reabsorption is decreased compared to N women, while in SF men, PT Ca reabsorption is significantly decreased with a more modest reduction in distal Ca reabsorption compared to normal men. Among female CaP SF we found an abnormality of unbound free Ca to PTH that appears to affect post PT Ca reabsorption. Among female CaP and CaOx SF and male CaOx SF we found a clear difference of urine Ca response to ultraltrate Ca concentration. This difference was absent in male CaP SF who had a unique increase in the development of distal Ca delivery on lithium reabsorption in the PT. CaOx male SF also had other PT abnormalities such as modeled urine Ca that was abnormally dependent on the urine-plasma lithium ratio. In addition, CaOx male SF had modeled lithium reabsorption that was abnormally responsive to both urine sodium, an ECF volume marker, and urine Ca concentration, presenting mediated through the Ca receptor (CaR). In contrast, CaP SF showed no abnormalities.

Conclusions: CaP and CaOx SF have differing abnormalities of Ca handling as compared to their same sex normals. In particular, phenotype specific abnormalities related to the CaSR exist in CaOx men and abnormalities related to the PTH receptor exist in CaP women.

Funding: NIDDK Support

P00328

Magnesium’s Roles in the Treatment of Hyperphosphatemia of CKD


Background: Hyperphosphatemia is causally related to atherosclerotic cardiovascular disease, the most important cause of death in all stages of renal failure and the single greatest threat to survival among ESRD patients undergoing dialysis. To meet the current K/DOQI guideline, patients use cationic binders to bind phosphate (Pi) in the gastrointestinal tract and prevent its uptake. FDA-approved phosphate binders include calcium acetate, lanthanum salts, sevelamer, and fudeside. Combination therapies of calcium and magnesium salts have the potential both for phosphate binding with reduced calcium load and for reduction in oxidative stress, vascular calcification, and bone dysfunction.

Methods: Recent literature describing treatment of hyperphosphatemia with phosphate binders composed of calcium acetate/magnesium carbonate and calcium citrate/magnesium carbonate was analyzed. The results highlight aspects of magnesium’s roles in the treatment of hyperphosphatemia of Stage 4-5 CKD and illustrate the potential benefits of these combination therapies in treatment of hyperphosphatemia.

Results: Recent clinical data strongly suggest that combinations of calcium and magnesium salts exhibit pleiotropic benefits for hyperphosphatemic Stage 4-5 CKD patients. In addition to reducing the calcium load, magnesium appears to act in the current K/DOQI guideline, patients use cationic binders to bind phosphate (Pi) in the gastrointestinal tract and prevent its uptake. FDA-approved phosphate binders include calcium acetate, lanthanum salts, sevelamer, and fudeside. Combinations of calcium and magnesium salts have the potential both for phosphate binding with reduced calcium load and for reduction in oxidative stress, vascular calcification, and bone dysfunction.

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amorphous calcium phosphate to secondary (insoluble) calcite/particles containing needle-like calcium phosphate particles, higher magnesium appeared to beneficially slow the rate of conversion. (4) Analyses of bone turnover parameters suggested that higher magnesium may have supported more normal bone remodeling.

**Conclusions:** Clinical data from several sources suggest that combinations of calcium and magnesium have unique potential for providing pleiotropic benefits to Stage 4-5 CKD patients of all ages. Additional preclinical studies are underway to confirm that calcium magnesium citrates and propionates can be effectively and safely administered to hyperparathyroidic ESRD patients.

**Funding:** Commercial Support - BioLink Life Sciences, Inc.

**PO0329**

**Vitamin D Deficiency, Investigating the Connection Between Osteoporosis and CKD**

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**Background:** Chronic kidney disease (CKD) is estimated to afflict thirty-seven million people in the United States and leads to drastic alteration in bone and calcium metabolism. Metabolic bone disease is a common complication, resulting in skeletal consequences and CKD-associated osteoporosis. This occurs due to a combination of abnormalities in calcium, phosphorus, parathyroid hormone, vitamin D metabolism, and dysregulation in both bone formation, and bone resorption. One mechanism of the pathophysiology of age-associated osteoporosis is the shift in lineage commitment of mesenchymal stem cells (MSCs) towards adipsogenesis at the expense of osteogenesis. Recent studies have implicated MSCs as mediators of osteoporosis due to the disrupted endogenous stem cell lineage owing individuals, similar to other individuals with CKD.

**Methods:** We performed a re-analysis of a published single cell transcriptomics dataset investigating differentiation of MSCs to osteoblasts and adipocytes. We applied a standard pipeline from the R package “Seurat” to examine transcriptional heterogeneity of undifferentiated mesenchymal stem cells. Additionally, we tested the effects of 1,25D on MSC differentiation towards the osteogenic lineage.

**Results:** Here, we demonstrate heterogeneity of bone-marrow derived MSCs at the transcriptional level, implying potential underlying functional heterogeneity. Using single cell transcriptomics, we characterize the subpopulations of MSCs, multipotent stem cells and cells poised for differentiation. Once we confirmed this heterogeneity, we investigated stem cell priming with the vitamin D metabolite 1α,25-dihydroxyvitamin D3 (1,25D), testing the memory of a prior exposure to stem cells influenced later lineage commitment choices. Vitamin D supplementation is a common therapeutic intervention for osteoporosis, however, the key for patients with CKD-associated osteoporosis is Vitamin D deficiency is prevalent in populations at-risk for developing osteoporosis and patients already diagnosed with CKD.

**Conclusions:** This project supports the commonly used treatment for development and prevention of osteoporosis and demonstrates functional heterogeneity of MSCs. Further steps in this project will explore the response to vitamin D priming at a higher resolution by employing single cell RNA-sequencing.

**Funding:** Other NIH Support - National Institute of Aging

**PO0330**

**Dissecting Ferric Citrate- and FGF-23-Associated Mineral Metabolism During the Anemia of CKD**

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**Background:** Ferric citrate (FC) is a dual therapy used in patients with chronic kidney disease (CKD). This drug is given as a phosphate (Pi) binder for dialysis-dependent CKD, and for iron deficiency anemia in non-dialysis CKD due to delivery of elemental iron. Elevated Pi and anemia both lead to increased FGF23 during CKD, however, the roles of iron and Pi are unique on CKD pathologies are unclear.

**Methods:** Iron and Pi utilization was tested in a mouse model of CKD receiving FC, with and without osteocyte deletion of FGF23 (flox-Fgf23/Dmp1Cre-). Male mice (n=4-7) with the genotype flox-Fgf23/Dmp1Cre- and -Cre were placed on a customized 0.2% adenine (AD)-containing diet for 6 weeks to induce FGF23 in the presence or absence of 0.5% Pi.

**Results:** After the diet regimen, iFGF23 increased significantly in all CKD mice (p=0.05-0.01), iFGF23 was lower in Cre+ mice fed FC (p=0.01), with Cre+ AD-only mice following a similar trend, demonstrating that the Dmp1-Cre was effective in reducing FGF23. Cre+ mice fed AD-only had higher serum Pi than Cre- controls (p=0.05), and regardless of treatment, the Cre+ mice had higher BUN (p<0.01), showing that FGF23 was required to maintain serum Pi and lessen renal disease. Total serum iron was higher in all mice receiving FC, demonstrating effectiveness of the drug. Consistent with increased serum iron in the FC fed mice, liver Tirc, BMP6, and hepcidin mRNA were increased regardless of genotype (p=0.05-0.01); liver IL6 showed decreased mRNA expression in FC fed mice (p=0.01). Key enzymes that control 1,25D production in kidney were also examined. In Cre+/+ mice fed FC the 1,25D adiabolic enzyme Cyp24a1 was higher (p=0.03-0.01), and calcitobin Cyp24a1 was lower (p=0.01), suggesting that FC may aid in restoring vitamin D metabolism in CKD.

**Conclusions:** In sum, delivery of FC during genetic reductions in FGF23 allowed the identification of FGF23-dependent and -independent actions in CKD. Loss of FGF23 was associated with higher serum Pi and worse renal function, demonstrating that FGF23 was protective of mineral metabolism, an effect independent of FC. In contrast, FGF23-dependent actions in CKD of FC included decreased serum Pi, correcting inflammation markers, and restoring the balance of Cyp24a1 and Cyp27b1 mRNAs, potentially providing beneficial effects on renal 1,25D metabolism.

**Funding:** Commercial Support - Keryx Biopharmaceuticals, Inc., a wholly-owned subsidiary of Akebia Therapeutics, Inc.
PO0333

CKD Decreases Cardiac PGC-1α Through Activin A Disrupting Mitochondrial Function

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Background: The CKD-MBD syndrome is a cause of cardiac risk. Our hypothesis was that a new component of the vascular disease, activin A, is responsible for systemic activation of activin receptor (ActRIIA) signaling in kidney disease, and is a mechanism of cardiac disease.

Methods: Two models of CKD were employed, Col4A5 Alport Syndrome mice and ablative CKD in Rosa26 cre ERT/+inhbafl/fl mice. Inhibition of Activin A in CKD was accomplished by either knockdown in Rosa26 cre ERT/+inhbafl/fl CKD mice or by monoclonal antibody in Alport mice. PGC-1α, mitochondrial gene expression and oxidative phosphorylation were measured by PCR and western analysis Cardiac mitochondrial respiration was measured by respirometry.

Results: In two kidney disease models, we show that activin A is the responsible ligand for cardiac and aortic ActRIIA activation in CKD. In untreated CKD mice, cardiac levels of pSmad2 and inhibin βa mRNA and preprotein (activin A monomer) were increased. Activin A inhibition, accomplished by either knockdown in Rosa26 cre ERT/+ inhbafl/fl CKD mice or by monoclonal antibody in Alport mice, prevents CKD-induced cardiac ActRIIA activation and loss of PGC-1α, the master regulator of mitochondrial biogenesis and fatty acid oxidative phosphorylation. Mitochondrial gene expression and oxidative phosphorylation were decreased by CKD but prevented by activin A inhibition in CKD. Cardiac hypertrophy by echocardiography and heart weight was increased by CKD and prevented by activin A inhibition in the absence of vascular stiffness and without change in FGF23 levels.

Conclusions: We conclude that activation of cardiac activin/ActRIIA signaling by CKD induces mitochondrial dysfunction through decreased PGC-1α which contributes to compensated cardiac hypertrophy in the early stages of CKD associated cardiac disease.

Funding: NIDDK Support, Commercial Support - Regeneron

PO0334

Response of Bone to Acid: Effect of Deletion of the Proton Receptor OGR1 in the Osteoblast

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Background: Metabolic acidosis induces bone resorption by inhibiting osteoblast (OB) bone formation and stimulating osteoclast (OC) bone resorption. Mice generate large amounts of endogenous acid and we have shown that OGR1 is the proton (H+) receptor in bone and is stimulated by this endogenous acid. Mice with a global deletion of OGR1 have increased bone density which appears due to increased bone formation. There is communication between OB and OC and OGR1 is present in both. To determine if the response of OGR1 in the OB is independent of a response in OC, we generated a global deletion of cardiac OGR1 which contributes to compensated cardiac hypertrophy in the early stages of CKD associated cardiac disease.

Funding: NIDDK Support, Commercial Support - Regeneron
PO0336
Using a Quantitative Systems Pharmacology Model of CKD-MBD to Guide Therapy Minimizing Calcium Flux from Bone and into Vasculature
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Background: CKD-MBD is characterized by bone loss and vascular calcification. Pharmacologic treatment of CKD-MBD involves dosing of three agents to minimize these complications through optimal balance of Calcium (Ca), Phosphorus (P), and PTH. Having developed a Quantitative Systems Pharmacology (QSP) model of CKD-MBD, we tested the hypothesis that an AI method called Deep QLearning (DQL) in conjunction with our model can be used to determine the impact of precision therapy on the mineralization defect in patients with End Stage Renal Disease (ESRD).

Methods: Applying a quantitative systems pharmacology (QSP) model of CKD-MBD to mimic disease progression, we trained a Deep Neural Network (virtual physician) to minimize the Ca bone efflux and the Ca vascular tissue influx regardless of achieved serum Ca, P, and PTH predicted by the model. The virtual physician observed Ca, P, PTH and adjusted the doses of P binder, vitamin D, and a calcimimetic. We evaluated a trained virtual physician through simulation of CKD-MBD treatment over 18 months on a population of 100 virtual ESRD patients with varying baseline Ca, P, PTH levels, P intake, and Ca sensing receptor sensitivity.

Results: Simulations produced an average 30% decrease in bone Ca efflux and a 20% decrease in Ca influx to vascular tissue over baseline values. Average P decreased from 7.4 to 5.1 mg/dL, average Ca increased from 8.5 to 9.2 mg/dL, median PTH decreased from 1650 to 315 pg/mL.

Conclusions: Using a QSP model of CKD-MBD, we trained an AI agent to minimize the Ca fluxes from the bone and into the vascular tissue by prioritizing optimization of Ca fluxes over the achievement of specific Ca, P, and PTH levels. Our approach demonstrates beneficial synergy of Systems Biology and AI in modeling complex biological processes.

Funding: Veterans Affairs Support

PO0338
Quantitative Systems Pharmacology Approach to the Treatment of CKD Metabolic Bone Disorder (CKD-MBD) Using Deep Learning
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Background: CKD-MBD is a common comorbidity that leads to serious skeletal and cardiovascular complications. Using a Systems Biology model of CKD-MBD and Artificial Intelligence (AI) - guided precision dosing approach, we tested the hypothesis that this approach can effectively achieve recommendations for Ca, P, and PTH by balancing the administration of vitamin D and a calcimimetic when faced with varying adherence to phosphate binder dosing.

Methods: Using a Quantitative Systems Pharmacology (QSP) approach to model the disease trajectory, we trained a Deep Neural Network AI-agent to adjust doses of a P binder, vitamin D, and a calcimimetic to drive Ca, P, and PTH to recommended targets. We evaluated the agent through treatment simulation in a cohort of 100 virtual patients (defined by dietary P and sensitivity of the Ca receptor) under 3 experimental conditions: 100%, 50%, and 0% adherence to P binder prescription. Using model derived doses of vitamin D and calcimimetic, we analysed the effect of P binder adherence on achieving the recommended Ca, P, and PTH target ranges. Dose adjustments were determined by simultaneously maximizing the percent in range of Ca, P, and PTH while minimizing the changes in bone Ca efflux and vascular Ca influx. Simulations were performed over 18 months.

Results: Results are shown in Table 1.

Conclusions: Using a QSP model of CKD-MBD, we trained an AI agent to guide precision dosing of P binder, vitamin D, and calcimimetic. We validated the agent under three simulated scenarios of P binder adherence. Simulation results show that control of intestinal P absorption is paramount in treatment of CKD-MBD. Failure to control P level severely compromises ability to control vascular tissue calcification even when Ca and PTH are controlled pharmacologically.

Funding: Veterans Affairs Support

PO0339
 Differences in 25-Hydroxyvitamin D Clearance by eGFR and Race: A Pharmacokinetic Study
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Background: 25-hydroxyvitamin D (25(OH)D) clearance is an essential yet often overlooked determinant of circulating 25(OH)D concentration, the prevailing marker of vitamin D status. Observational studies associate markers of low 25(OH)D clearance with poor clinical outcomes and suggest differences in 25(OH)D clearance by kidney function and race, but these potential variations have not been tested using gold-standard methods.

Methods: We administered intravenous deuterated 25(OH)D (d25(OH)D) in a pharmacokinetic study of 87 adults with a wide range of kidney function, including normal estimated glomerular filtration rate (eGFR ≥ 60 ml/min/1.73m2), non-dialysis chronic kidney disease (CKD; eGFR < 60 ml/min/1.73m2, n=24), and kidney failure treated with hemodialysis (n=20). We measured d25(OH)D and deuterated 24,25-dihydroxyvitamin D, concentrations 5 minutes-12 hours, and 1, 4, 7, 14, 21, 32, 42, and 56 days post-administration. We calculated 25(OH)D clearance using non-compartmental analysis of d25(OH)D concentrations over time. We re-measured 25(OH)D clearance in a subset of participants after 12-16 weeks of 2000 IU/day of oral vitamin D3 (n=18).

Results: We recruited 85 pts in 29 months and included 69 pts in the study. Mean age 50±12.4 years, 48 men, 53 caucasian (78.9%), 53 non-Hispanic black (81.5%), mean BMI 24.5, 53 caucasian (78.9%), 53 non-Hispanic black (81.5%), median dialysis vintage 55 (42 – 84). We observe a significant reduction on P, Mg, PTH, calcitomin, sclerostin, bAP and FGF23. Both Ca and alpha-kloho levels increased, with no significant changes in vitD levels. With restoring renal health (time 1) and comparing with time 0, PTH maintain the negative correlation with sclerostin (p=0.002) and the positive correlation with FGF23 (p=0.002); modify the correlation with P, becoming a negative correlation instead of positive (p=0.001) and gain new correlations with Ca (p=0.001) and vitD levels (p=0.03). Also, PTH correlated with the delta FGF23 (rho=0.4, p=0.003) and sclerostin correlated with delta PTH (p=0.01). FGF23 showed a radical statistical association with P or Ca levels after transplant, contrasting with positive associations in pre transplant (p=0.002, p<0.0001). On the contrary, sclerostin developed a new correlation with P (p=0.0004) and a negative correlation with Ca (p=0.01). We didn’t find correlations between these molecules and alpha-kloho.

Conclusions: It seems that sclerostin influences PTH levels and that PTH is the stimulus for the increase or decrease of FGF23 serum levels. Levels of Ca and P seemed to be directly influenced by the level of PTH in post transplant, and those minerals seemed to be key factors for sclerostin secretion.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO0337
Mineral Metabolism Changes in Renal Transplantation
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Background: Successful renal transplant restores many physiological abnormalities. The aim of this study was to analyse the evolution of CKD-MBD patients (alpha-kloho, fibroblast grow factor (FGF) 23, sclerostin, parathyroid hormone (PTH), bone alkaline phosphatase (bAP), calcitomin, vitamin D (vitD), phosphorus (P), Calcium (Ca) and Magnesium (Mg)) pre and post transplantation.

Methods: Prospective cohort study of de novo renal transplant patients (pts). A inclusion and after 12 months (time 0 and 1) pts performed laboratory evaluation. The difference over the achievement of time1 - time 0) is the delta value. Associations between variables were performed by Wilcoxon matched-pairs test and Spearman correlation test. STATA software was used and p < 0.05 was considered statistically significant.

Change in Ca flux distributions over time in the simulated patient cohort.
PO0340
The Vitamin D Metabolite Ratio and Change in Bone Density and Fracture Risk in Older Adults

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Background: Recent studies have suggested that 25-hydroxyvitamin D [25(OH)D] may be a poor biomarker of bone health. Higher concentrations of its catabolic product 25,26-dihydroxyvitamin D [25,26(OH)2D3] and a higher ratio of 25,26(OH)2D3 to 25(OH)D (the vitamin D metabolite ratio [VMR]) may provide additional information on vitamin D receptor activity and bone health.

Methods: We measured 24,25(OH)D3, 25(OH)D3, 25(OH)D3 and serial bone densitometry scans over a 9-year period, in 761 community dwelling older adults, that participated in the Health Aging and Body Composition Study. Participants were followed for a median time of 11 years for any fractures. 24,25(OH)D3 and 25(OH)D3 were used to calculate the VMR. We used linear mixed models to assess the relationship between 24,25(OH)D3, 25(OH)D3, 25,26(OH)2D3, and the VMR with annual change in hip, lumbar and thoracic spine bone mineral density (BMD). We used Cox models to assess the relationships between these parameters and fracture risk.

Results: Study participants had mean age 75±3 years, 49% were female, 42% were black, 23% had CKD. 24,25(OH)D3 in participants with normal eGFR (71 ml/min/1.73m2, 95% CI: 16.1 125), but not in those with CKD or kidney failure (p-for-interaction = 0.052). 25(OH)D clearance did not differ after compared with before vitamin D supplementation, although lower 25(OH)D clearance was correlated with a larger increase in serum 25(OH)D concentrations following supplementation (r = 0.31).

Conclusions: Through prospective pharmaco kinetic measurements, these findings confirm impaired 25(OH)D clearance as a feature of disorder mineral metabolism in CKD, and may help understand racial differences in vitamin D metabolism. Surrogate measures of 25(OH)D clearance may allow clinicians to more accurately anticipate individual response to vitamin D supplementation.

Funding: NIDDK Support, Other NIH Support - National Center for Advancing Translational Sciences of the National Institutes of Health

PO0341
The Vitamin D Metabolite Ratio Is Independent of Vitamin D Binding Protein Concentration

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Background: 25-hydroxyvitamin D [25(OH)D] may be a poor biomarker of bone health. Higher concentrations of its catabolic product 25,26-dihydroxyvitamin D [25,26(OH)2D3] and a higher ratio of 25,26(OH)2D3 to 25(OH)D (the vitamin D metabolite ratio [VMR]) may provide additional information on vitamin D receptor activity and bone health.

Methods: We measured 24,25(OH)D3, 25(OH)D3, 25,26(OH)2D3, 1,25(OH)2D3, and VDBP in 1,259 participants with normal eGFR, CKD and kidney failure respectively (p = 0.02). 25(OH)D clearance was independent of VDBP concentration, whereas VDBP was strongly directly associated with 25(OH)D concentration following supplementation (r = -0.41).

Conclusions: In diverse cohort of community dwelling older adults, the VMR was independent of vitamin D supplementation whereas VDBP was strongly directly associated with the individual vitamin D metabolite concentrations. The VMR may serve as an important biomarker of vitamin D status and clinical outcomes that can be utilized in populations with a large spectrum of VDBP concentrations.

Funding: NIDDK Support, Private Foundation Support

PO0342
Meta-analysis of the Impacts of Supplementation with Nutritional Vitamin D on Mineral and Bone Markers in Non-Dialysis CKD

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Background: Secondary hyperparathyroidism (SHPT) is a critical component of mineral and bone disorder in chronic kidney disease (CKD-MBD), characterized by excessive parathyroid hormone (PTH) secretion and low levels of vitamin D. Nutritional vitamin D (NVD) supplements are frequently used to treat SHPT, especially in early CKD. The objective of this meta-analysis (MA) was to evaluate the impact of NVD supplements on PTH, vitamin D (25D), calcium (Ca), phosphate (P) and fibroblast growth factor 23 (FGF23).

Methods: Study level results were pooled using a fixed effect model with inverted-variance weighting. The impact of the NVDs was measured in two ways: as change versus placebo or ‘no treatment’ and as change within the NVD study arm (before versus after NVD supplementation).

Results: Overall changes in PTH from NVD supplementation were small when measured within the NVD study arms (pooled reduction of 10.53 pg/ml, 95% confidence interval (CI): -16.33 to -4.73) but larger when compared to placebo/no treatment (reduction of 49.74 pg/ml, 95% CI: -70.17 to -29.3). NVDs tended to increase levels of 25D both within the NVD study arms (increase of 20.62 ng/ml, 95% CI: 19.58 to 21.65) and when compared to placebo/no treatment (increase of 26.87 ng/ml, 95% CI: 24.44 to 29.30). At the end of the study periods, average levels of 25D in the NVD study arms were -30 ng/ml in all but two RCTs and >50 ng/ml in only five of the included RCTs. Ca levels increased statistically significant from supplementation with NVDs versus placebo/no treatment (increase of 0.05 mg/dl, 95% CI: -0.12 to 0.34 mg/dl). Only small and statistically non-significant impacts were observed on levels of P and FGF23.

Conclusions: Our results suggest that the magnitude of 25D increase caused by NVD may be insufficient to effectively and consistently lower PTH. While supplementation with NVDs can be used to correct vitamin D insufficiency, the potential of NVDs to actively reduce PTH in ND-CKD patients with SHPT is limited.

Funding: Commercial Support - Vifor Pharma

PO0343
Fibroblast Growth Factor 23 (FGF-23), Calcification Propensity, and Heart Failure with Preserved Ejection Fraction (HFpEF) in Patients with CKD: The CRIC (Chronic Renal Insufficiency Cohort) Study

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Background: HFpEF represents half of all HF events and is common in patients with CKD. Given lack of treatments, identifying factors that impact HFpEF development is critical. FGF-23 is an osteocyte-derived hormone involved in phosphorous homeostasis and is implicated in HF development. Calcification propensity (TSO) is an in vitro assessment of the time for secondary calciprotein particle formation.

Methods: Multivariable adjusted Cox proportional hazards models, we investigated the associations of FGF23 and TSO with incident HFpEF. FGF23 and TSO were measured at the baseline and Year 1 visits, respectively. Incident HFpEF was
defined as ejection fraction > 50% on echocardiogram at the time of event or by a CRIC Study echocardiogram within 1 year. After excluding individuals with baseline HF and individuals with HF events prior to analyte measurement, we included 3502 and 3029 individuals for our FGF23 and T50 analyses, respectively.

Results: In the FGF23 cohort, 333 incident HFpEF events occurred over a median follow-up of 10.8 years. In the T50 cohort, 259 incident HFpEF events occurred over a median follow-up of 10.2 years. Individuals in the highest FGF23 and lowest T50 quartiles had the highest rates of incident HFpEF (Figure). When adjusted for demographics, cardiovascular risk factors and kidney function, elevated FGF23, but not T50, was independently associated with incident HFpEF (Table).

Conclusions: FGF23, but not T50, was associated with incident HFpEF in patients with CKD. These data are consistent with studies demonstrating cardiac toxicity of FGF23 and may inform future trials of HFpEF development in CKD.

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PO0345
Renal Clearance of Intact and C-Terminal FGF-23 in Man
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Background: The ratio of C-terminal (cfGF23) to Intact FGF23 (iGF23) is higher in persons with higher eGFR. Mechanisms are unclear. Differential renal clearance is one possibility.

Methods: Patients were referred for clinically suspected renal artery stenosis (RAS), and maintained off BP meds for 21 days before angiography. This study includes those found without RAS (N=93). Blood was obtained from the aorta (Ao) and bilat. renal veins (RV), and renal blood flow (RBF) was measured using 133Xenon washout. Single pass % reductions of each measure (Ao – RV/Ao) were 100 calculated, left and right was averaged, and multiplied by RBF to provide renal clearance in ml/min/100g kidney tissue. To determine the relative renal clearance, we calculated the cfGF23/iGF23 clearance ratio (C/I ratio) and evaluated its relationship with eGFR.

Results: Mean age was 52±11 years, 22% were women, all were white, eGFR was 77±26 ml/min/1.73m² and directly measured Cr clearance was 72 ± 42 ml/min/100g. Renal clearance of cfGF23 was similar to Cr, while iGF23 was 37% higher (C/I ratio 0.73 ± 0.10). The clearance of cfGF23 and iGF23 were directly correlated to eGFR (r=0.31 and 0.35). However, their relative clearance was similar across the range of eGFR (r=0.01). Results were similar in models adjusted for age, sex, and BMI.

Conclusions: Renal cfGF23 clearances (which measures both iGF23 and c-terminal fragments) is similar to Cr, whereas iGF23 clearance is higher, suggesting that renal clearance of c-terminal fragment clearance is low. While renal cfGF and iGF23 clearance were both reduced in persons with lower eGFR, the relative efficiency of clearance of cfGF23 vs. iGF23 appeared similar across the range of eGFR.

Funding: NIDDK Support

Single Pass Percent Reduction and Renal Clearance of C-terminal and Intact FGF23 in Man (N=93)

PO0346
Association of Changes in Levels of eGFR and Fibroblast Growth Factor 23 from Midlife to Late Life with Risk of Mortality: The ARIC Study
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Background: Aging from midlife to late-life involves the dynamics of levels of eGFR and fibroblast growth factor 23 (FGF23). Whether changes in levels of eGFR and FGF23 from midlife to late-life are independently and jointly associated with subsequent risk of mortality is unknown.

Methods: We included 5639 participants of the Atherosclerosis Risk in Communities Study who had eGFR and serum level of FGF23 measured during midlife (visit 3, 1993-1995, mean age 58 [SD, 5] years, 58% women, 23% black race) and late-life (visit 5, 2011-2013, mean age 76 years). We used Cox regression to examine the associations of past changes in levels of eGFR and FGF23 levels (in quartiles)– separately and jointly– with mortality from visit 5 (2011-2013) through December 31, 2017.

Results: The median eGFR 15-year decline (from visit 3 to 5) was 20.5 ml/min/1.73m² (from median eGFRs 87.8 to 65.7 ml/min/1.73m²). The median FGF23 increase was 17.4 pg/ml (median FGF23s 37.5 to 54.8 pg/ml). During a median follow-up of 5.5 years after visit 5, 868 participants died. Adjusted HRs of mortality were 1.93
**PO0347**

**Intact and C-Terminal Fibroblast Growth Factor 23 Assays: Do Kidney Function, Inflammation, and Iron Deficiency Influence Relationships with Clinical Outcomes?**

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**Background:** Higher fibroblast growth factor-23 (FGF23) concentrations are associated with heart failure (HF) and mortality, but strengths of associations differ depending upon FGF23 assay type. We investigated whether iron deficiency, inflammation, and kidney function account for these differences.

**Methods:** In 844 Cardiovascular Health Study participants, using a case-cohort design, we examined associations of intact and C-terminal FGF23 with risk of mortality and HF, using modified Cox models to account for case-cohort design, adjusting sequentially by iron status, inflammation, kidney function or their combinations.

**Results:** C-terminal FGF23 more strongly correlated with ferritin (r = -0.26) and CRP (r = 0.21) than intact FGF23 (r = 0.04 & r = 0.07, respectively). The two FGF23 assays moderately correlate with one another (r = 0.47). During follow up, there were 658 deaths, and 220 incident HF events. FGF23 measured by either assay was associated with mortality in unadjusted analysis (intact FGF23 HR per two-fold higher 1.45; 1.25-1.68) to 1.16 (0.97, 1.38). Adjustment for iron deficiency and inflammation completely attenuated the association of intact FGF23 with mortality (β change from 0.99 to 0.76, 1.28) with eGF23 and albuminuria adjustment, whereas C-FGF23 went from 1.45 (1.25, 1.68) to 1.16 (0.97, 1.38). Adjustment for iron deficiency and inflammation did not meaningfully influence the differential associations of the two assays with either endpoint.

**Conclusions:** The associations of biologically active FGF23 with clinical endpoints may be weaker than previously thought.

**Funding:** NIDDK Support

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**PO0348**

**Factors Associated with Change in Fibroblast Growth Factor 23 Levels from Midlife to Late-Life: The ARIC Study**

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**Background:** Factors associated with change in fibroblast growth factor 23 (FGF23) levels from midlife to late-life are not well-characterized in the general population.

**Methods:** Among 5,981 participants of the Atherosclerosis Risk in Communities Study who had serum level of FGF23 measured during midlife (visit 3, 1993-1995, mean age 58 years, 58% women, 23% black race) and late-life (visit 5, 2011-2013, mean age 76 years), we explored demographic and clinical factors associated with change in FGF23 levels. Change in FGF23 levels was regressed on pre-specified factors assessed at visit 3 (age above vs. below median), sex, race, ever smoke, high BMI (BMI ≥ 30 kg/m²), hypertension, diabetes, history of CVD, and reduced eGFR (HR vs. <60 ml/min/1.73m²) using multivariable linear regression models.

**Results:** The mean FGF23 levels increased by 21.0% (95%CI, 20.3-21.6) pg/mL from 39.7 at visit 3 to 60.6 pg/mL at visit 5. Reduced eGFR, diabetes, hypertension, female, older age, and white race were significantly associated with a greater increase in FGF23 levels (Table). Although history of CVD demonstrated a similar magnitude as race, the β coefficient was not significant. We also did not observe significant associations for BMI or smoking. The associations were strongest for reduced eGFR and diabetes with similar degrees of associations (ΔFGF23, 6.7 [95%CI, 2.7 to 10.6] pg/mL for reduced eGFR and 6.7 [4.4 to 9.0] pg/mL for diabetes) independent of each other.

**Conclusions:** In addition to reduced GFR, we identified diabetes, hypertension, female, older age, and white race as predictors of an increase in FGF23 levels from midlife to late-life. Among these, the strong association of diabetes independent of kidney function deserves future investigations.

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**PO0349**

**Fibrogenesis Is Induced by Glucocorticoid Stimulation In Vivo and In Vitro: Translational Approach**

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**Background:** Previous data have suggested that glucocorticoid (GC) treatment may induce plasma fibroblast growth factor 23 (FGF23). Recently, we have reported that in prepubertal renal transplantation children, chronic GC treatment was associated with increased plasma FGF23 levels, that was related to decreased bone growth in vivo and in vitro. Our objective was to evaluate whether GC treatment modulate FGF23 in adult patients.

**Methods:** Translational approach. This included an observational clinical study of patients who began GC treatment (prednisone 1 mg/kg/day), estimated glomerular filtration rate (eGFR) over 60 ml/min/1.72m². Measurements of intact FGF23 were performed before initiation and 2 months later. Also we performed in vitro and in vivo analysis with cell cultures and experimental rat models which were treated with GC, measurements of plasma and bone FGF23 expression were performed.

**Results:** We recruited 10 patients who began GC treatment. We observed a significant increase in plasma intact FGF23 levels at 2 months (57% increase as compared to baseline values): baseline values: 18.9 +/- 4.2 pg/mL; 2 months: 29.7 +/- 5.2 pg/mL; p<0.001. No significant changes in renal function were detected. Also, rats treated with prednisone had a significant increase in plasma FGF23 and bone FGF23 expression after GC treatment. Finally, pharmacological blockage of glucocorticoid receptor alpha in vitro prevented the increase of FGF23 expression in bone tissue.

**Conclusions:** Sustained glucocorticoid treatment is associated to increased FGF23 expression and plasma levels. This effect should be evaluated in larger groups of patients to evaluate its potential relevance.

**Funding:** Government Support - Non-U.S.
PO0350

PTH 1-84 and Bone Alkaline Phosphatase Are Independently Associated with Mortality, Whereas FGF-23 Predicts Dialysis Initiation in CKD Patients

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Background: Despite the fact that CKD-MBD is a risk factor for CKD morbidity and mortality, details of its role regarding the role of individual biomarkers are variable. In addition, dimensionality reduction techniques have not been applied in CKD-MBD. The aim of our study was to evaluate a panel of CKD-MBD biomarkers, namely Ca, P, PTH 1-84, FGF-23, 25-vitamin D, 1,25-vitamin D, bone alkaline phosphatase (BAP) and sclerostin, individually and collectively related to death and KRT.

Methods: Events of death and KRT in 454 participants of the Progressor Cohort (Sao Paulo, Brazil) with predominantly CKD G3 and G4 were ascertained after a median follow-up of 6 years. Those with missing values were excluded (n=25) and 4 were lost to follow-up. The association of individual CKD-MBD parameters (DiasSort® assays) and factors derived from factorial analysis was evaluated through Cox and Competitive Risk models (R package “cmpmrk”).

Results: Mean age was 68(12)y, mean eGFR was 38(15) mL/min/1.73m², 63% were male and 56% diabetic. In univariable analysis, sclerostin, BAP, PTH, and factor 1 were associated with death and 1.25vitD, DM, MI, AUC, smoking. After adjustments, BAP, PTH, and factor 1 remained associated with death, and FGF-23 remained associated with death (p<0.01). The addition of PFG-23 with interaction with P significantly improved the model fit for KRT (p=0.0046).

Conclusions: PTH and BAP are positively associated with death and improved its prediction model. This finding suggests that BAP could be reflecting not only bone turnover but also vascular calcification. FGF-23 is associated with the risk of death and improved the model fit for KRT (p=0.0046).

Funding: Government Support - Non-U.S.

PO0351

Parathyroid Hormone Serum Levels and Mortality Among Hemodialysis Patients in the Gulf Cooperation Council Countries: Results from the DOPPS (2012-2018)

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On behalf of the GCC-DOPPS Study Group12 1Arbor Research Collaborative for Health, Ann Arbor, MI; 2The Royal Hospital, Ministry of Health, Muscat, Oman; 3Dubai Medical College, Dubai, United Arab Emirates; 4Jahra Hospital, Jahra, Kuwait; 5DSPH, Jeddah, Saudi Arabia; 6King Abdulaziz University, Jeddah, Saudi Arabia; 7Hamad General Hospital, Doha, Qatar; 8Salmaniya Medical Complex, Manama, Bahrain; 9King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia; 10Amgen UAE, Dubai, United Arab Emirates.

Background: The prospective Dialysis Outcomes and Practice Patterns Study (DOPPS) has collected data since 2012 in all six Gulf cooperation council (GCC) countries (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates). Here, we report the relationship of PTH with mortality in the largest GCC hemodialysis (HD) patient cohort studied to date.

Methods: Data were from randomly-selected national samples of HD facilities in GCC DOPPS phases 5 and 6 (2012-2018). PTH descriptive findings and case-mix adjusted PTH-mortality Cox regression analyses were based on 1825 and 1422 randomly-selected HD patients, respectively.

Results: Mean patient age was 55 years (median dialysis vintage = 2.1 years). Median PTH ranged from 259 pg/mL (UAE) to 437 pg/mL (Kuwait), with 22% having PTH <150 pg/mL, 24% (PTH 150-300), 34% (PTH 301-700), and 20% (PTH >700 pg/mL. Patients with PTH >700 pg/mL, were younger, on dialysis longer, less likely to be diabetic, have urine<200 mL/day, prescribed 3.5 mEq/L dialysate calcium, had higher mean serum creatinine and phosphorus levels, lower white blood cell counts, and more likely to be prescribed cinacalcet, phosphate binders, or IV vitamin D. A U-shaped PTH/mortality relationship was observed with >2-fold and 1.5 fold higher adjusted HR of death at PTH>700 pg/mL and <300 pg/mL, respectively, compared to PTH 301-450 pg/mL.

Conclusions: Secondary hyperparathyroidism is highly prevalent among GCC HD patients, with a strong U-shaped PTH/mortality relationship seen at PTH <300 and >450 pg/mL. Future studies are encouraged for further understanding this PTH/mortality pattern in relation to unique aspects of the GCC HD population.

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PO0352

Effect of PTH Dosing Frequency and Amplitude on Bone Health: From Anabolism to Catabolism

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Background: In patients with chronic kidney disease or primary hyperparathyroidism, chronically elevated parathyroid hormones (PTH) levels exert catabolic effects on the bone. In contrast, PTH cycling or daily application of teriparatide (TP) promotes bone formation. These responses have important clinical and therapeutic implications. Although the anabolic effects of PTH cycling are widely accepted, the underlying dynamics are not well understood.

Methods: We developed a physiology-based model quantitating the interrelations of osteoclasts, osteoblasts and osteocytes on bone remodeling (Cherif et. al., NDT 33(1), 2018, i165-6). Using the validated model, we explore the effect of altered PTH (TP) dosing (e.g., dosing frequency and amplitude) on bone catabolism and anabolism, respectively.

Results: The model accurately predicts differential responses of anabolic and catabolic effects of continuously and intermittently elevated PTH (TP) levels, respectively. We observe that intermittent dosing of PTH with a high frequency and amplitude induces bone catabolism similar to that seen with chronically elevated PTH. We see a more than 3-fold change from baseline in osteoclastic over osteoblastic activities, resulting in catabolism. Low PTH frequency with high dosing amplitude induces both osteoclastic and osteoblastic activities, but the net result is bone anabolism. Figure 1 shows a region where high osteoclastic activities exceed osteoclastic resorption. These findings suggest the existence of optimal PTH (TP) frequency-amplitude values that enhance anabolic gains, beyond which there can be a detrimental effect on bone.

Conclusions: Our results suggest that both frequency and amplitude of PTH (TP) cycling affect the balance of catabolic and anabolic effects. Understanding the underlying mechanism of differential responses induced by intermittent and continuous levels of PTH, respectively, may provide new therapeutic options for patients and minimize unintended, unforeseen consequences of intervention.

Illustrates regions with high osteoclastic and osteoblastic activities corresponding to anabolic gains and/or catabolic loss in bone health as a function of dosing frequency and amplitude.
PO0353

Chemical Characterization and Quantitation of Circulating Intact Parathyroid Hormone and Parathyroid Hormone Fragments by High-Resolution Mass Spectrometry in Chronic Renal Failure

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Background: The precise concentrations of full-length parathyroid hormone (PTH 1-84) and the identity and concentrations of PTH fragments in patients with various stages of chronic renal failure (CRF) are unknown.

Methods: We developed a liquid chromatography-high resolution mass spectrometry (LC-HRMS) method to characterize and quantitate PTH 1-84 and PTH fragments in the serum of 221 patients with progressive renal dysfunction. Following capture by matrix-bound amino-terminal or carboxyl-terminal region-specific antibodies and elution from matrix, full-length PTH and PTH fragments were identified and quantitated using LC-HRMS. PTH was simultaneously measured using an intact PTH (iPTH) immunoassay.

Results: Full-length PTH 1-84 and eight PTH fragments (PTH 28-84, 34-77, 34-78, 34-84, and 45-84) were unequivocally identified and were shown to increase significantly when the eGFR declined to less than 17-23 mL/min/1.73 m². Serum concentrations of PTH 1-84 were similar when measured by LC-HRMS following capture by amino-terminal or carboxyl-terminal immunoisolation methods. Serum PTH 1-84 concentrations measured by LC-HRMS were significantly lower compared with PTH measured by an iPTH immunoassay in patients with eGFRs of less than 30 mL/min/1.73 m². PTH 7-84 was below the lower limit of quantitation of the method (<50 pg/mL).

Conclusions: LC-HRMS accurately quantitates full-length PTH, carboxyl-terminal PTH fragments, and mid-region PTH fragments, in the serum of patients with progressive renal failure. Serum concentrations of PTH 1-84 and PTH fragments increase when eGFR declines to less than 17-23 mL/min/1.73 m². Values measured by LC-HRMS are lower than those obtained from an iPTH immunoassay in severe CRF.

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PO0354

Management of Secondary Hyperparathyroidism Among Patients Who Transition from Daily At-Home to Three-Times-Weekly Oral Cinacalcet

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Background: Results of a small phase 1 clinical trial demonstrated the safety and potential utility of 3X weekly in-center administration of cinacalcet to control secondary hyperparathyroidism (SHPT) in hemodialysis (HD) patients. Moreover, a larger observational study demonstrated comparable control of SHPT among HD patients who initiated 3X weekly cinacalcet in-center to those who initiated cinacalcet at home. The present study assessed the effectiveness of 3X weekly in-center cinacalcet among HD patients who transitioned from cinacalcet administered daily at home in the management of SHPT.

Methods: Patients included in this analysis were ≥18 years of age, receiving standard in-center HD, Medicare beneficiaries, and had 90% compliance to transitioning from daily at-home cinacalcet to cinacalcet given 3X weekly in-center (July 2018 to December 2019). Patients were followed forward in time for up to 9 months after transition to in-center cinacalcet or until loss to follow-up or end of study. Generalized linear models and 95% confidence intervals (CIs) were calculated for parathyroid hormone (PTH), calcium (Ca), and phosphorus (Phos). Hypocalcemia events were defined as Ca <8.4 mg/dL.

Results: We identified 874 qualifying HD patients who transitioned from at-home to in-center cinacalcet administration during the study period. Among patients with baseline PTH <800 pg/mL, PTH levels initially increased but stabilized after transition. Among patients with baseline PTH 800 to 1599 pg/mL and PTH >1600 pg/mL, PTH levels initially decreased but then stabilized following transition. Ca and Phos levels were generally stable for all patients following transition. Hypocalcemia was observed in approximately 25% to 38% of patients during follow-up.

Conclusions: These results suggest that SHPT can be stably maintained by transitioning patients from daily at-home cinacalcet to cinacalcet given in-center 3X per week. We postulate that increased prescription adherence is the likely factor mediating this effect.

PO0355

Real-World Experience with Etecalcitide in an Academic Dialysis Program

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Background: High parathyroid hormone (PTH) levels may increase fracture risk, vascular calcification, and cardiovascular disease in end-stage kidney disease (ESKD) patients. Treatments include phosphorus binders, Vitamin D analogues, and cinacalcet. However, most ESKD patients persist with high PTH levels. Etecalcitide (ETC) is an injectable calcimimetic recently approved to treat hyperparathyroidism in ESKD. To date, few studies have described the safety and efficacy of ETC on calcium (Ca) and PTH levels in real world usage.

Methods: This retrospective chart review of 195 in-center HD patients describes those who received a stable dose of ETC for at least 12 consecutive weeks. ETC dose, Ca, and PTH levels were obtained monthly x 3 months prior to ETC start and up to 9 months post. 23 patients were included for 2 or more doses of ETC. Overall and severe hypocalcemia were defined as corrected Ca <8.3 and <7.5 mg/dL, respectively.

Results: See Table 1. PTH changed from +3.37% (2.5mg) to -32.57% (10mg) to -3.19% (15mg). As expected, ETC use yielded a statistically significant lower PTH when compared to pre-treatment average of 1 and 2 months pre-drug PTH values versus 3 months post drug average (p<0.0034 via t-test for related samples). Corrected Ca decreased in a dose dependent fashion from 0.22% (2.5mg) to 11.89% (15mg). Overall, hypocalcemia occurred in 36.6% of patients. Severe hypocalcemia ranged between 0% (2.5, 5, 12.5, 15mg) and 1% (7.5, 10mg).

Conclusion: Prior studies have used aggressive PTH lowering targets (>300mg/mL or >30% reduction from baseline) yielding high rates of hypocalcemia (61-68%). Our study is the first to describe results of a typical real world dosing strategy. Our results suggest that PTH levels decrease in a dose dependent fashion and severe hypocalcemia is rare at doses >10mg diminishing PTH reductions which could be due to a preponderance of patients with refractory / tertiary hyperparathyroidism. Rates of overall and severe hypocalcemia were lower here. Limitations of this study include limited adjustment for confounding variables, retrospective nature and small population at higher doses.

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PO0356

The Cost Effectiveness of Alternate-Day Cinacalcet Therapy for Secondary Hyperparathyroidism (SHPT) in Hemodialysis Patients

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Background: CKD defines as abnormalities of kidney structure or function, present for more than 3 months with implication for health. Secondary hyperparathyroidism (SHPT) is one of implication of CKD, which eventuate with decrease in GFR. The initial treatment starts with incremental approach, constrain of Dietary Phosphorus, use of calcium and non-calcium phosphorus binders and additional Vit D Analogues. Next approach to Secondary hyperparathyroidism (SHPT) after poor response to initial therapy is to use Cinacalcet. Cinacalcet act by activating calcium sensing receptor of parathyroid hormone gland directly and it bypass normal physiological process. It has half-life of 30-40 hours, Cinacalcet is excreted 80% through kidney and 20% through liver.

Methods: We did prospective control study by following Dialysis patients (N=88) who were receiving alternate day Cinacalcet either by physician’s choice or due to noncompliance to home medications. We followed Intact PTH every 3 months, Serum Calcium and serum phosphorus every month after start of alternate day therapy until six months and compared it with 6 months data before start of alternate day Cinacalcet. Data was analyzed by using paired T-Test.

Results: A total of 88 patients were enrolled in the study, who were on hemodialysis for at least one year. The mean age of patients was 49.17±15.80, and 50.8 percent of them were males. The mean duration of dialysis was 6.68 ± 5.27 years and 40.9 percent of patients had diabetic nephropathy as a cause of End stage renal disease. The patients were transferred from once daily dosing to 3 times per week hemodialysis dose. The mean post hemodialysis dose of cinacalcet was 62.73 ± 27.71 mg. The baseline mean PTH value before shifting to alternate dose was 986.69 ± 503.370 mg and after was 798.24 ± 526.92 and the P value was 0.001. The mean serum calcium before was 8.28 ± 2.30 and after it was 8.72 ± 1.42 with a p value of 0.03. Serum phosphorous before and after was, 4.66 ± 1.53, 4.86 ± 1.19 with a P-value of 0.147.

Conclusion: Cinacalcet effectively controls secondary hyperparathyroidism even with modified regimen as used in our study. Cinacalcet showed significant reductions of PTH with intermittent (3/week) dosing and thus is more cost effective and has better directly observed compliance.
A Real-World Observational Study of Calcimetic Use in Hemodialysis (HD) Patients with Secondary Hyperparathyroidism (SHPT) in Europe

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Background: Calcimetics, oral calcineal (CIN) and intravenous etelcalcetide (ETEL), are approved for treating SHPT in adult patients on maintenance HD. Data on real-world use of calcimetics are needed to provide guidance in clinical practice.

Methods: In this observational study, Chronic HD patients treated with calcimetics for >3 months were included in analyses conducted within 90 days before and after a calcimetic initiation. Data on demographics, clinical history, laboratory values and calcimetic use were abstracted from medical charts.

Results: Interim data for 503 HD (96 CIN and 407 ETEL) patients from 57 sites across 15 countries are reported. At baseline, values were within normal limits within 90 days before a calcimetic initiation, were included. Data on demographics, clinical history, laboratory values and calcimetic use were abstracted from medical charts. For ETEL, the primary outcomes were: (i) the percent change in PTH from baseline (CIN vs. ETEL); (ii) the proportion of patients achieving >30% reduction in PTH levels from baseline (CIN vs. ETEL).

Conclusions: This is the largest real-world study on calcimetics following 2016 approval of ETEL in Europe. There were marked reductions in PTH, Ca, and P levels. Gastrointestinal events did not differ between ETEL and CIN groups.

Indirect Comparison of Treatments for Secondary Hyperparathyroidism Through a Network Meta-Analysis

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Background: Secondary hyperparathyroidism (SHPT) is a complication of chronic kidney disease (CKD) affecting mineral and bone metabolism and characterized by excessive parathyroid hormone (PTH) production and parathyroid hyperplasia. Currently, there is a need for well-tolerated treatment options. The objective of this study was to compare the efficacy and safety of ERC and PCT by assessing their effect on biomarkers PTH, Ca, and phosphate.

Methods: A systematic literature search (SLR) was performed in PubMed to identify randomized controlled trials (RCTs) to be included in a Network Meta-Analysis (NMA). In all articles, the comparator groups were consisting of placebo. A quality assessment was done using the GRADE method. The treatment effects of ERC and PCT were compared using random effects in a frequentist setting, and a sensitivity analysis was performed using a Bayesian approach. The study was registered in the PROSPERO database.

Results: Nine RCTs comprising a total of 1426 patients were included in the analyses. Compared to placebo, treatment with both PCT and ERC lowered levels of PTH in a statistically significant manner. No statistically significant differences in PTH reduction were found between PCT and ERC. Treatment with PCT significantly increased calcium levels compared to placebo (effect size: 0.30 mg/dL; 95% CI: 0.21-0.40 mg/dL), while the estimated effect of ERC on calcium (effect size: 0.10 mg/dL) was not significant (95% CI: -0.43 to 0.23 mg/dL). The calculated difference of effects between treatment with PCT and ERC shows that PCT significantly raises levels of calcium by 0.2 mg/dl (95% CI: -0.37 to -0.04 mg/dl).

Conclusions: This NMA showed that ERC is non inferior in lowering PTH levels vs. PCT. ERC displayed avoidance of clinically relevant increases in serum phosphorus and calcium, offering a new and well-tolerated treatment option for the early management of SHPT in patients with HD CKD.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.

Parathyrodeectomy Improves Muscular Function but Not Muscle Mass in Hemodialysis Patients with Severe Hyperparathyroidism

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Background: Increased levels of parathyroid hormone (PTH) are associated with a negative impact on the bone-muscle axis including sarcopenia and osteoporosis, and it is possible that treating hyperparathyroidism (HPT) could ameliorate these disturbances. However, the effects of parathyrodeectomy (PTX) on muscle mass, strength and performance have not been thoroughly investigated. This study aims to evaluate the impact of PTX on muscle mass, strength, and performance, body fat and resting energy expenditure (REE) in patients with severe HPT.

Methods: We are prospectively evaluating muscle mass, strength and performance of 30 patients before and after 6 months of PTX by using Actigraph GT3X accelerometer, timed-up-and-go (TuG), sit-to-stand-to-sit (STS) and muscle strength tests (dynamometry). Body composition was assessed by bioelectrical impedance x-ray apparatus, and REE was examined by indirect calorimetry. Participants completed the SARC-F questionnaire.

Results: At 6 months after PTX, 20 patients who already completed the protocol, showed a significant drop in PTH ([510(1360-1885) vs. 90(38-260) pg/mL, p<0.01], a significant increase of number of days/steps ([4759(3572-6185) vs. 6343(4123-8540) p 0.01] and improvements of strength tests: IHS(27a14 vs.31±14 kg p 0.01); SP(26±15 vs.31±16 kg p 0.01) and LP[24±23 vs.50±9 kg p 0.01]. In addition, there was an improvement of SARC-F score [1 parathyroid hormone value (PTH) recorded within 90 days before 90 days from parathyroidectomy. Therefore, we strongly feel that there is a need for larger controlled studies to elucidate specific guidelines for treating refractory HPT.

Indications and Justification for Parathyrodeectomy in Secondary Hyperparathyroidism

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Introduction: Hyperparathyroidism (HPT) is a common complication of CKD, which is treated by diet, medications and surgery. Parathyrodeectomy (PTX) is reserved for patients with refractory HPT. There are no guidelines for the timing or type of surgery. Our findings suggest that PTH-associated sarcopenia is mediated not only by a decrease in muscle mass but also by muscle dysfunction.
Introduction: Secondary hyperparathyroidism (SHPT) is a common complication of end stage kidney disease (ESKD) causing loss of bone density through increased osteoclastic activity. Imbalanced bone resorption and peri-trabecular fibrosis causes formation of hemosiderin-laden giant cell granulomas – brown tumors. Here is a case of palatal brown tumor in an ESKD patient which led to complications of hungry bone syndrome after parathyroidectomy.

Case Description: A 57 yo F with ESKD on HD and SHPT presented with a growing palatal mass. She reported difficulty chewing and shortness of breath. A friable mass was located over the hard palate. Labs showed serum calcium (Ca) 9.5 mg/dL, PTH 4477 pg/mL, phosphate 5.1 mg/dL, and alkaline phosphatase (ALP) 1124 U/L. Parathyroid scan showed a focus of activity in the left thyroid bed. She underwent a mass resection and parathyroidectomy. Pathology revealed an atypical parathyroid adenoma without features of carcinoma. Her postoperative course was complicated by hungry bone syndrome with prolonged hypocalcemia, hypomagnesemia and hypophosphatemia which persisted despite aggressive Ca supplementation and high Ca dialysate. She was also started on teriparatide to stimulate osteoblast activity and bone formation. After a long hospital course, she was discharged on oral supplemental Ca and calcitriol with close follow-up.

Discussion: Despite the advent of effective management strategies for renal osteodystrophy, we must be mindful of brown tumors. Surgical excision with parathyroidectomy is the preferred treatment. Post-operatively, patients must be monitored for hungry bone syndrome. As bone formation increases, rising ALP levels can serve as a biomarker for increasing Ca requirements requiring escalating dosage of supplements. Teriparatide is a recombinant human PTH which can be used to augment bone density.

PO0362

A Case of a Hemodialysis Patient with Secondary Hyperparathyroidism, Effectively Treated with Cinacalcet Hydrochloride but Not with Etelcalcetide

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Introduction: Although both cinacalcet hydrochloride and etelcalcetide are calcimimetics that directly inhibit the parathyroid hormone (PTH) secretion by activating the calcium (Ca)-sensing receptor, their binding sites are different.

Case Description: We report a rare case of a hemodialysis (HD) patient with secondary hyperparathyroidism, in whom cinacalcet was effective to reduce serum intact PTH (i-PTH) level but not etelcalcetide. A HD patient underwent total parathyroidectomy with autotransplantation to his right forearm 19 years ago. His i-PTH level had been almost controlled with 100 mg of cinacalcet. At a month after switching to etelcalcetide, serum i-PTH level increased from 269 pg/ml to 716 pg/ml. Although the dose of etelcalcetide was gradually increased to 45 mg/week, the maximal dose of etelcalcetide, serum i-PTH level increased to 919 pg/ml. Therefore, etelcalcetide was switched to 50 mg/day of cinacalcet, and his i-PTH level decreased to 208 pg/ml.

Discussion: Thus, the present case has resistance to etelcalcetide treatment but not cinacalcet, suggesting that his parathyroid gland might have partial deletion or mutation in the extracellular domain of the Ca-sensing receptor. Therefore, we should consider the possibility of resistance to etelcalcetide treatment while treating secondary hyperparathyroidism.

PO0363

Hypercalcemia Resulting from Spindle Cell Tumor-Induced Calcitriol Production

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Introduction: Less than 1% of cases of hypercalcemia of malignancy are caused by overproduction and release of 1,25-dihydroxy vitamin D (calcitriol) by tumor cells.1 Calcitriol excess has been identified most often in sarcoidosis, hematologic malignancy, and infection.2 We present a patient who developed severe hypercalcemia from a spindle cell tumor and acute kidney injury as a result of spindle cell neoplasm-mediated calcitriol excess, with normalization of serum calcium and creatinine in response to treatment with prednisone.

Case Description: A 65yo man with a history of a large retroperitoneal mass presented with malaise. He was not taking calcium or vitamin D supplements. Initial labs showed serum calcium 15.7 mg/dL, 1,25-dihydroxy Vit. D 126 pg/mL (elevated), and creatinine 4.5 mg/dL. His PTH 8 pg/mL, PTHrP 0.8 pmol/L, and 25-hydroxy Vit. D 26 ng/mL were suppressed or normal. SPEP, UPEP, serum immunofixation, and serum free light chains were unremarkable. Pathology of the mass revealed a spindle cell neoplasm embedded within fibrous stroma. Prednisone was prescribed to suppress tumor-associated calcitriol production. His serum calcitriol level fell to 33.2 pg/mL, with a serum calcium of 10.9 mg/dL, after taking prednisone 40 mg/day for 2 weeks. His calcitriol 39.2 pg/mL, calcium 8.7 mg/dL, and creatinine 0.81 mg/dL levels were normal while on prednisone 20 mg/day at 76 days after starting corticosteroids and before any anti-tumor therapy or surgical debulking.

Discussion: The conversion of 25-hydroxy Vit. D to calcitriol is catalyzed by 1-alpha hydroxylase, a phenomenon that can occur in extra-renal tissues, such as within macrophages in sarcoid tissue.3,4 We hypothesize that elevated 1-alpha hydroxylase activity in spindle tumor cells or in activated macrophages within tumor stroma was responsible for excess calcitriol production and the resultant hypercalcemia. Corticosteroids inhibit the 1-alpha hydroxylase conversion of 25-hydroxy Vit. D to calcitriol and have been used successfully to reduce malignancy-induced calcitriol production.5,6 This case provides evidence of severe hypercalcemia due to endogenous production of calcitriol associated with a large spindle cell neoplasm, with rapid normalization of both serum calcium and calcitriol levels in response to treatment with prednisone, without anti-tumor therapy or surgical debulking.
Unexplained Persistent Hypercalcemia After Liver Transplantation
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Introduction: Hypercalcemia has been reported as a sequela of chronic liver disease in association with hyperbilirubinemia. Previous reports of hypercalcemia post liver transplant were thought to be potential rare complication of altered bone metabolism under intense immunosuppression and from prolonged immobilization. However the pathogenesis of this rare phenomenon has not been clarified to this date. We present cases of unexplained severe persistent hypercalcemia in three liver transplant recipients.

Case Description: Hypercalcemia post liver transplant in 3 recipients described in Table 1 and calcium trends shown in Figure 1.

Discussion: Extensive work up for hypercalcemia was negative in our patients. Although immobilization could be contributory, other unrecognized possibilities are plausible. Immunosuppression with steroids and other agents, especially cyclosporine, has been hypothesized to cause calcium imbalance by inhibiting T cell activation and transcription of interleukin-2 which are involved in bone turnover. Depletion of T cells upregulates osteoclastogenesis through prostaglandin production; by interfering with receptor activator of nuclear factor kappa ligand (RANK-L) and osteoprotegerin on osteoblasts. However, only one patient was on cyclosporine. Other, yet unidentified factors modifying calcium metabolism could be involved. We would like to draw attention to this fascinating phenomenon in order to gain more insight. Low dialysate calcium, pharmacotherapy (Calcitonin, Pamidronate and Denusomab) along with improved mobility had successfully lowered serum calcium in these patients. One patient had hypocalcemia after Denusomab administration, hence needed careful monitoring.

Descriptions of hypercalcemia cases post liver transplant.

PO0365

A Rare Case of Hyperthyroidism Presenting with Symptomatic Hypercalcemia
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Introduction: Primary hyperparathyroidism and hypercalcemia are by far the most common causes of hypercalcemia in clinical practice. Asymptomatic hypercalcemia with minimally raise calcium levels have been documented in 20% of cases of hyperthyroidism as well and is related to increased bone resorption by osteoclasts and subsequent release of calcium into circulation. We describe a rare case of hypercalcemia with symptomatic hypercalcemia as the first clinical manifestation.

Case Description: A 60 year old male with a history significant for chronic kidney disease, stroke and hypertension was admitted to the hospital following a syncopal event. Physical examination and baseline investigations were normal other than elevated calcium levels of 12.1 mg/dL. PTH levels and PTHp levels were normal ruling out hyperparathyroidism and paraneoplastic related hypercalcemia. Vitamin D levels were also normal. Work up for hyperthyroidism was done which showed extremely low levels of TSH (<0.005 mU/L) with elevated T3 and T4 levels (12.9 ng/dL and 5.52 ng/dL respectively). Thyroid scan was performed which showed significant thyroiditis. Thyrotrphin receptor antibody test also came positive. The patient was diagnosed with Graves’ disease based on the laboratory investigations and subsequently started on 5 mg methimazole TID. He also received one dose of zolendronic acid in the hospital. His calcium levels stabilized, falling from 12.4 to 9-10 mg/dL within 1 month. Patient received methimazole for a total of 7 months after which it was discontinued as his TSH levels (1.38 mU/mL), T3 levels (2.19 ng/dL) and T4 (0.78ng/dL) normalized. Patient further underwent radioiodine ablation for the treatment of Graves’ disease.

Discussion: In past, multiple cases have been reported of concurrent hyperparathyroidism or vitamin D deficiency in hyperthyroid patients. This case is unique as the patient presented with symptomatic hypercalcemia in the absence of other causes and in the absence of other common symptoms of hyperthyroidism. To our knowledge, only 2 cases of hyperthyroidism have been reported previously with hypercalcemia as the first clinical manifestation. Clinicians should be aware of association of hyperparathyroidism with hyperthyroidism as it will facilitate early diagnosis and appropriate intervention.

PO0366

Low Phosphate and Low Calcium Levels Predict Higher Risk for Adverse Events of Maintenance Hemodialysis
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Background: It is well known higher serum levels of phosphate (P) and calcium (Ca) associated with higher risk of cardiovascular disease (CVD) and premature death of hemodialysis (HD) patients. However, in the current situation that guidelines penetrated widely, there are few reports which investigated the association CKD-MBD related factors and adverse events of HD patients.

Methods: The study design was the multiple centers, observational study for 3 years. 989 HD patients were enrolled in this study. Hb, ferritin, creatinine, total protein, albumin, total cholesterol, Ca and P levels were measured every 3 months. High-sensitivity C-reactive protein (hsCRP) and intact-parathyroid hormone (int-PTH) were also measured every six months. The correlation between CKD-MBD factors and adverse events were evaluated by the time depended cox hazard model.

Results: 82% (P), 83% (Ca), and 78% (int-PTH) of patients were maintained in a target range. After correlated with age, sex, past history of CVD, Hb, albumin, and hsCRP, compared with the patients with target levels of P, patients with low P levels were significantly higher risk for CVD (P=0.042, HR:2.27), hospitalization (P=0.034, HR:2.44), and all caused mortality (P=0.03, HR:2.29). Compared with the patients who maintain target int-PTH levels, patients with lower (P=0.025, HR:1.46) and higher (P=0.04, HR:1.44) int-PTH were significantly higher risk for hospitalization. Furthermore, compared with the patients who maintain the target levels both of Ca and P, the patients with target Ca and low P levels (P=0.042, HR: 2.75) were significantly higher risk for CVD. And compared with the patients who maintain the target levels both of Ca and P, the patients with low Ca and low P levels (P<0.001, HR: 4.4) and target Ca and low P levels (P=0.22, HR: 2.0) were significantly higher risk for hospitalization.

Conclusions: Although after correlated by several clinical factors, we found that patients who maintain the low serum P levels beared significantly higher risk for CVD and all caused mortality than patients who maintained higher Ca and P levels. Without doubt, extremely higher serum P, Ca, and int-PTH levels should be treated according to guidelines. However, in the current situation that guidelines penetrated widely, CKD-MBD managements which considered the clinical conditions of low P, Ca, and int-PTH are needed.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: Patient level data was collected via an online, HIPAA-compliant form in June 2019 as part of an independent cohort study. A total of 1,615 patient records (789 in-center HD, 200 PD, and 26 home HD) were submitted by 159 nephrologists. Patients had been on dialysis for at least six months (Mean: 26; Median: 15) and most were in LDO-affiliated units.

Results: Patients in the consistently high group had a dialysis vintage longer than those consistently in target or in the target-high variability group (36 months vs. 23 months) and were also younger on average (53 years vs. 61 years). Those in the consistently high and high-target group (CH/HT) had a 37% higher daily pill burden (from binders) than those consistently in target. Patients dialyzing in Fresenius units were the most likely to be consistently in target (27%). Compared to those consistently in target, those in the CH/HT group were significantly more likely to have diabetes, obesity, heart failure and coronary artery disease. They were also six times as likely to have poorly controlled hypertension. Ethically also was correlated with phosphate control with a disproportionate percent of non-white patients in the consistently high and high-target variability groups.

Conclusions: Not only is hyperphosphatemia rampant at any given time, but only a small minority of patients on phosphate binders (19%) are able to achieve consistent control, most patients fluctuate in and out of target. Increased phosphate binder dosing was not associated with better control and suggests that a new approach to the management of hyperphosphatemia is warranted.

PO0368

Hyperphosphatemia with Elevated Serum FGF-23 and PTH, Reduced Calciuretic, and Normal FGF7 Concentrations Characterizes Chronic Renal Failure in Humans

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Background: Fibroblast growth factor 23 (FGK23), a phosphatonin produced by osteocytes, regulates phosphate (Pi) homeostasis and is increased in CKD. A recent study showed plasma low serum (s) concentrations of FGF7 may contribute to hyperphosphatemia in patients with hypophosphatemia, and are elevated in some patients with tumor-induced osteomalacia and hypophosphatemia. We hypothesized that FGF7 might play a role in compensating for elevated Pi concentrations in CKD.

Methods: We measured serum concentrations of intact FGF7 (iFGF7, R&D Systems), iFGF23 (Eagle Biosciences), intact parathyroid hormone (iPTH) by enzyme-linked immunosorbent assays and determined s Pi, and 1,25-dihydroxyvitamin D (1,25(OH)2D, by mass spectrometry) among 75 non-kidney transplant patients with varied estimated glomerular filtration rate (eGFR). Relationships between these parameters and eGFR were explored.

Results: For iFGF7 of 60 or more (n=29), 45-59 (n=14), 30-44 (n=9), 25-29 (n=13), and under 15 u/mL 1.73 m2 (n=10), the median (IQR) s FGF7 concentrations were 41.9 (33-147.4), 56.4 (47-458.6), 62.9 (53.2-75.6), 117.5 (87.6-137.2), and 327.5 (195.1-456.3) pg/mL, respectively (P<0.01). At comparable eGFRs, median (IQR) s FGF7 concentrations were 46.1 (40.8-56.1), 43.1 (39.2-49.2), 45.4 (38.5-53.8), 47.7 (38.5-54.6), and 46.1 (40.8-54.6) pg/mL, respectively (P<0.01). Negative correlations between Pi (r = -0.46; P<0.01), iPTH and iFGF7 (r = -0.33; P<0.05), and a positive correlation between 1,25(OH)2D and eGFR (r = 0.51; P<0.01) were demonstrated. Significant increases in iFGF23, iPTH, and Pi were observed at eGFRs of less than 33 (95% CI, 26.40-40.05), 29 (95% CI, 22.51-35.36) and 22 mL/min/1.73 m2 (95% CI, 19.25-25.51), respectively. More significantly, significant decreases in 1,25(OH)2D were observed at eGFRs of less than 35 mL/min/1.73 m2 (95% CI, 36.57-81.43). iFGF7 concentrations did not significantly correlate with eGFR, Pi, iFGF23, iPTH, and 1,25(OH)2D.

Conclusions: Increases in serum concentrations of Pi, iFGF23, iPTH, but not iFGF7, and decreases in 1,25(OH)2D are observed as renal function declines in CKD.

Funding: Other NIH Support - R01DK107870

PO0369

Effects of a Reduced Phosphorous Diet on the Circulating Metabolome in Healthy Adults

Shejiut Paul, Orlando M. Gutierrez. University of Alabama at Birmingham, Birmingham, AL.

Background: Excess phosphorus intake is linked to hypertension, heart failure, and disorders of bone and mineral metabolism. The reasons for these associations are unclear. Most prior work on the effects of diet phosphorus have focused on changes in specific endocrine factors in the blood. Less is known about the effects of nutritional phosphorus on the human metabolome, which represents the integrated biologic response to changes in diet.

Methods: In 37 healthy adults, we performed a global metabolomic analysis using untargeted mass spectrometry in plasma samples obtained after consuming a high phosphorus diet (1000 mg/day) for 2 weeks (considered baseline for this study) and after consuming a reduced phosphorus diet (1200 mg/day) fo 6 weeks. Metabolomic profiling was conducted by Metabolon, Inc. using standard protocols. Matched pairs t-tests were used to identify analytes that significantly changed from baseline to six weeks, with each individual serving as his or her own control.

Results: The mean age of study participants was 34±12 years, 36% were black and 49% were men. A total of 222 metabolites significantly changed from baseline to six weeks on a reduced phosphorus diet using a false discovery rate <0.05 to take into account multiple comparisons. Major analytes which differed in six-week vs. baseline samples included metabolites related to tryptophan metabolism, microbiome related biochemicals, urea cycle, bile acids, corticosteroids and androgenic steroids, and acyl carnitines. Changes in specific analytes of note within each of these pathways are depicted in the Figure.

Conclusions: In healthy adults, a reduced phosphorus diet altered metabolites related to the microbiome, urea cycle, steroid hormones, energy and lipid metabolism.

Funding: Private Foundation Support

PO0370

Hospital Admission Rates Among Hemodialysis Patients with Persistent Hyperphosphatemia Who Were Prescribed Changes in Phosphate Binder Treatment: A Retrospective Analysis of Real-World Data

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Background: Phosphate binders (PB) may have different formulations, potency, and pill burden, however, there is limited data on hard outcomes to support decisions in PB therapy. The goal of this retrospective analysis is to determine the rate of all-cause hospital admissions of patients who, at baseline, remained hyperphosphatemic despite treatment with sevelamer carbonate (SC) and had prescriptions to either (1) switch to monotherapy sucroferic oxihydroxyde (SO) or (2) switched to Non-SO binders [Calcium Acetate, Lanthanum Carbonate, or Ferric Citrate] or added one of these PBs to SC therapy.

Methods: Deidentified clinical and prescription data were retrospectively extracted from the Fresenius Kidney Care database and pharmacy records. All prescription changes were the result of routine clinical care. We aimed to control for selection bias by using Inverse Probability of Treatment Weighting (IPTW). This method was chosen due to its ability to balance baseline characteristics between the two groups and maintain adequate sample size.

Results: We identified 1,076 patients with baseline hyperphosphatemia despite SC prescription who switched PB therapy, including 319 patients with SO therapy and 757 patients with Non-SO therapy. Patients switched to SO had 27 fewer hospital admissions per 100 patient-years compared to patients with Non-SO therapy (Table 1).

Conclusions: In a retrospective database analysis of hemodialysis patients previously treated with sevelamer carbonate and switched to SO or Non-SO phosphate binder therapy, patients switched to SO monotherapy had a lower rate of hospital admissions than patients switched to other, non-SO phosphate binders.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

Variables included in the Poisson regression model: HD vintage, congestive heart failure status, serum phosphorus and categories, iPTH and categories, (iPTH)
PO0371
An Observational Analysis of Hospital Admissions and Total Member Costs Associated with the Use of Various Phosphate Binders Used in Dialysis Patients Included in ESRD Seamless Care Organizations
Kristian C. Lindemann,1 Christina Ajala,1 Melissa M. Rosen,2 Claude Mullon,2 Robert J. Kossmann,3 Terry L. Ketchersid,2 Linda Ficciocchi,2 Fresenius Medical Care North America, Waltham, MA; 1Fresenius Medical Care Renal Therapies Group, Waltham, MA; 2Fresenius Medical Care North America, Waltham, MA.

Background: A prior observational study using real world data and estimates of hospitalization costs based on national data, found patients continuing sucralfate oxycodroxide (SO) therapy had fewer hospital admissions and expected lower healthcare costs when compared to patients switching to another phosphate binder (PB). End Stage Renal Disease (ESRD) Seamless Care Organizations (ESCOs) coordinate treatment for patients with chronic kidney disease (CKD). The purpose of this study was to review hospitalization costs and costs associated with various PBs prescribed to dialysis patients in ESCOs.

Methods: Patients included in the analysis had PBs prescribed during 2016-2018 in ESCOs along with parathyroid (PTH) levels <600 pg/ml. Aggregated utilization and cost data from 24 ESCOs were used over 3 years. Total hospital admissions and member months (MM) were used to calculate hospital admission rates and rate ratios. The statements contained in this document are solely those of the authors and do not necessarily reflect the view or policies of CMS. The authors assume responsibility for the accuracy and completeness of the information contained in this document.

Results: Hospital admission rates were found to be lower for SO (Table). Compared to MM treated with SO, an increased hospital admission rate of 11%, 20%, 32%, and 42% was observed for MM treated with SEV, CaAC, FC, and LC, respectively. In addition, the total per member per month (PMPM) healthcare costs were lower for SO ($5670) compared to FC ($5908), LAN ($6104), CaAC ($6303), and SEV ($6354), respectively.

Conclusions: Data from 24 ESCOs showed differences in hospital admission rates with the lowest rate in SO (7.97 per 100-member month (MM)) and the highest in CaAc (11.28 per 100-MM). In addition, total costs of care per MM where SO was prescribed were lower when compared to other PBs.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO0372
Determining the Value of Pharmaceutical Treatment of Hyperphosphatemia with Phosphate Binders: A Systematic Review
Lindisella Mullon,1 Melissa M. Rosen,1 Michael S. Anger,1 Robert J. Kossmann,2 Claude Mullon,1 Fresenius Medical Care Renal Therapies Group, Waltham, MA; 1Fresenius Medical Care North America, Waltham, MA.

Background: Phosphate binders (PBs) are the primary therapeutic treatment for hyperphosphatemia in ESRD patients receiving dialysis. Medication spending on PBs has been estimated to be over $1.5 billion. There is increased focus on value-based prescribing as a method to control rising healthcare spending in the U.S. However, guidance to support such decisions is limited. The purpose of this study was to review economic evaluations of PBs to understand if specific binders are associated with greater value to patients and payers.

Methods: We conducted a systematic literature review with results restricted to economic evaluations published in English in peer reviewed journals between January 2015 and May 2020. Studies included in the review reported cost-effectiveness outcomes. Studies were included if they reported cost-effectiveness outcomes.

Results: After removing irrelevant articles and duplicates, 8 publications were found that met our inclusion criteria. Four (50%) studies compared either sevelamer carbonate (SEV) or lanthanum carbonate (LC) to calcium-based binders. SEV or LC was cost-effective compared to calcium-based binders. Two studies focused on ferric citrate (FC) with one comparing FC to the standard of care (either calcium acetate, SEV, or LC), and the other to SEV or calcium acetate. The results favored FC based on differences in the use of erythropoiesis-stimulating agents and hospitalization risk. However, these studies did not examine the potential for unsafe levels of iron absorption associated with FC use. The remaining two studies evaluated sucralfate oxycodroxide (SO). One study found SO to be cost-effective relative to SEV based on clinical trial data. The other analysis looked at patients prescribed SO for two years compared to those who discontinued use after 90 days and switched to another binder. This model estimated that SO use had the potential to be cost-saving based on reduced risk of hospitalization. We were unable to find an economic evaluation that compared the two iron-based binders, SO to FC.

Conclusions: This review demonstrates the need for more economic evaluations of phosphate binders. One of the cost-effectiveness analysis was found that compared two non-calcium binders (SO vs SEV) head-to-head. In addition to cost analyses, payers may benefit from reviewing real-world data to examine the clinical benefits of specific phosphate binders.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO0373
Effect of Lanthanum Carbonate on Blood Pressure in CKD: The COMBINE TRIAL
Mitra Jamshidian,1 Brett Larive,1 Jennifer J. Gassman,1 Kalani L. Raphael,4 Michel Chonchol,2 Joachim H. Ix,1 Charles Ginsberg,1 Cleveland Clinic, Cleveland, OH; 1University of Colorado Denver School of Medicine, Aurora, CO; 2University of California San Diego School of Medicine, La Jolla, CA; 3University of Utah Health, Salt Lake City, UT.

Background: Higher serum phosphate concentrations are associated with vascular calcification, cardiovascular events, and all-cause mortality. Emerging data suggests that higher serum phosphate may also be associated with increased blood pressure (BP). The effect of phosphate-lowering medication on BP has not been studied in a chronic kidney disease (CKD) cohort.

Methods: We evaluated patients from the CKD Optimal Management with Binders and Nicotinamide (COMBINE) Trial, a randomized, double-blind, placebo-controlled trial of phosphate binders and/or nicotinamide in patients with eGFR 20-45 ml/min/1.73m2. Our primary end point for this analysis was 12-month change in systolic BP (SBP). Randomization to lanthanum vs non-lanthanum treatment arms was our primary predictor variable. The secondary predictor variable was 24-hour urine phosphate excretion (a marker of dietary phosphate intake).

Results: 205 participants underwent randomization. The mean ± SD baseline age was 69±12 years, eGFR was 32±7 ml/min per 1.73 m2, and SBP was 129±17 mmHg. Over the 12-month trial, compared to the non-lanthanum arms (N=102), SBP in the lanthanum arms (N=103) rose by 5 mm Hg (P value 0.0497) after adjusting for baseline BP, age, sex, baseline eGFR, clinical center and number of anti-hypertensives over time. Within the lanthanum arms SBP rose by 5 mm Hg (95% CI 1, 9 mm Hg) and diastolic BP rose by 2 mm Hg (95% CI 0.4, 4 mm Hg). BP did not change in the non-lanthanum arms. There was no association between 24-hour urine phosphate excretion and change in BP.

Conclusions: Among trial participants with moderate to severe CKD, randomization to lanthanum carbonate was associated with increased SBP. Future studies should determine whether lanthanum carbonate influences absorption of anti-hypertensive medications.

Funding: NIDDK Support, Commercial Support - Shire, Private Foundation Support

PO0374
Efficacy of Tenapanor for the Control of Serum Phosphorus in Patients with CKD on Dialysis: Novel Mechanism of Action Allows for Both Monotherapy and Dual-Mechanism Approach
David P. Rosenbaum, Yang Yang, Ardelyx Inc, Fremont, CA.

Background: Tenapanor (TEN) is an investigational, first-in-class, non-binder, phosphate absorption inhibitor being developed to control serum phosphorus (sP) in patients with chronic kidney disease (CKD) on dialysis. It has a unique mechanism of action and acts locally in the gut to inhibit the sodium-hydrogen exchanger 3 (NHE3). This results in the tightening of epithelial cell junctions, reducing paracellular uptake of phosphate, the primary pathway of phosphate absorption, thereby reducing serum phosphorus concentrations.

Methods: Two Phase 3 studies were completed. An 8-week, double-blind (DB), randomized treatment period (RT) with a 4-week placebo (PBO)-controlled randomized withdrawal period (WR) examining the efficacy of TEN as monotherapy to treat hyperphosphatemia (HP) in patients with CKD on dialysis (NCT03427125) and a 4-week, randomized, DB, PBO-controlled study examining the efficacy of TEN administered with phosphate binders (BIND) using a dual mechanism approach to treat patients with uncontrolled HP (≥5.5 mg/dL) in patients with CKD on dialysis (NCT 03824587).

Results: In the monotherapy study, 219 patients were randomized to the RT, 164 patients completed the RT, and of these, 152 (93%) completed the WR. TEN achieved the primary endpoint with a LS mean difference of -0.8% (95% CI: -1.4, -0.2, p=0.01) in sP between TEN and PBO during the WR period. Approximately 50% of the patients treated with TEN achieved a mean sP reduction of 2.56 mg/dl from baseline to the end of the RT period. In the dual mechanism study, 236 patients were randomized to treatment. At week 4, the mean change in sP was significantly greater in the TEN+BIND arm (−0.84 mg/dl v. −0.19 mg/dl in the PBO+BIND arm, p=0.0004). Twice as many patients achieved sP<5.5 mg/dl with TEN+BIND than with PBO+BIND (up to 49.1% v. up to 23.5%, p<0.01). In both studies, the most common adverse event for patients treated with TEN was low stools/diarrhea, leading to discontinuation in 7.8% and 3.4% of patients respectively.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0375
Efficacy and Safety of Add-on Tenapanor to Phosphate Binders for Refractory Hyperphosphatemia in Japanese Patients on Hemodialysis: A Phase 2, Double-Blind Study
Tadato Akizawa,1 Yu Sato,2 Masayuki Takamura,3 Hironori Kanda,2 Masafumi Fukakusa4 (Showa University School of Medicine, Tokyo, Japan), 2Kyoyuki Kirin Co., Ltd., Tokyo, Japan; 3Tokai University School of Medicine, Kanagawa, Japan.

Background: Among hemodialysis (HD) patients, some patients have poorly controlled serum phosphorus levels, even while using phosphate binders (PB). Tenapanor is a novel agent, which reduces phosphate uptake by selectively inhibiting sodium/hydrogen exchanger isoform NHE3 on the apical surface of the enterocytes and therefore decreasing paracellular phosphate permeability. The mechanism of action is different from conventional PB used to treat hyperphosphatemia. The additional treatment of tenapanor is expected to reduce serum phosphorus levels in HD patients with poorly managed serum phosphorus levels by PB. Here, we evaluated the efficacy and safety of adding tenapanor to PB for refractory hyperphosphatemia in patients on HD.

Methods: This was a multicenter, randomized, double-blind, placebo (PLA)-controlled, Ph2 study. The study consisted of a screening period, a 2 or 3-week observation period, and a 6-week treatment period. Patients whose serum phosphorus level was ≥6.1 and <10.0 mg/dL with PB were randomized to either tenapanor (TEN) or PB-PLA group in 1:1 ratio. Starting dose of tenapanor was 30 mg BID, which could be reduced in a step-wise manner (30, 20, 10 and 5 mg BID) at the investigator’s discretion, based on GI tolerability. The primary endpoint was the change in serum phosphorus level from baseline value at the end of treatment.

Results: 47 subjects were randomized. Mean change in serum phosphorus level from baseline was 1.99 mg/dL in the tenapanor group and 0.08 mg/dL in the PB group (95% CI: −2.89, 1.26 mg/dL, p<0.001). The achievement ratio of target serum phosphorus level (≤3.5, ≥3.0 mg/dL at the end of treatment was 87.0% in the tenapanor group and 37.5% in the PLA group. Diarrhea was the most frequent adverse event (tenapanor=65.2%; PLA=16.7%), all of which were of mild to moderate severity.

Conclusions: Tenapanor showed a significant decrease in serum phosphorus levels compared with PLA (p<0.001) under PB combination. This result suggests that coadministration of tenapanor with PB could satisfy the unmet needs to better control serum phosphorus in HD patients with refractory hyperphosphatemia.

Funding: Commercial Support - Kyoyuki Kirin Co., Ltd.

PO0376
Tolerability of Tenapanor, an Investigational, First-in-Class, Non-Binder Therapy for the Control of Serum Phosphorus in Patients with CKD on Dialysis
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Background: Phosphate binders are associated with gastrointestinal (GI) tolerability issues including constipation, diarrhea, nausea, and vomiting. Tenapanor (TEN), a first in class non-binder therapy, blocks the paracellular absorption of phosphate in the GI tract by local inhibition of the sodium-hydrogen exchanger (NHE3), and may have a different GI profile because of its unique mechanism which also reduces dietary sodium absorption, increasing the sodium and water content of stool.

Methods: Data from a 12-week monotherapy study (TEN201), a 52-week monotherapy study (PHREEDOM), and a 4-week combination study (AMPLIFY) were analyzed to evaluate the GI tolerability of TEN. Adverse events were coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA). A linear mixed model with generalized estimating equations (GEE) was used to compare the primary endpoint of diarrhea incidence between the groups (least square means, 95% CI).

Results: 47 subjects were randomized. Mean change in serum phosphorus level from baseline was −1.99 mg/dL in the tenapanor group and 0.08 mg/dL in the PLA group (95%CI: −2.89, −1.26 mg/dL, p<0.001). The achievement ratio of target serum phosphorus level (≤3.5, ≥3.0 mg/dL at the end of treatment was 87.0% in the tenapanor group and 37.5% in the PLA group. Diarrhea was the most frequent adverse event (tenapanor=65.2%; PLA=16.7%), all of which were of mild to moderate severity.

Conclusions: Tenapanor showed a significant decrease in serum phosphorus levels compared with PLA (p<0.001) under PB combination. This result suggests that coadministration of tenapanor with PB could satisfy the unmet needs to better control serum phosphorus in HD patients with refractory hyperphosphatemia.

Funding: Commercial Support - Kyoyuki Kirin Co., Ltd.

PO0377
Changes in Serum Phosphorus Among Patients Who Switch from Sevelamer Carbonate to Sucroferric Oxylolate or Other Phosphate Binders After Persistent Hyperphosphatemia
Vidhya Parameswaran,1 Linda Ficocelli,1 Claude Mullon,1 Robert J. Kossmann,2 Michael S. Anger,1 Sagar U. Nigwekar,3 1Fresenius Medical Care Renal Therapies Group, Waltham, MA; 2Fresenius Medical Care North America, Waltham, MA; 3Massachusetts General Hospital, Boston, MA.

Background: Despite being prescribed phosphate binders (PB), many HD patients have persistent hyperphosphatemia. The current analysis examines serum phosphorus (sP) and pill burden changes among patients who have 3 months of sP > 5.5 mg/dL despite prescription of sevelamer carbonate (SC) and switched to (1) sucroferric oxylolate (SO) monotherapy, or (2) Non-SO binders [Calcitral (Caltrate®) + Calcium Carbonate, or Ferric Citrate] monotherapy or added one of these PBs to SC therapy.

Methods: All deidentified clinical and prescription data were extracted retrospectively from the Fresenius Kidney Care database. Follow-up was divided into quarters (Q1-Q4) to determine mean sP and PB pills/day. We applied Propensity Score Matching (PSM), Coarsened Exact Matching (CEM), and Inverse Probability of Treatment Weighting (IPTW) to address potential confounding/seletion bias. PSM and CEM were used to match patients using overall PSM or agreement with each variable (CEM), and IPTW used weights on all patients.

Results: We identified 1,076 SC patients with baseline hyperphosphatemia who switched to SO (319 patients) and Non-SO (757 patients) PB therapy. Results from IPTW method that allowed retention of the entire sample size (n=1,076) are presented in Table 1. Application of CEM and PB pill burden method identified 197 and 257 matches for SO patients, respectively and noted results comparable to IPTW.

Conclusions: In a retrospective database analysis of HD patients with persistent hyperphosphatemia despite being prescribed SC, patients switched to SO had a mean sP decrease of 1.1 mg/dL compared to 0.79 mg/dL decrease among patients prescribed non-SO PBs. The PB pills/day decreased by 6.3 for SO-treated and 2.2 for Non-SO-treated patients.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean sP (mg/dL)</th>
<th>Mean P (Pills/day)</th>
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</thead>
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<tr>
<td>SC</td>
<td>5.5±2.7</td>
<td>1.63±0.43</td>
</tr>
<tr>
<td>SO</td>
<td>4.7±2.5</td>
<td>1.63±0.43</td>
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<tr>
<td>Non-SO</td>
<td>6.0±2.6</td>
<td>2.54±0.43</td>
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</tbody>
</table>

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Endnotes:
1Showa University School of Medicine, Tokyo, Japan; 2Michael Mullon, Fresenius Medical Care, Inc., Waltham, MA; 3Massachusetts General Hospital, Boston, MA.

Poster 164
Changes in Serum Phosphorus and Pill Burden in Peritoneal Dialysis (PD) Patients Treated with Sucroferric Oxyhydroxide (SO) as Part of Routine Clinical Care: A Contemporary Cohort

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Background: Previous real-world analyses of SO in PD patients (pts) included pts first prescribed SO within the first 2 years of SO availability in the US (2014 Cohort: Kalantar 2018). A more contemporary cohort of pts prescribed SO may have different patient characteristics or treatment patterns than earlier SO pts. The current retrospective study assessed changes in serum phosphorus (sP) and phosphate binder (PB) pill burden in PD pts recently and previously prescribed SO.

Methods: Included were adult Fresenius Kidney Care PD pts first prescribed SO monotherapy during 5/2018- 5/2019 with PB monotherapy during a 3-month baseline (BL), and sP measured the month before SO initiation (-M1) and 6-months of the follow-up (2108 Cohort). Means were calculated monthly (-M1, M1-M6) for PB pills/day and monthly labs and quarterly for iPTH using mixed-effects linear regression.

Results: At BL, the 2018 Cohort (n=201) included slightly older pts (52.3 vs 50.6 yrs) with shorter dialysis vintage (22 vs 29 months) and different BL PB: sevelamer (42 vs 63%), calcium acetate (35 vs 21%), lanthanum (3 vs 5%), ferric citrate (12 vs 0%), or switched PB (8 vs 11%) compared to 2014 cohort. Lower pill burden (7 vs 10) and sP (6.52 vs 6.59) at BL were observed in 2018 cohort. In the 2018 cohort, pts achieving sP≤5 mg/dL increased from 21.9% at -1M to 40.5-47.3% during follow-up and the pattern was similar in 2014 cohort (25.8% at -1 M to 35.3-44.4% at follow-up). Mean SO pill-day was higher (4.7) in 2018-2019 cohort than the 2014 cohort (4.3).

Conclusions: PD pts prescribed SO as part of routine care in 2018 and 2014 experienced significant reductions in sP, and PB pill burden, and an increase in pts with sP≤5mg/dL.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group
PO0382

Dose-Response Efficacy and Tolerability of Tenapanor on Hyperphosphatemia in Japanese Hemodialysis Patients: Results of a Randomized Phase 2 Study

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Background: Tenapanor is a novel, non-binder, targeted therapy that reduces paracellular phosphate absorption in the gut by selectively inhibiting the intestinal sodium/hydrogen exchanger isoform NHE3. In a US clinical trial by Ardelyx, Inc., tenapanor significantly reduced serum phosphate level in hemodialysis (HD) patients with hyperphosphatemia as compared to the placebo (PLA). The purpose of this study was to confirm the efficacy, dose-response and tolerability of tenapanor on hyperphosphatemia in Japanese HD patients.

Methods: This was a multicenter, randomized, double-blind, PLA-controlled, parallel-group and dose-finding Ph2 study. The study consisted of a screening, a 2 or 3-week 1st washout (WO) period, a 6-week treatment period, and a 3-week 2nd WO period. Patients were enrolled when screening serum phosphate level was 3.5–6.0 mg/dL and increased by at least 0.1 mg/dL after 1–1.9 mg/dL after 1st WO. Thereafter patients were randomized to one of five groups (PLA, tenapanor 5 mg, 10 mg, 30 mg or 30 mg down titration (DT) twice/day). 30 mg DT group could be down-titrated in a step-wise manner to 10, 5 and 0 mg on the basis of GI tolerability. The primary endpoint was the mean change in serum phosphate level from baseline to end of treatment in each group.

Results: 207 subjects were enrolled (41 or 42 subjects were randomized to each group). The mean change in serum phosphate at the end of treatment from baseline was 0.64 mg/dL in the PLA group, −0.93 mg/dL, in the 10 mg group, −1.36 mg/dL, in the 30 mg group and −1.99 mg/dL in the 30 mg DT group (p<0.001 in all tenapanor groups vs PLA). The major adverse event was diarrhea, which occurred in a dose-dependent manner (PLA: 22.0%, tenapanor 5 mg: 57.1%, 10 mg: 65.9%, 30 mg: 76.2%, 30 mg DT: 70.7%). Most of the events were mild in severity, and, in each tenapanor group, only 1 to 3 subjects were discontinued from the study due to diarrhea.

Conclusions: Tenapanor was well tolerated in Japanese HD patients and significantly decreased serum phosphate level in a dose-dependent manner compared with PLA (p<0.01).

Funding: Commercial Support - Kyowa Kirin Co., Ltd.

PO0383

CKD and Vitamin D Status Alter Vitamin D Metabolism

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Background: Up to 90% of people with chronic kidney disease (CKD) are vitamin D (ViD) deficient. ViD is subsequently prescribed and has documented health benefits, including nephro-protective, cardio-protective and immune-protective. This paired study sought to evaluate and compare ViD metabolism in CKD patients and healthy controls (HC) under both ViD deficiency and repletion.

Results: Compared to the 2014 Cohort, the 2018 cohort (n=208) was larger (vs 424), older (56 vs 51 years with shorter dialysis vintage vs 56 months), more likely prescribed calcium acetate (42 vs 22%) and less likely prescribed sevelamer (41 vs 63%). The 2018 Cohort had better BL sP control (25.7 vs 15.6%) with sP 5.5 mg/dL, yet in both cohorts SO conversion was associated with significant reductions in sP (6.39 to 6.00 vs. 6.86 to 6.41) and PB pills/day (7.6 to 4.4 vs. 9.7 to 4.0). % pts with sP ≤ 5.5 mg/dL increased from 15.6 to 30.4% in 2014 Cohort and 25.7 to 41.3% in Cohort 2018.

Conclusions: Similar to the 2014 Cohort, a contemporary cohort of HD pts converted to SO experienced improved in sP and achieving ≤ 5.5 mg/dL with fewer PB pills/day. Physicians are prescribing SO to a broader patient population with different distributions of baseline PB therapy.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO0384

Long-Term Safety and Efficacy of Tenapanor for the Control of Serum Phosphorus in Patients with CKD on Dialysis

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Background: Tenapanor (TEN) is an investigational, first-in-class, non-binder therapy that targets the primary pathway of phosphate absorption, providing a novel approach to treating hyperphosphatemia. TEN blocks the paracellular absorption of phosphate in the GI tract by local inhibition of the sodium-hydrogen exchanger isoform NHE3 and is dosed as one small pill (<12x7 mm) twice daily. Two previously conducted pivotal trials of TEN met their primary efficacy endpoint.

Methods: A 52-week study consisting of a 26-week, open-label, randomized treatment period (RT) with a 12-week placebo-controlled randomized withdrawal period (RW), followed by a 14-week open label safety extension period (SE). Patients on maintenance dialysis with serum phosphorus (sP) ≥ 6.0 mg/dL and <10 mg/dL and a 1.5 mg/dL increase in sP following washout were randomized 3:1 to receive one 30 mg TEN tablet BID or sevelamer carbonate (SEV; a safety control) dosed per package insert. At end of RT all patients in the TEN arm were re-randomized 1:1 to either TEN or placebo for the RW. Primary endpoint was the mean change in sP from the end of RT to the end of the RW and was compared between TEN and placebo for the efficacy analysis set, defined as patients demonstrating a 1.2 mg/dL decrease in sP at the end of RT.

Results: The study achieved its primary endpoint demonstrating a statistically significant difference in least squares (LS) mean sP change (-1.4 mg/dL, p=0.0001), between TEN and placebo. For the efficacy analysis set (n=131), the mean sP decreased from 7.7 mg/dL at baseline to 5.1 mg/dL at the end of the 26-week TEN treatment, with a mean reduction of 2.6 mg/dL. During the 26-week treatment period, 77% of TEN-treated patients in the intent-to-treat population (n=407) had a decrease in sP, with a mean reduction from baseline of 2.5 mg/dL. TEN was generally well tolerated; the only AE with incidence >5% during RT was loose stools/diarrhea (53.0%), the majority of which were mild-to-moderate and transient in nature. In the RT, 17.4% of tenapanor-treated patients compared to 23.4% of sevelamer-treated patients experienced a serious adverse event.

Conclusions: The trial results suggest that among patients on maintenance dialysis with hyperphosphatemia, TEN dosed one tablet twice daily is safe and efficacious as monotherapy.

Funding: Commercial Support - Ardelyx, Inc.
Diagnosis of Static Bone Histomorphometry Parameters to Define Low Bone Turnover

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Background: Tetracycline labeling for bone biopsy allows pathologists to measure the pace of new bone production, which is critical to defining bone pathology in CKD. In the setting of clinical fractures, bone tissue is available, but tetracycline labeling is not possible. Therefore, we sought to determine the diagnostic accuracy of static measures of bone turnover relative to that measured by tetracycline in CKD patients undergoing iliac crest biopsy and histomorphometry.

Methods: We evaluated 147 individuals ages 12.4 ± 8.9 who had undergone iliac crest bone biopsy with tetracycline labeling for clinical indications of CKD-MBD. Using the tetracycline labels under fluorescence, we defined bone formation rate relative to bone surface (bFR/BS) as our gold standard to define low bone turnover. A blinded investigator used light microscopy without fluorescence to measure static bone turnover parameters. We then compared the area under the ROC curve (AUC), sensitivity, and specificity of each bone turnover parameter with low turnover based on tetracycline using the Youden J Index, which is the point on the ROC curve farthest from the line of equality that maximizes sensitivity and specificity.

Results: Among the 147 biopsies, 35 (24%) had low bone turnover based on tetracycline. We evaluated 5 parameters available by static bone microscopy, among which Osteoblast Surface relative to Bone Surface (O/S:BS), Osteoclast Surface relative to Bone Surface (Oc/S:BS), Boster Osteoid Volume to Bone Volume (OV/IV) had the highest AUCs for low bone turnover based on tetracycline labeling. Using the best cutoffs from the AUC curves, a 0.5 S:BS of 82% had a sensitivity and specificity of 80% and 75% for low bone turnover.

Conclusions: Static measures of bone turnover have high specificity and sensitivity for identifying low bone turnover defined by tetracycline labeling at the iliac crest in CKD patients. Bone tissue without tetracycline labeling may be useful clinically to define bone turnover.

Funding: Other NIH Support - NIA (R01 AG065876)

Acid-Base Status More Than Dietary Acid Intake Determines Urine Citrate Excretion in CKD

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Background: Lower urine excretion of the pH-sensitive metabolite citrate (UcitV) might be a clinically useful biomarker of steady-state acid (H+) retention not evident by plasma acid-base parameters in patients with CKD. Ongoing dietary H+ intake might also be an important determinant of UcitV and possibly confound its utility as a biomarker of underlying H+ retention.

Methods: We examined the influence on 8-hour UcitV (UcitV), its plasma citrate concentration (Pcit), and kidney clearance (UcitV/Pcit) components, and 8-hour urinary net acid excretion (8hNAE) of 1) ongoing dietary acid addition assessed by potential renal acid load (PRAL) and 2) steady-state acid-base status assessed by plasma total CO2 (PtcO2) and by H+ retention [estimated by comparing observed to expected PtcO2, increase in response to retained HCO3 (administered minus HUO3CO2H) 2 hours after oral NaHCO3 bolus (0.5 mmol/kg bw), assuming 50% body wt HCO3, apparent space of distribution] in 224 patients with CKD stages 1-3 due to macroalbuminuric, non-diabetic, renal acid load (PRAL) and 2) steady-state acid-base status assessed by plasma total CO2 (PtcO2) and by H+ retention associated inversely with each measure of citrate homeostasis. The data show that steady-state acid-base status is a more important determinant of UcitV than dietary acid intake and support continued exploration of UcitV as a biomarker of underlying H+ retention in CKD.

Funding: Government Support - Non-U.S.

Calciaphylaxis (Calciﬁc Uremic Arteriopathy) in a Predominantly African-American Urban US Patient Population

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Background: Calciﬁc Uremic Arteriopathy (CUA) which is commonly called calciaphylaxis is a rare and serious condition characterized by painful skin ulcerations due to ischemia with necrosis of the skin. The disorder carries a mortality rate > 50% in the first year, and death is often due to recurrent infections. Risk factors for calciaphylaxis includes end-stage renal disease (ESRD), a history of diabetes, obesity, female gender, Caucasian race, and the use of medications such as warfarin. We present clinical characteristics of CUA patients admitted to a large academic medical center which serves as a CUA referral center due to the presence of a wound center with hyperbaric oxygen therapy available.

Methods: Retrospective chart review of CUA patients from 2001-2019 in our single center academic hospital. Baseline data reported included age, calcium, phosphorus, PT, albumin, hemoglobin, creatinine, BUN, the use of medications such as warfarin or steroids, and treatment options.

Results: There were 110 patients included. Patient identified racial (n=108) make-up included African-American (n=89), Caucasian (n=18), and Asian (n=10). Average age was 56±14 years and 80% of patients were female (n=88). Also, 59% (n=65) of patients were diabetic. Dialysis modalities included hemodialysis (n=82) and peritoneal dialysis (n=24). Also 4 patients with CKD not yet on dialysis at the time of diagnosis. Average calcium levels of 8.9±1.1 mg/dL and phosphorus of 5.1±1.9 mg/dL. The average PTI was 569.6±714.9 pg/mL, albumin 2.5±0.7 g/dL, and hemoglobin 9.8±1.7 g/dL. Approximately 50% of patients received hyperbaric oxygen therapy as inpatient, 25% received sodium thiosulfate therapy, and 20% received a surgical intervention during the admission. Approximately 33% of patients were currently or recently on warfarin therapy, and approximately 25% were currently or recently exposed to high dose steroids.

Conclusions: We reported the largest single center and predominantly African-American (81%) calciaphylaxis case series. In comparison to other reported calciaphylaxis series our average PTI was lower and a high percentage of our patients were using warfarin or steroids. The PTI levels were higher in the African American group compared to others. Also, with a lower than expected parathyroidectomy rate which is likely due to our lower than average PTI.

PO0387

Citraic Acid-Containing Dialyate (CD) Attenuates Vascular Calcification in Hemodialysis Patients (HD)

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Background: The main causes of death in patients with CKD, especially in HD, are heart failure, cardiovascular, and cerebrovascular disease, which are due to a high degree of systemic vascular calcification. Progression of aortic calcification, simply evaluated by chest radiography, was reported to be significantly associated with overall and cardiovascular mortality in HD. Recently, it was reported that the use of CD reduced blood calciprotein particles (CPPs) associated with arteriosclerosis and inflammation in HD. Therefore, we investigated the effect of using CD on blood CPPs and vascular calcification in HD in a retrospective observational study.

Methods: The subjects were 262 HD who were visiting the Jiban Hospital in Japan. These patients were divided into two groups, those who continued to use acetate-containing dialyate (AD) or switched to CD from October 2017. A one-year retrospective observational study was conducted on the association with blood, laboratory test values, and aOACS (aortic arch calcification score) evaluated by chest X-ray. At baseline, patients with aOACS>50%, bisphosphonate, and warfarin use were excluded. Univariate, multivariate, subgroup analyses were used for statistical analysis. The main outcome was the presence or absence of aOACS exacerbation of 5% or more in one year.

Results: A total of 115 patients with AD and 102 patients with CD matched to the criteria were included. As a result, the use of CD (HR 0.53, 95% confidence interval (CI) 0.30-0.92), P = 0.026, ALP (HR 0.97, 95 %CI 0.94-0.99, P = 0.013), and aOACS (HR 1.36, 95% CI 1.15-1.63, P = 0.0004) were significantly associated with an exacerbation of aOACS. Subgroup analyses showed the characteristics of patients who benefit from using CD are those older than 75 years old, those with non-diabetes as the underlying disease, low nPCR(normalized protein catabolic rate), high blood CRP, and not severe calcification. In other words, patients with MIA syndrome can benefit from the use of CD.

Conclusions: Among patients with mild to moderate vascular calcification, HD with CD had a significantly reduced progression of aOACS compared with AD. The results indicate that the dialysis method using CD in HD may be a useful therapeutic method for suppressing vascular calcification.

Funding: Government Support - Non-U.S.
PO0389
Vascular Calcifications in Renal Transplantation
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Background: The aim of this study was to analyse the progression of vascular calcifications (VC) in a cohort of renal transplanted patients.

Methods: Prospective cohort study of de novo renal transplant patients. All patients were submitted to X-ray of the pelvis and hands (Adragão score); bone biopsy; laboratorial and echocardiographic evaluation at baseline and after 12 months (time 0 and 1). At the end of the study, bone densitometry and non-contrast cardiac CT (Agatston score) were performed. Associations between variables were performed using Wilcoxon rank sum test and Spearman correlation test. STATA software was used and p < 0.05 was considered statistically significant.

Results: We recruited 85 patients during 29 months and 69 were included in the study (6 patients refuse to perform the 2nd evaluation, 5 had primary non-function of the kidney graft, I had no sample on bone biopsy in time 0 and 4 patients died). Mean age 50.1±12.7 years, 59 men (69.4%), 66 caucasian (77.6%), median BMI 25.1±1.34. The median baseline and 12 months Adragão score had no differences. The median coronary artery calcium score (CACS) was 48.5 (0 – 535) and median percentile was 80 (0 – 92.5). Valvular calcifications were present in 15 and 16 patients and baseline and after 1 year (p>0.05). CACS were correlated with age (p=0.001), both Adragão score (p=0.001), presence of valvular calcification in time 1 (p=0.004), baseline calcium (p=0.02), baseline and 12 months sclerostin (p=0.01; p=0.04). CACS were higher in patients with highest values of FGF23 at baseline (p=0.04). Using a pairwise correlation, vitamin D levels (r=0.4, p>0.05) were correlated with the score. Coronary calcium percentile was correlated with Adragão score (p=0.0004), iPTH (r=0.6, p<0.001) and total cholesterol levels (r=-0.3, p=0.01) were correlated with the presence of valvular calcification in time 1 (p=0.02), baseline and 1-year calcium levels (p=0.004; p=0.02) and baseline sclerostin (p=0.01).

Conclusions: VC stabilize after renal transplantation. Adragão score can assess VC in renal transplanted patients. Calcium and sclerostin correlated with Agatston scores.

PO0390
Vascular Calcification and Progression of CKD
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Background: Vascular calcification, particularly the medial form, is common in advanced chronic kidney disease (CKD) and leads to poor outcomes. However, the extent to which medial calcification affects the kidneys and could exacerbate CKD is unknown.

To this end, progression of CKD was compared in women with and without breast arterial calcification (BAC), a marker of systemic medial arterial calcification, and the prevalence of other calcifications was assessed radiologically and histologically in patients undergoing nephrectomy.

Methods: Women with CKD (eGFR <60 ml/min/1.73m2) were identified from previous studies of breast arterial calcification, and those with a subsequent measurement of serum creatinine at least 1 year later were included. Consecutive patients with CKD and nephrectomies were identified from a computerized search of medical records. Computed tomography (CT) scans were reviewed for aortic and renal artery calcification, and histology (hematoxylin and eosin staining) was reviewed for calcification of main renal arteries and parenchymal arteries. Current or past warfarin use was an exclusion in all cohorts.

Results: Women with (n=51) and without (n=67) breast arterial calcification had similar yearly eGFR declines (1.55 vs. 1.60 ml/min/1.73 m2) despite a greater age (75.4 ± 13.7 vs 70.4 ± 1.5) and lower baseline eGFR (33.8 ± 1.8 vs 39.2 ± 1.6) in women with BAC. There was no correlation between the quantity of BAC and the decline in eGFR (r = 0.10). Of 246 patients with nephrectomies who were screened, 50 had an eGFR < 30. End-stage renal disease was present in 82% and 36% had diabetes. CT scans were available in 34 patients and showed aortic and renal artery calciumization in 59% and 38%, respectively. Prevalences of histologic calcification of renal artery and intraparenchymal arteries were 16% and 15%. When present, calcification of parenchymal arteries was usually very mild, and was severe in only 3 cases and limited to large arteries. In patients with CT scans, only those with renal artery calcification had parenchymal artery calcification (4 of 11 vs. 0 of 17 without, p=0.016).

Conclusions: Vascular calcification does not contribute to the progression of CKD. This is explained by the surprisingly low prevalence and severity of calcification in intrarenal arteries. Patients without renal artery calcification on imaging are at low risk for parenchymal artery calcification.

Funding: Clinical Revenue Support

PO0391
Clinical Outcomes in Patients with Calcinifications on Kidney Biopsy
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Background: Calcification is often noted on kidney biopsies, but the consequences of this finding is not known.

Methods: We searched a biobank for specimens with at least two years of linked clinical data and identified those which had calcification on report. Biopsy specimens were further classified to be described as calcium oxalate (CO), calcium phosphate/dystrophic (DC), or both. Linked clinical data was examined in 3 month intervals before and after index date of kidney biopsy. Cox proportional hazard analysis was performed using a split time model to evaluate relationships between presence of calcification, type of calcification, and clinical endpoints. Linked clinical data was examined in 3 month intervals before and after index date of kidney biopsy. Cox proportional hazard analysis was performed using a split time model to evaluate relationships between presence of calcification, type of calcification, and clinical endpoints.

Results: Patients with any calcification (n=429) vs. without (n=3936) were (p = 0.05) older, more likely to be white, have diabetes, lower eGFR and higher AKI/ATN on kidney biopsy specimen (31 vs. 13%). Patients with COX (n = 126) vs. DC (n = 260) were older, less diabetes, lower eGFR, more likely to have malabsorption or gastric bypass, and used more vitamin D. By univariate analyses, patients with any calcification were more likely to have a decline in the slope of creatinine at 6 months, 1 year, and 2 years; these relationships persisted even after adjustment for baseline eGFR, htn, proteinuria, negative biopsy findings, CAD (for 1 year beta 0.029, p < 0.001). When adjusted for age, diabetes, and baseline eGFR, patients with any calcification were less likely than those without calcification to advance to ESKD (HR 0.59; 95%CI 0.38-0.92; p = 0.05) but not to meet the outcome of death.

Conclusions: The presence of calcification on kidney biopsy specimen is associated with lower progression to ESKD and decrease in rate of decline of eGFR over time at 6 months, 1 year, and 2 years. This paradoxical finding may be due to increased AKI with recovery, rather than progressive chronic disease but requires further analyses.

PO0392
Urinary Phosphate Excretion and Microvascular Function in a Population-Based Cohort
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Background: Higher serum phosphate is associated with cardiovascular events and all-cause mortality. While these associations have largely been attributed to an increased risk of large vessel calcification, our previous work demonstrated a higher morning serum phosphate level is associated with microvascular dysfunction. However, the relationship between 24-hour urinary phosphate excretion ([UPE]) a surrogate for dietary phosphate] and microvascular function has not been explored.

Methods: We performed a cross-sectional analysis of 3,116 community-living participants that underwent a 24-hour urine collection and skin capillaroscopy, laser-Doppler flowmetry, and flicker-light induced retinal vessel responses as part of the Maastricht Study. The primary outcome was post-occlusive finger skin capillary recruitment. Secondary outcomes included capillary recruitment during venous congestion, heat-induced skin hyperemic response, and flicker-light induced retinal artery and vein dilation.

Results: The mean age of the cohort was 60 years, 48% were women, 7% had an eGFR< 60ml/min/1.73 m2, and the mean serum phosphate concentration was 3.2mg/dl. The mean UPE was 874 ± 315 mg/day. UPE was not associated with any of the microvascular outcomes (Table 1) and there were no significant interactions between UPE and sex, diabetes status or eGFR on any of the outcomes (P>0.43). We found an inverse relationship between UPE and serum phosphate (r=−0.26, p<0.001).

Conclusions: We found no relationship between UPE and microvascular function in community-living individuals predominantly with normal kidney function. Relationships between urine phosphate, serum phosphate and microvascular function require further exploration.

Funding: NIDDK Support, Private Foundation Support

Table 1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>UPE (mg/day)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary recruitment</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heat-induced skin</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Flicker-light response</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Relationships are adjusted for age, sex, both body mass index, smoking status, baseline proteinuria, diabetes, use of non-steroidal anti-inflammatory medication, use of bone modifying medications, phosphate reabsorption status, eGFR, and serum calcium.*

*Data for capillary recruitment from our study, Clingen et al. CLINRISK 2019.*
PO0393
Complete Resolution of Calciphylaxis in a Renal Transplant Patient with Calcifediol
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Introduction: Calciphylaxis is a rare but lethal disorder (mortality 60-80%) characterized by occlusion of microvasculature in the subcutaneous adipose tissue and dermis, resulting in excruciating painful, ischemic skin lesions. It commonly occurs in dialysis patients but only few cases in transplants reported. Treatment options are meager, and a multidisciplinary approach (dermatology, nephrology, nutrition, pain, palliative medicine, plastic surgery, and wound care), with surgical debridement, antimicrobial therapy, optimization of calcium-phosphorus product, dialysis adequacy, sodium thiosulfate, and hyperbaric oxygen has been suggested.

Case Description: A 62-year-old female with a LDKT (2008) complicated with CKD II, lupus nephritis, hypothyroidism, presented with painful, bilateral, medial calf ischemic ulcerations, which on punch biopsy revealed calciphylaxis. Her baseline iPTH, calcium, phosphorus, and 25-hydroxy-vitamin D, was 372 pg/mL, 9.4 mg/dL, 3.8 mg/dL, and 17.4 ng/mL, respectively. She was on calcitriol 0.75 mg/daily, ergocalciferol 50,000 units weekly and cinacalcet 30 mcg every other day. We started her on Calcifediol 30 mg, which increased to 60 mg daily. Her calcitriol and ergocalciferol doses were reduced slowly, while cinacalcet remained the same. This led to gradual increase in 25-hydroxyvitamin D and reduction in iPTH levels without effect on the calcium-phosphorus product. Over 1-year follow-up, her ulcers completely resolved as shown in the images with marked improvement in the pain.

Discussion: Treatment of hyperparathyroidism is limited as calcitriol and ergocalciferol worsen the calcium-phosphorus product while calcimimetics cause hypocalcemia, which hinders the attempt to lower calcitriol. Calcifediol is well tolerated and causes a progressive increase in serum 1,25-dihydroxy vitamin D and reductions in plasma iPTH without a significant effect of serum calcium and phosphorus levels. This led to remarkable clinical improvement with resolution of calciphylaxis in this case. Large clinical trials mandated to test these findings.

PO0394
Rapidly Growing “Calcified Cauliflower” in the Lung of an Orthotopic Heart Transplant (OHT) Recipient on Hemodialysis (HD)
Rui Song, Ali Arif, Chandra Dass, Iris J. Lee, Dina Abdelwahab. Lewis Katz School of Medicine at Temple University, Philadelphia, PA.

Introduction: Pulmonary calcinosis is commonly seen in ESRD patients but rarely in OHT recipients. We report a rare case of an OHT recipient who developed AKI requiring RRT. CT chest was noted for rapid progressive calcifications of lungs with both dystrophic and metastatic features.

Case Description: A 48-year old male with non-ischemic cardiomyopathy who underwent OHT. The post-transplant course was complicated by biventricular failure requiring VA-ECMO and IABP support, aortic anastomotic bleeding, multiple surgeries, recurrent bacterial and viral pneumonia dependent on mechanical ventilation, and ischemic acute tubular injury requiring CRRT then switched to HD. The imaging was noted for cardiac calcification, followed by rapidly progressive lung calcification. CT chest showed diffuse ground-glass opacity and “calcified cauliflower” signs with a mixture of dystrophic and metastatic lung calcifications. Work up for hyperparathyroidism, vitamin D toxicity, malignancy was negative. Contributing factors for pulmonary calcinosis included multiple surgeries, infections of the lungs, massive transfusion with subsequent IV calcium repletion, calcium concentration in replacement fluid of CRRT, use of calcium acetate. Subsequently, the patient was put on the lowest calcium bath and longer HD sessions.

CT chest: cauliflower calcification bilaterally

Discussion: Dystrophic pulmonary calcification occurs in the injured lung due to inflammation, infection, or hemorrhage. While metastatic calcification is more common in ESRD patients, primary and secondary hyperparathyroidism, or malignancy. Our case report emphasizes the importance of bone mineral disease as an underlying etiology for pulmonary calcinosis in dialysis-dependent OHT patients. The supportive approach includes avoidance of massive transfusions, IV calcium infusion, and calcium-based phosphorus binder, use of low calcium bath in HD.

PO0395
Calciphylaxis and Ectopic Parathyroid Gland: Chicken or the Egg?
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Introduction: Calciphylaxis is a vascular calcification disorder that is classically seen in patients(pts) with end stage renal disease on hemodialysis. It is most common in caucasian females and risk factors include hypercalcaemia, hyperphosphatemia, hyperparathyroidism, coumarine and iron therapy. This is a case of a patient with severe calciphylaxis, ectopic primary hyperparathyroidism with chronic kidney disease(CKD) not yet on dialysis.

Case Description: 64 year old female with CKD-4, obesity, HTN, pulmonary embolism not on anticoagulation, undiagnosed mediastinal mass came with lower extremity pain and a non-healing ulcer over the left anterior shin. Initial labs showed BUN:68mg/dl, Creatinine:5.4mg/dl, Calcium:11.3mg/dl, PTH:3,059 pg/ml. She underwent punch biopsy of the skin lesion that was consistent with calciphylaxis and was subsequently initiated on hemodialysis and sodium thiosulphate infusion. A nuclear uptake scan showed an anterior mediastinal mass that was consistent with ectopic parathyroid adenoma after surgical excision.

Discussion: This case highlights a rare cause of calciphylaxis in a pt. with undiagnosed ectopic primary hyperparathyroidism and CKD. Our pt. had hypercalcemia and a mediastinal mass which upon work-up was found to be a hypervascular ectopic parathyroid adenoma that likely triggered her calciphylaxis in the setting of concomitant secondary hyperparathyroidism due to chronic kidney disease as evident by hypercellularity of the reamining three parathyroid glands. Only 12 known cases of calciphylaxis are attributed to primary hyperparathyroidism and none due to an ectopic adenoma. Our pt. underwent hemodialysis, parathyroidectomy of the adenomatous gland and sodium thiosulphate infusion after which her PTH and calcium levels significantly improved and her skin lesions healed with no recurrence.
PO0396

Penile Calciphylaxis: Challenges in Its Diagnosis and Management
Isabelle Dominique V. Tomas Cruz, Carl Arenos, Sachiko S. Estreller, Blythe N. Ke, Shahara Abalos-Babaran, Elizabeth Montemayor. Philippine General Hospital, Manila, Philippines.

Introduction: Penile calciphylaxis is an uncommon presentation of a rare systemic disorder.

Case Description: We discuss 2 cases of penile calciphylaxis in patients with end stage kidney disease on hemodialysis presenting with painful ulcerations and eschar formation on their penile shaft. Diabetes mellitus, hyperphosphatemia and vascular calcifications on radiographs were common in both patients. A multidisciplinary approach to management involved wound care with irrigation followed by application of petrolatum-impregnated wet-to-dry dressing, antibiotic therapy, intensification of hemodialysis and use of intravenous sodium thiosulfate. Both patients showed good wound healing on discharge.

Discussion: Skin biopsy may aid in confirmation, but should be weighed against the risks of provoking nonhealing wounds & secondary infection. A high index of suspicion and multidisciplinary management are key components; but, prognosis is poor with survival rates reported to be less than a year upon diagnosis.

Case 1. Penile ulcer

Case 2. A&B. Penile and lower extremity lesions. C. Vascular calcifications on radiograph. D. Punch biopsy of the leg ulcer consistent with calciphylaxis (H&E stain, 40x). E. Thready calcium deposits in the lobular panniculus together with calcification of a medium-sized vessel (H&E stain, 10x)
PO0397
High Turnover Bone Disease After Successful Parathyroidectomy in a Dialysis Patient
Yahya R. Ahmad, Katherine M. Donaldson, Matthew Shea, Florence Lima, Madhumathii Rao. University of Kentucky Department of Nephrology University of Kentucky, Lexington, KY.

Introduction: We report a patient with end stage renal disease (ESRD) on hemodialysis (HD) with history of successful near-total parathyroidectomy (PTX) and normal to low parathyroid hormone (PTH) levels, found to have high-turnover hyperparathyroid (HPT) bone disease on biopsy (tx).

Case Description: 54-year-old female with ESRD on HD for 10 years presented with declining bone density and osteoporosis (left radial T-score of -2.7). She had a near-total PTX in 2014 for secondary hyperparathyroidism and bx proven severe HPT bone disease, complicated by calciphiaxis treated with wound care and sodium thiosulfate. Patient also has history of focal segmental glomerular sclerosis of her native kidneys, gastric bypass, uterine cancer requiring radiation, and psoriatic arthritis and gout requiring steroids. Labs showed corrected calcium 9.4 mg/dL, serum phosphorus 7.9 mg/dL, 25-OH-vitamin D3 16.9 ng/mL, bone specific alkaline phosphatase 12.8 ug/L, intact PTH level 34 pg/mL (consistent with past values), PTH-(1-84)-(7-84) ratio 1.1 (Scantibodies CA). She was started on weekly ergocalciferol. Bone bx showed persistent high-turnover/HPT bone disease with normal mineralization and low bone volume (2019, Figure 1). Relative to her prior bx, however, there was a demonstrably decrease in bone turnover and volume.

Discussion: Bone bx studies showing the evolution of bone disease after PTX in ESRD patients are limited. Development of adynamic bone disease is often presumed, but not established. In this patient, osteoporosis was related to high bone turnover, despite near-total PTX and successful reduction of serum PTH. These observations suggest that more research is needed into mechanisms other than PTH that contribute to bone turnover and loss in ESRD patients.

Figure 1: Anterior iliac crest bone biopsy: 1A – Trichrome stain 10x showing osteoclastic activity with tunneling in trabecular bone and increased osteoid volume and surface 1B – Fluorescent microscopy for tetracycline labeling 10x showing double labels and diffuse uptake in woven bone

PO0398
Successful Treatment of Severe Osteoporosis with Romosozumab in a Patient Undergoing Combined Peritoneal Dialysis and Hemodialysis: A Case Report
Hyeryong Lee, Kazuhiito Fukuoka, Shinya Kaname. Kyorin University School of Medicine, Department of Rheumatology and Nephrology Kyorin Daigaku, Mitaka, Japan.

Introduction: Recently osteoporosis is becoming a bigger problem as aging of population distribution increases. However, the use of anti-osteoporotic drugs is limited because of concerns for increased rates of adverse events associated with decreased drug clearance and comorbidities such as CKD-MBD in dialysis patients. Here we present a case of severe osteoporosis that was successfully treated with romosozumab.

Case Description: A 57-year-old woman ESKD patient due to lupus nephritis had been on peritoneal dialysis (PD) combined with hemodialysis for the last 4 years. She has been suffering from systematic lupus erythematosus and complicated by severe osteoporosis probably due to long-term use of glucocorticoids and renal dysfunction. Although she was treated with vitamin D3 analogues, bisphosphonates, and denosumab, severe pains continued and had pelvic bone and vertebral fractures, followed by repeated pathological bone fractures of the ribs. Thus, we decided to use romosozumab. After administration of romosozumab, bone pains dramatically improved and fragile bone fractures became less frequent, without progression of bone destruction. Four months later levels of tartrate-resistant acid phosphatase-5b decreased, total type 1 procollagen N-terminal propeptide increased, and bone mineral density significantly improved. Serum calcium and inorganic phosphate levels slightly decreased, and intact PTH slightly increased, but no overall adverse effects were noted.

Conclusion: Romosozumab is a humanized anti-sclerostin monoclonal antibody that has recently been introduced for the treatment of osteoporosis. While it demonstrates strong effects on osteogenesis and bone resorption, it also raises concerns about increased cardiovascular events. Our case suggests that romosozumab can be safely and effectively used for the treatment of osteoporosis, at least for a short period, in patients undergoing dialysis, although further study is clearly required to evaluate the efficacy of the agent.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**PO0401**

**Ethnic Differences in the Association of Kidney Function and Low Bone Density**

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**Background:** Chronic kidney disease (CKD) is an important risk factor for bone disease and fracture. Here, we examined the relationship between reduced kidney function (RKF) and bone mineral density (BMD) in women. We also examined PTH and calcium levels among a subset of patients with advanced CKD and low BMD (osteoporosis range).

**Methods:** We examined femoral neck BMD in 118,484 women age 60-79 with an ambulatory creatinine/eGFR within 1 year of the BMD scan and compared the proportion with low BMD (T-score ≤ -2.5) by kidney function. Presence of hyperparathyroidism (PTH > 65) and hypercalcemia (Ca ≥ 10.5 mg/dL) was examined in a subset of 257 patients with low BMD and advanced CKD G3B (eGFR < 45) and G4/G5 (eGFR < 30) who had PTH, calcium, and confirmatory eGFR measured within 2 years of BMD scan.

**Results:** Among 118,484 women, 83% had eGFR ≥ 60, 12% had eGFR 59-45, 4% had eGFR 44-50, and 1% had eGFR < 40. Overall, 12% of women age 60-69 and 21% of women age 70-79 had low BMD, but this varied by race/ethnicity. Asians had the highest burden of low BMD. Within each race/ethnicity group, the burden of low BMD varied by RKF/eGFR (Figure). In the subset with low BMD, advanced CKD, and measured PTH and calcium, 9.7% of G3B (n = 145) and 5.4% of G4/G5 (n = 112) patients were hyperparathyroidic. Of these hyperparathyroidic patients, 57% with G3B had PTH > 65 pg/mL (28.6% had PTH > 130 pg/mL), and all with CKD G4/G5 (n = 6) had PTH > 65 pg/mL (n = 4 > 130 pg/mL). Of the remainder with normal/low calcium, 57% with G3B and 84% with G4/G5 had PTH > 65 pg/mL. (19% of G3B and 53% of G4/G5 had PTH > 130 pg/mL).

**Conclusions:** The burden of low BMD and the association of RKF with low BMD varied by race/ethnicity. The majority of patients with advanced CKD and low BMD also had evidence of hyperparathyroidism when laboratory data were assessed. Our findings support guidelines for PTH and BMD screening in advanced CKD patients to optimize bone health.

**Funding:** Private Foundation Support

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**PO0402**

**Serum Biomarkers, but Not Dual-Energy X-ray Absorptiometry, Predict Cortical Bone Mineral Density in Children and Young Adults with CKD**

Samira Andromachi Mtsioni,1 Lorenzo Biassoni,2 Amrit Kaur,10 Manish Sinha,2 David C. Wheeler,8 Neil D. Duncan,7 Joyce Popoola,11 David Milford,3 Jin Long,4 Mary B. Leonard,3 Mary Hewett,3 12 Rukshana Shroff.12 Great Ormond Street Hospital For Children NHS Foundation Trust, London, United Kingdom; 2University College London Institute of Child Health, London, United Kingdom; 3Birmingham Women’s and Children’s NHS Foundation Trust, Birmingham, GB, Birmingham, United Kingdom; 4Children’s Hospital “P. & A. Kyriakou”, Athens, Greece; 5Evelina London Children’s Hospital, London, United Kingdom; 6University College London College, London, United Kingdom; 7Imperial College Healthcare NHS Trust, London, London, United Kingdom; 8Stanford University, Stanford, CA, US, Stanford, CA; 9University Hospitals Birmingham NHS Foundation Trust, Birmingham, Birmingham, GB, Birmingham, United Kingdom;10Manchester University NHS Foundation Trust, Manchester, United Kingdom; 11St Georges Healthcare Trust, London, United Kingdom.

**Background:** Currently available serum biomarkers and Dual-energy X-ray Absorptiometry(DXA) are thought to be poor predictors of bone mineral density(BMD). We set out to determine the clinical utility of DXA and routine clinical biomarkers in the young CKD population, by comparing them with tibial cortical BMD measured by peripheral Quantitative Computed Tomography(pQCT).

**Methods:** A multi-centre cross-sectional study with 77 patients on dialysis and 26 in CKD4-5 (n=103 total, ages 5-30 years). Participants underwent hip and lumbar spine (LS) DXA, tibial pQCT [for cortical (cortBMD) and trabecular BMD (trabBMD)] and measurement of routine serum biomarkers. All bone measures were expressed as Z-scores adjusted for age, sex, race and height. Tibial cortical BMD Z-scores was used as the gold standard to evaluate the predictive value of other measures.

**Results:** Bone pain was present in 58%, hindering activities of daily living. 10% had suffered at least one previous low-trauma fracture. DXA LS Z-scores were higher in the CKD compared to the dialysis population, with a corresponding higher trabBMD Z-score on pQCT (p<0.001). CortBMD cortical and mineral content Z-scores were significantly lower in dialysis compared to CKD patients (p<0.01 & p<0.05 respectively). Hip and LS DXA Z-scores did not correlate with any biomarkers or cortBMD. CortBMD Z-scores were negatively associated with PTH (r=-0.44, p<0.001) and alkaline phosphatase (ALP) (r=-0.22, p=0.03) and positively with calcium (r=0.33, p<0.001). None of the patients with PTH levels less than three times the upper limit of normal had a Z-score less than -2 SD (OR 95%CI 7.331 to infinity). Multivariable linear regression analysis showed the independent predictors of cortBMD Z-scores were PTH (β=-0.43, p<0.001), ALP (β=-0.36, p<0.001) and serum calcium (β=0.21, p<0.005), which together predicted 57% of variability in cortBMD. DXA imaging did not improve this model.

**Conclusions:** Routinely used biomarkers are moderate predictors of tibial cortical BMD. DXA is not a clinically useful tool and should not be performed routinely in children and young adults with CKD4-5 and on dialysis.

**Funding:** Other NIH Support - UK NIH, Kidney Research UK, Kids Kidney Research

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**PO0403**

**Advanced Glycation End Products Are Related with Cortical Bone Quality and Increased Risk for Fractures in CKD Patients**

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**Background:** The risk of bone fractures is higher in chronic kidney disease (CKD) patients than general population. We aim to investigate the relationships between advanced glycation end-products (AGEs) and cortical bone in a cohort of CKD patients.

**Methods:** 86 CKD patients (stages 3-4, N=26; hemodialysis, N=32; peritoneal dialysis, N=28) were included. AGEs levels were measured in serum (pentosidine and glycated hemoglobin), in skin (by AGE-Reader device) and in cortical bone by immunohistochemistry; receptor activator of nuclear factor kapp-B (RANK) and its
ligand (RANKL) and SOST mRNA expression were evaluated by real-time PCR. Bone histomorphometry was performed to measure cortical porosity, thickness and volume. Fracture risk was predicted using FRAX tool.

Results: Age was 51±13 years; 48 (56%) were male, 41 (48%) Caucasian and 16 (19%) diabetics; dialysis vintage was 21 (10-44) months. AGEs levels in skin were 3.06 ± 0.7 AU (reference: <2.0 AU), serum pentosidine 71 (44-121) pmol/mL and glycated hemoglobin 5.4 (3-12.1%). Cortical bone volume, thickness and porosity were 22.3 ± 0.7 AU (reference: <2.0 AU), serum pentosidine 71 (44-121) pmol/mL and glycated hemoglobin 5.4 (3-12.1%).

Conclusions: AGEs were detected in cortical bone and skin of CKD patients and correlates with their risk for osteoporotic fractures. Serum pentosidine levels were associated with low thickness of cortical bone. Cortical porosity was associated with serum glycated hemoglobin levels. SOST and RANKL mRNA expression. RANK was positively influenced by serum pentosidine levels. Together these data point to a direct relationship between AGEs and fractures in patients with CKD.

Funding: Government Support - Non-U.S.

PO0404
Low Bone Turnover and Increasing Calcification with Lower Trabecular Bone Score in Early CKD Patients
Amr E. Mohamed, Mohamed Ahmed, Michael Winkler, Habib Sour, Daniel Devoserop, Marie-Claude M. Faugere, Hartmut H. Mullache, University of Kentucky University of Kentucky, Lexington, KY.

Background: Little information is available on turnover abnormalities early during the development of loss of kidney function. Vascular calcifications may develop in association with bone turnover abnormalities. This study was designed to evaluate bone changes and cardiovascular calcification in early CKD patients without clinically known bone or cardiovascular disease.

Methods: This is a cross-sectional analysis of 32 adult volunteers with CKD stage 2-4. All patients underwent 1) dual energy x-ray absorptionmetry including trabecular bone score (TBS). 2) Non-contrast CT for cardiovascular calcium scoring, and 3) anterior iliac crest bone biopsy after double tetracycline-labelling and mineralized bone histology with histomorphometry.

Results: The mean age of the patients was 61±11 years. Patients tended to be obese (75%), white (72%), and female (59%). The mean eGFR was 44 ± 16 ml/min/1.73 m2. On histomorphometry.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO0405
Bone-Derived Hormones, Mineral Metabolism, Cardiovascular Disease, and Patient Survival in ESRD
Ana Carina Ferreira,1,2 Marco Mendes,1,2 Cecilia Silva,1 Patricia Cotovio,1 Ines Aires,1,2 David Navarro,1 Fernando C. Pereira,1,2 Rute M. Salvador,2 Bruna F. Correia,1 M. Guadalupe Cabral,2 Fernando E. Nolasco,1,2 Varvara Mitsioni,4 Lorenzo Biassoni,1 Amrit Kaur,2 Manish Sinha,1 David C. Wheeler,3 Neil D. Duncan,4 Joyce Popoola,1 Simon Mcguirk,2 Kristian H. Mortensen,2 David Milford,1 Jin Long,2 Mary B. Leonard,2 Mary Fewtrell,6,7 Rukshana Shroff,3,8 1Great Ormond Street Hospital For Children NHS Foundation Trust, London, London Kingdom; 5Evelina London Children’s Healthcare, London, United Kingdom; 2University College London Institute of Child Health, London, United Kingdom; 3Birmingham Women’s and Children’s NHS Foundation Trust, Birmingham, United Kingdom; 4University of Glasgow, Glasgow, United Kingdom; 4University College London, London, GB, London, United Kingdom; 9Manchester University NHS Foundation Trust, Manchester, Manchester, United Kingdom; 3University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; 1St Georges HealthCare Trust, London, United Kingdom.

Background: The aim of this study was to analyse the associations between chronic kidney disease-mineral and bone disorder (CKD-MBD) players [alpha-klotho, fibroblast growth factor (FGF) 23, sclerostin, parathyroid hormone (PTH), bone alkaline phosphatase (bAP)] with cardiovascular disease and patient survival in ESRD patients.

Conclusions: Low bone turnover, normal total bone volume and absence of bone formation defects were all associated with normal total bone volume and absence of bone formation defects in these early CKD patients. There were increased vascular calcifications with low TBS pointing to a relationship between bone quality and vascular calcifications.

Table 1

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PO0406
Bone Mineral Density Is Not Associated with Coronary Artery Calcification in Children and Young Adults with CKD
Alexander D. Lalavaniannis,1,2 Nicola J. Crabtree,1 Charles Ferro,1 Varvara Askitis,4 Andromachi Mitiisoni,4 Lorenzo Biassoni,1 Amrit Kaur,2 Manish Sinha,1 David C. Wheeler,3 Neil D. Duncan,4 Joyce Popoola,1 Simon Mcguirk,2 Kristian H. Mortensen,2 David Milford,1 Jin Long,2 Mary B. Leonard,2 Mary Fewtrell,6,7 Rukshana Shroff,3,8

Methods: Patients with CKD4-5 or on dialysis aged 5-30 years underwent tibial pQCT and measurement of vascular health to examine the association between bone demineralization and vascular calcification in a young CKD population.

Results: One hundred participants [median 13.82 years(IQR 10.7 to 16.5), 20% above 18 years, 44% female, 77% on dialysis] underwent tibial pQCT [for cortical/medulla (bMD) and trabecular BMD (tBMD)] and ultrasound for carotid intima-media thickness (cIMT), carotid-femoral pulse wave velocity (cfPWV) and measurement of routine serum biomarkers. All measures were expressed as Z-scores and adjusted for age, height. cIMT was expressed as Agatston score (AS).

Conclusions: Low bone turnover, normal total bone volume and absence of mineralization defect are seen in early stages of CKD. There are increased vascular calcifications with low TBS pointing to a relationship between bone quality and vascular calcifications.
Conclusions: Despite a high prevalence of bone and cardiovascular disease (CVD), there was no increase in bone mineral density (BMD) or serum concentrations of CAC or surrogates of CVD in this cohort of children and young adults with CKD-5D. The skeleton accretes calcium until the third decade of life, perhaps allowing a buffering effect that protects against vascular calcification. Confirmation through longitudinal studies is required.

PO0407
A Randomized, Double-Blind, Placebo-Controlled Trial Assessing Efficacy of Standard and Low-Dose Hydrochlorothiazide Treatment for Prevention of Recurrent Calcareous Nephrolithiasis (NOSTONE Trial)

Nasser Dhayat,1 Olivier Bonny,2 Beat Roth,3 Grazia M. Cereghetti,2 David Schilling,4 Pina Pusztai,5 on behalf of the NOSTONE Investigators6 Inselstippt Universitätsklinik Bern, Bern, Switzerland; 1University of Bern, CTU Bern, Bern, Switzerland; 2Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

Background: Nephrolithiasis is a global healthcare problem with a current lifetime risk of up to 18.8% in men and 9.4% in women. Without specific treatment, 5- and 20-year recurrence rates are 40% and 75%, respectively. Given the high cost of medical treatments and surgical interventions as well as the morbidity related to symptomatic stone disease, medical prophylaxis for stone recurrence is an attractive approach. Efficacy of thiazides for kidney stone prevention was tested in 11 trials in the past. However, all these trials had major methodological deficiencies. Nowadays, thiazides are widely used in the treatment of recurrent nephrolithiasis and arterial hypertension, but at significantly lower doses. In the case of recurrent nephrolithiasis, however, this practice is not supported by randomized evidence. Thus, evidence for benefits and harms of thiazides in the prevention of kidney stones remains unclear.

Methods: NOSTONE is a multicenter, randomized, placebo-controlled, double-blind, parallel-group trial with the purpose to assess the dose-response relationship for three different dosages of hydrochlorothiazide (placebo, 12.5mg, 25.0mg, 50.0mg) in kidney stone prevention. The primary outcome is incidence of stone recurrence (a composite of symptomatic or radiologic recurrence) at 3 years, a low-dose CT will be performed at the beginning and the end of the trial. Patients from 12 hospitals throughout Switzerland were included in the trial.

Results: NOSTONE received all necessary approvals by the end of February 2017. Recruitment started in Bern on the 9th of March 2017, all study sites are operative since June 2017. Altogether, 416 patients were randomized in the trial was reached and therefore recruitment stopped (www.nostone.ch). In March 2020 the first patient randomized in the trial completed the treatment phase. All patients are expected to reach end of treatment by the end of August 2021.

Conclusions: The study will provide critical information to physicians for the treatment of kidney stones. The impact of the results of this study will affect many patients currently treated with hydrochlorothiazide for the prevention of recurrent nephrolithiasis.

Funding: Government Support - Non-U.S.

PO0408
Roux-en-Y Gastric Bypass and Kidney Stones


Background: Roux-en-Y gastric bypass (RYGB) is a bariatric surgical procedure that is highly effective in the management of morbid obesity but also associated with higher risk of stone formation after surgery. It is not known why RYGB is associated with higher kidney stone risk but it may be due to changes in urine composition, such as high urine calcium oxalate supersaturation (CaOx SS) and calcium phosphate supersaturation (CaP SS). It is not known who is at risk for high urine CaOx SS after surgery. We examined 24-hour urine composition in 18 men and women before and after RYGB to look for predictors of urine high CaOx SS and CaP SS.

Methods: Patients were recruited from a bariatric surgery clinic prior to scheduled laparoscopic long-limb RYGB. Three consecutive 24-hour urine collections performed in a Clinical Research Center both before and 1 year after surgery. We performed Welch’s 2-sample and paired t-tests to compare mean urinary values for pre- to post-RYGB collections and to compare men to women in the post-RYGB collections. We used linear regression to evaluate predictors of urine CaOx SS and CaP SS.

Results: Seven men and eleven women completed pre- and post-RYGB urine collections. Post-RYGB, women had a significantly higher urine CaOx SS (13.1 ± 4.6 vs. 12.5 ± 4.0, p = 0.002), CaP SS (5.9 vs. 1.9, p = 0.05), and lower urine volumes (1.7 vs. 2.7L, p = 0.001) compared with men. There were no differences by sex in CaOx SS or urine volume pre-RYGB. Both men and women had high oxalate in the pre- and post-RYGB collections. Urine volume was most strongly associated with urine CaOx SS and a difference in urine CaOx SS of -6.4 (-8.7 to -4.0) for every 1 liter of urine volume excretion. Calcium was also associated with change in -0.01 (-0.01 to -0.002) per mg of citrate. Calcium and oxalate associated with change in -0.01 (-0.01 to -0.002) per mg of citrate. Calcium and oxalate were most strongly associated with urine CaP SS, higher urinary citrate, calcium and pH (1.3 ± 0.7 vs. 1.7 were associated with higher CaP SS (Calcium 0.01mg, 0.008 to 0.12mg; pH 1.3, 0.8 to 1.7). Higher urine volume (-0.4 -0.6 to -0.1) was associated with lower CaP SS and citrate was not significant.

Conclusions: There are important differences in urinary parameters by sex that may contribute to differences in kidney stone risk after RYGB. Women may be at higher risk for kidney stone formation after RYGB compared with men.

Funding: Clinical Revenue Support

PO0409
Nephrocalcinosis at Baseline Did Not Increase the Risk of Nephrocalci- nosis Progression After Long-Term Burosumab Treatment in Adults and Children with X-Linked Hypophosphatemia (XLH)

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Background: In patients with XLH, excess FGF23 induces hypophosphatemia, leading to musculoskeletal impairments. In two Phase 3 trials (NCT02526160, NCT02015705), burosumab significantly improved serum phosphorus concentrations in adults and children with XLH. We examined subject characteristics and long-term safety of burosumab by the absence or presence of nephrocalcinosis (NC) at baseline (BL) from these trials.

Methods: Adults were randomized (1:1) to burosumab 1.0 mg/kg every 4 weeks or placebo for 24 weeks; after 24 weeks, adults received burosumab through 96 weeks. Children were randomized (1:1) to burosumab 0.8 mg/kg every 2 weeks or oral phosphate and active vitamin D (Pi/D) for 64 weeks. NC was determined at BL and during study by ultrasound and graded by central readers from 0 (normal) to 4 (stone formation).

Results: In adults, NC was found in 73/134 patients (54%) at BL. Age, sex, and duration of treatment with Pi/D as adults did not differ by baseline NC group. Compared with adults within NC at BL, those with NC longer duration of treatment with Pi during childhood (mean [SD] 13.2 [3.2] vs 11.4 [4.0] years) but not with D. After 96 weeks in adults, median 24-hr urine calcium increased by 35% overall but remained within the normal range. NC scores increased by +1 in 5/73 adults with NC at BL and 5/61 adults without NC at BL. In children, NC was found in 14/61 (23%) at BL. Compared with children without NC at BL, children with NC were older (7.6 [2.8] vs 5.7 [3.4] years), more likely to be male (71% vs 36%), treated longer with Pi/D pre-enrollment (4.8 [3.3] vs 3.6 [3.0] years), and had higher 24-hr urine calcium (4.4 [5.4] vs 2.3 [1.9] mg/kg/day [normal <4.9 mg/kg/day]). After 64 weeks in children, median urine calcium decreased by 50% overall. At week 64, NC scores did not increase in any child and decreased by 1 in 8 children. Serum creatinine and estimated GFR did not change in adults or children.

Conclusions: In adults with NC at BL was associated with longer duration of Pi during childhood. In children with NC at BL, NC was associated with longer duration of Pi and D pre-enrollment and with BL hypercalciuria. With long-term burosumab, the presence of NC at BL did not increase the risk of NC progression.

Funding: Commercial Support - Ultragenyx Pharmaceutical Inc.

PO0410
Proton-Pump Inhibitors Are Associated with Decreased Urinary Citrate Excretion

Parth M. Patel,1 Alexander Kandabarov,1 Escosa Aiwerioghoiene,1 Enrique Blanco-Martinez,2 Spencer Hart,2 David J. Leehey,2-3 Ahmer Farooq,2 Kristin Baldea,4 Thomas Turk.5 Loyola University Health System, Maywood, IL; 2Edward Hines Junior VA Hospital, Hines, IL.

Background: Proton-pump inhibitors (PPIs) may increase the risk of kidney stone formation, but the mechanism(s) have not been elucidated. PPI-associated hypomagnesaemia is due to impaired intestinal magnesium absorption thought to result from changes in intestinal pH that decrease binding of magnesium to its transporters. Citrate is a tricarboxylic acid with α-ketavalues of 2.9, 4.8, and 5.6. Since citrate is transported primarily in the divalent form (citrate2-) by the intestinal sodium dicarboxylate transporter (NaDC1), changes in intestinal pH by PPIs might decrease the amount of the divalent form, thus reducing intestinal absorption of citrate, thereby decreasing alkaline load and urinary citrate excretion.

Methods: We performed a retrospective review of nephrolithiasis patients treated at our institution and compared patients who were taking PPIs or not at the time of their 24-hour urine collections. Patients taking PPIs were older and more likely to have medical comorbidities associated with metabolic syndrome such as hypertension, diabetes, and dyslipidemia (p<0.01). Controlling for these factors, patients taking PPIs were found to have lower 24-hour urine citrate excretion (p=0.12, ΔF=4.24, n=904). 24-hour urine magnesium excretion was numerically but not significantly lower in patients taking PPIs. There were no other differences in urinary composition between the groups.

Conclusions: Our findings suggest that patients who take PPIs regularly may be at risk for decreased urinary citrate excretion, which is a known risk factor for kidney stone formation. It is possible that the decrease in urinary citrate with PPIs may have clinical significance, particularly in patients with idiopathic hypercalciuria or other conditions associated with hypocitraturia such as genetic polymorphisms of the renal-sodium-citrate (renal-NaDC1) transport system or chronic metabolic acidosis, hypercalcemia, or chronic metaphosphoric acid or anhydride inhibitors, high animal protein diet intake, and incomplete distal RTA.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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PO0411
Dietary Intake and Risk of Incident and Recurrent Kidney Stones
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1Mayo Clinic Minnesota, Rochester, MN; 2VA Maine Healthcare System, Augusta, ME.

Background: Dietary factors associated with recurrent kidney stones (KS) may differ from those associated with incident KS.

Methods: We recruited adult incident symptomatic KS formers and controls from local residents surrounding the Mayo Clinics in Minnesota and Florida between 2009 and 2018. Participants were administered a Viocare Food Frequency Questionnaire, a KS survey, and completed a 24h urine chemistry evaluation at a baseline study visit. Medical records of stone formers were reviewed for symptomatic recurrence with a visit lower confirmed stone through May 2019. Analyses compared baseline dietary factors between incident symptomatic stone formers and controls and assessed whether these same dietary factors predicted symptomatic recurrence.

Results: There were 416 incident symptomatic KS formers (74 had a recurrence during follow-up) and 384 controls. Higher dietary potassium, calcium and phytate were associated with lower odds of an incident symptomatic KS adjusting for age, race, BMI, underlying diseases, family history of KS, education status, fluid and energy intake. During median follow-up time of 4.1 years, higher dietary calcium and lower oxalate intake predicted a lower risk of symptomatic KS recurrence (Hazard ratio for highest tertile vs lowest tertile = 0.53, 95%CI [0.28, 0.99] and 2.09, 95%CI [1.18, 3.69], respectively) adjusting for BMI, fluid and energy intake, and Recurrence of Kidney Stone score. (Table)

Conclusions: Certain dietary factors may differ in their association with incident and recurrent KS. In particular, dietary oxalate intake may be more important for preventing recurrence than for preventing a first KS episode.

Funding: NIDDK Support, Private Foundation Support

PO0413
Type 3 Renal Tubular Acidosis in Association with a Pelvic Kidney

Introduction: The association of renal tubular acidosis (RTA) from carbonic anhydrase isoenzyme II (CA II) deficiency, cerebral calcifications and osteopetrosis is now known as marble brain disease

Case Description: 21-year-old woman with a medical history of multiple fractures since childhood, recurrent episodes of nephrolithiasis and, renal tubular acidosis (RTA), presented to establish care at our clinic. Genetic testing had revealed she had CA II gene mutation. Her brother had the same condition but her sisters were healthy. Her medication included potassium citrate and vitamin D3. Laboratory assessment revealed the following: serum Na+ 143 mmol/L, K+ 3.9 mmol/L, Cl- 109 mmol/L, HCO3 21 mmol/L, creatinine 0.73 mg/dl, Ca2+ 9 mg/dl, PO43- 4.4 mg/dl, vitamin D 7.6 mg/dl. Urine pH was 6. CT urogram revealed a normal right kidney and an ectopic left kidney with numerous small stones. (Figure 1). Spine X rays showed osteoporosis of vertebral endplates and MRI brain showed calcifications in basal ganglia. Pyelolithotomy of the pelvic stone was performed and stone analysis revealed 90% calcium phosphate and 10% calcium oxalate. 24-hour urine showed a low urine citrate with low urine volume. Thus the findings were consistent for RTA with low serum bicarbonate, low urine citrate and calcium phosphate predominant stones.

Discussion: CA II deficiency syndrome is a rare autosomal recessive disorder that results in Type 3 RTA (combined proximal and distal RTA). Pelvic kidneys, which result from a failure of mesonephros to ascend normally during early gestation, are prone to urolithiasis due to poor urinary drainage. In our patient RTA, along with altered urine flow due to pelvic kidney predisposed to nephrolithiasis.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

Table of results

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<th>Table</th>
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CI, confidence interval

PO0412
Cross-Sectional Study of Metabolomic Profiles and the Association with Kidney Stone Disease in the Nurses' Health Studies I and II
Panupat Maprangpho,1 Yukun Li,1 Raji Balasubramaniam,1 Eric N. Taylor,1,2 Gary C. Curhan.1 Bringham and Women’s Hospital Channing Division of Network Medicine, Boston, MA; 1Mahidol University Faculty of Medicine Siriraj Hospital, Bangkok, Thailand; 1VA Maine Healthcare System, Augusta, ME; 2University of Massachusetts Amherst, Amherst, MA.

Background: Kidney stone disease is a painful and expensive health condition with a high recurrence rate and substantial morbidity; however, the mechanisms underlying the disease remain incompletely understood. Metabolomics is one novel approach that might provide important insights into the etiology of stone disease.

Methods: In a subset of participants from the Nurses’ Health Study I and II cohorts (NHSI and NHSII), subjects were divided into stone and non-stone former groups. Data from existing mass-spectrometry based plasma metabolomic profiling that had been performed in multiple case-control studies of other diseases were used. Multivariable logistic regression models were employed to identify metabolites which were associated with kidney stone history after adjusting for multiple comparisons using false detection rate correction.

Results: We included 230 prevalent kidney stone cases among 5380 NHSI participants and 114 cases among 2283 NHSII participants. 277 metabolites were measured and passed the 10% missing threshold. In NHSI, one metabolite was significantly inversely associated with kidney stones (p=0.01) and passed the false-detection rate correction for multiple testing. The identified metabolite was cinnamoylglycine (HMDB0011621), which is a metabolite in the carboxylic acids and derivatives class. There were no significant metabolites in NHSII. When the cohorts were combined, HMDB0011621 was significantly inversely associated with stone history (p<0.01). The odds ratio per standard deviation increase in the metabolite for the combined cohorts was 0.87 (0.81, 0.95).

Conclusions: We identified one plasma metabolite associated with a history of kidney stones. The metabolite has been recently identified as one of the potential biomarkers of proximal tubule function, colonic epithelial resistance and prostate cancer. Larger studies are needed to identify other potential metabolites that may be involved in kidney stone formation.

Funding: NIH Support, Private Foundation Support
Ectopic (pelvic) left kidney with multiple stones with a normal looking right kidney

PO0414
Incidence and Characteristics of Kidney Stones in Patients on a Ketogenic Diet: A Meta-Analysis
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Background: Very-low-carbohydrate diets or ketogenic diets have frequently been used for weight loss in adults and as a therapy for epilepsy in children. The incidence and characteristics of kidney stones in patients on ketogenic diets are not well studied.

Methods: A systematic literature search was performed using MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews from the databases’ inception through April 2020. Observational studies or clinical trials that provide data on the incidence and/or types of kidney stones in patients on ketogenic diets were included. We applied a random-effects model to estimate the incidence of kidney stones.

Results: A total of 36 studies with 2,795 patients on ketogenic diets were enrolled. The estimated pooled incidence of kidney stones was 5.6% (95% CI, 4.4%-7.1%) in patients on ketogenic diets at mean follow-up time 3.7±2.9 years. Subgroup analyses demonstrated the estimated pooled incidence of kidney stones of 5.6% (95% CI, 4.3%-7.2%) in children and 5.6% (95% CI, 2.3%-12.6%) in adults, respectively. Within reported studies, 48.7% (95% CI, 33.2%-64.6%) of kidney stones were uric stones, 36.5% (95% CI, 10.6%-73.6%) were calcium based (CaOx/CaP) stones, and 27.8% (95% CI, 12.1%-51.9%) were mixed uric acid and calcium based stones, respectively.

Conclusions: The estimated incidence of kidney stones in patients on ketogenic diets is 5.6%. Its incidence is comparable among adults and children. Uric acid stones are the most prevalent kidney stones in patients on ketogenic diets followed by calcium based stones. These findings may impact the prevention and clinical management of kidney stones in patients on ketogenic diets.

PO0415
Association of Urine Findings with Metabolic Syndrome (met-s) Traits in Patients with Nephrolithiasis
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Background: Met-s is a health concern related to lifestyle habits including acidicogenic and high protein diets. The odds of nephrolithiasis increases with an increasing number of met-s traits. Prior studies have shown relationships among the number of met-s traits and decreasing urine pH and other acid excretion markers. We evaluated associations of urine factors including acid excretion and stone composition with the number of met-s traits in a large cohort of stone-forming patients.

Methods: A retrospective review was performed of 24-hour urine studies (Litholink, Litholink, Chicago, IL) from patients seen in Urology and Nephrology divisions, UVMCC July 2009 to December 2018. Patients <18 years and those with improper collections based on creatinine/kg were excluded. Patient variables, laboratory values, associated diagnoses, and medications were identified within 6 months of urine collection and 1 year of kidney stone composition. Four groups based on the number (0, 1, 2, 3-4) of met-s traits were calculated using linear contrasts in analysis of variance.

Results: 1250 unique patients, 494 females, 1250 unique patients, 494 females, 703 with stone composition criteria for inclusion. Met-s groups n were 0=509, 1=381, 2=203, 3+4=157. There was no difference or trends among the groups for urine volume, calcium or citrate. There was a significant trend p<0.001 for increasing number of met-s traits with decreasing urine pH and SS calcium phosphate (CaP) and increasing age, weight, protein intake, urine uric acid (UA), SS UA, oxalate, sodium, potassium, phosphorus, urea nitrogen, chloride, estimated net acid excretion and p<0.05 for sulfate (S), ammonium, magnesium. When adjusted for age and protein intake the trend remained significant only for urine pH and a reversed trend for S. There was a significant trend for more UA and fewer predominately CaP stones in those with more met-s traits.

Conclusions: High protein intake accounted for most of the difference in urinary markers of stone risk except low urine pH. The latter facilitates more UA and less CaP contribution to stone composition. Future studies could determine if changing diet can reduce risk for stones in met-s.

Funding: Clinical Revenue Support

PO0416
Primary Hyperoxaluria (PH) Types 1 and 2 with Kidney and/or Liver Transplant Achieve Best Health-Related Quality of Life (HRQoL)
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Background: Our previous study showed that PH without a transplant (tx) had worse HRQoL compared to the US Standard Population and worsened with increased stone frequency. We now show the first longitudinal HRQoL profiles for PH patients with transplants.

Methods: PH patients were enrolled from the Rare Kidney Stone Consortium registry. HRQoL was measured with a generic non-disease specific instrument (SF-36v2). Results were calculated as norm-based scores (NBS) based on US Standard Population
(Mean domain score = 50). We created three groups based on the time of last stone event (≥30 days, 31–365 days, >366 days). The study compared HRQoL for participants with a kidney and/or liver transplant over 5 different time points.

**Results:** This sub-sample included 100 surveys of 32 PH participants (16 males and 16 females) with a tx. The mean age was 47 years for both males and females. This sub-sample includes 24 participants with liver/kidney tx (75%) and 8 with kidney tx only (25%). Participants with only a kidney tx reported significantly more stone events within a year (26% vs 13%, χ² = 0.028). Two way ANOVA did not find a change in HRQoL profiles over time for PH participants with kidney/liver tx (figure). Most mean domain scores are 50 or above, except for the domain of General Health which was less. Participants with only a kidney tx scored significantly lower in role physical, bodily pain, general health, social function, and physical component score (data not shown) than participants with kidney/liver tx. There was no difference between male and female participants over time.

**Conclusions:** PH participants with kidney/liver tx achieve better HRQoL, measured with a non-disease specific generic instrument, than those with kidney alone; both are better when compared to the US Standard Population. The majority of PH participants with a tx are stone-free, with a direct beneficial impact on their HRQoL.

**Funding:** NIDDK Support

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**PO0417**

Assessment of Blood Oxalate Concentrations in Patients with CKD

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**Background:** Alterations in oxalate homeostasis are associated with kidney stone disease and progression of chronic kidney disease (CKD). However, accurate measurement of plasma oxalate (Pₐ) concentration is challenging as prompt processing and acidification of samples has been deemed necessary. In the present study we examined the effects of variations in sample handling on Pₐ results. Subsequently, a standardized analytical protocol was established, and Pₐ concentrations were measured in a large cohort of patients with CKD.

**Methods:** We tested the effects on Pₐ results of storage time at room temperature (RT), storage on dry ice and maintenance of samples at -80°C. Pₐ results were calculated using the Student t-test, one-way ANOVA and Pearson's correlation using GraphPadPrism, version 8.0. A P value of <0.05 was considered significant for all analyses.

**Results:** Pₐ concentrations increased rapidly when samples were maintained at RT. This was most relevant for Pₐ < 10 μM as concentrations more than doubled within a few hours. Immediate freezing on dry ice and storage at -80°C provided stable results and allowed postponement of acidification for >1 year. In the GCKD study, mean (SD) eGFR at the time of Pₐ measurement was 44.0 (17.9) ml/min/1.73 m². More than half of the patients had a Pₐ concentration below 2.0 μM. Pₐ correlated positively with urinary albumin to creatinine ratio and inversely with eGFR (P < 0.001). The lowest eGFR quartile, median eGFR was 25.1 ml/min/1.73 m² (IQR 20.3 - 28.1) with a median Pₐ of 2.7 μM (IQR 1.9 – 4.2).

**Conclusions:** We conclude that immediate freezing and maintenance of plasma samples at -80°C facilitates the sample collection process and allows accurate Pₐ assessment in large patient cohorts. Our study presents a critical and useful modification of the complex preanalytical procedure. Moreover, we demonstrate that Pₐ concentrations in patients with CKD are substantially lower than previously reported. The present study may serve as a reference for sample handling to assess Pₐ in clinical trials and to determine its role in CKD progression.

**Funding:** Commercial Support - Dicerna Pharmaceuticals, Cambridge, USA; Private Foundation Support, Government Support - Non-U.S.

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**PO0418**

Safety and Efficacy of Reloxaliase in Enteric Hyperoxaluria (EH): An Aggregate Review of Completed Studies

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**Background:** EH occurs when excess oxalate is absorbed from the gastrointestinal (GI) tract due to underlying fat malabsorption, increasing renal oxalate load and as a result, risk of both kidney stones and chronic kidney disease. Reloxaliase is a first-in-class enzyme that specifically targets and degrades oxalate within the GI tract to treat EH. An aggregate safety and efficacy assessment of reloxaliase in subjects with EH across completed clinical trials was performed.

**Methods:** There were a total of four Phase 2 and 3 trials that enrolled EH subjects; 2 were single-arm and 2 were randomized, placebo (PBO) controlled. Subjects took reloxaliase orally (7,500 units/dose) to 3 times/day, for 4 days to 12 weeks. The efficacy endpoint in all trials was change in 24-hr urine oxalate (UOx) excretion (mg/d). For this aggregate analysis, percent change from baseline was calculated using the average of all values obtained during treatment.

**Results:** There were a total of 168 randomized subjects with EH (94 reloxaliase and 74 PBO), most with bariatric surgery as the cause of malabsorption. Baseline estimated glomerular filtration rate (eGFR) ranged from normal to as low as 33 ml/min/1.73 m². In subjects with baseline UOx ≥ 50 mg/d, reloxaliase treatment consistently reduced 24-hr UOx by a mean of 23 to 35% across the studies, despite differences in dosing frequency and duration of treatment. Efficacy appeared to be unrelated to baseline eGFR. Adverse events (AEs) were reported in 67% of reloxaliase subjects compared to 51.4% on PBO, with GI AEs most common in both groups. There were no treatment-related serious AEs or deaths, and none of the reloxaliase treated subjects withdrew from the study due to a related AE.

**Conclusions:** Reloxaliase reduces 24-hr UOx excretion and is well tolerated in EH patients independent of eGFR, dosing frequency, or duration of treatment. Further studies are ongoing to assess the long-term benefits of reloxaliase and its potential to decrease kidney stone events and preserve kidney function.

**Funding:** Commercial Support - Allena Pharmaceuticals

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**PO0419**

Trends in Treatment of Secondary Hyperparathyroidism and Association with Post-Transplant Outcomes


**Background:** Secondary hyperparathyroidism (SHPTH) affects nearly all patients with kidney failure on maintenance dialysis and has been independently associated with increased mortality and cardiovascular disorders. Treatment includes vitamin D analogs, calcimimetics, or parathyroidectomy. However, treatment choice for SHPTH on outcomes after kidney transplantation (KT) is not well understood. The primary objectives of our study were to understand treatment trends in SHPTH and their association with post-transplant outcomes.

**Methods:** Using SRTR and Medicare claims data, we identified 12,372 adults (age ≥ 18) who received KT in 2007-2016 and had a diagnosis of SHPTH during dialysis. We examined the association between treatment method for SHPTH and development of tertiary hyperparathyroidism, delayed graft function, graft failure, and death using adjusted Cox proportional hazards models.

**Results:** Of 12,372 patients with a diagnosis of SHPTH, 4,554 (36.8%) received cinacalcet, 205 (1.7%) underwent parathyroidectomy, and 7,613 (61.5%) had no treatment prior to KT. Cinacalcet use increased throughout the duration of the study period with 18.4% of patients receiving it 2007 versus 46.2% in 2017 (p<0.001). Utilization of parathyroidectomy increased from 0.8% in 2007 to 3.1% in 2016 (p=0.005). Compared to patients treated with cinacalcet, those treated with parathyroidectomy had a lower risk of developing tertiary hyperparathyroidism (aHR = 0.49, 95%CI: 0.29-0.82) at 3 years post-KT and those who received no treatment had lower odds of delayed graft function (aOR = 0.87, 95%CI: 0.78-0.96). There was no association between treatment of SHPTH and post-transplant death-censored graft failure, all-cause graft failure or death.

**Conclusions:** The use of calcimimetics and parathyroidectomy to treat SHPTH has been steadily increasing since 2007. Importantly, patients who underwent parathyroidectomy for SHPTH had lower risk of developing tertiary hyperparathyroidism post-transplant. Therefore, patients treated with cinacalcet pre-transplant may need closer surveillance post-transplant for development of tertiary hyperparathyroidism.

**Funding:** Other NIH Support - NIA

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**PO0420**

A Combined MicroRNA and Target Protein-Based Panel for Predicting the Probability and Severity of Uremic Vascular Calcification

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**Background:** Vascular calcification (VC) increases the future risk of cardiovascular events in uremic patients, but effective therapies are still unavailable. Accurate identification of those at risk of developing VC using pathogenesis-based biomarkers is of particular interest and may facilitate individualized risk stratification. We aimed to uncover miRNA-target protein-based biomarker panels for evaluating uremic VC probability and severity.
Methods: We created a 3-tiered in vitro VC model and an in vivo uremic rat model receiving high phosphate diet to mimic uremic VC. RNAs from the in vitro and in vivo models underwent miRNA and mRNA microarray, with results screened for differentially expressed miRNAs and their target genes as biomarkers. Findings were validated in all models and human cells, followed by functional assays of identified miRNAs, and tests of sera from end-stage renal disease (ESRD) and non-diagnosis dependent chronic kidney disease (CKD) patients without and with VC.

Results: Totally 122 down-regulated and 119 up-regulated miRNAs during calcification progression were identified initially; further list-narrowing based on miRNA-mRNA pairing, anti-correlation, and functional enrichment left 16 and 14 differentially expressed miRNAs and mRNAs. Levels of 4 miRNAs (miR-I08-5p, miR-195, miR-125b-2-3p, and miR-378a-3p) were shown to decrease throughout all models tested, while 1 mRNA (SULT1F, a potential target of miR-378a-3p) exhibited the opposite trend concurrently. Among 77 ESRD (88.3% with VC) (Figure A) and 59 CKD patients (61% with VC) (Figure B), serum miR-125b-2-3p and miR-378a-3p decreased with greater VC severity, while serum SULT1F levels increased. Adding serum miR-125b-2-3p, miR-378a-3p, and SULT1F into regression models for VC substantially improved performance compared to using clinical variables alone.

Conclusions: Using a translational approach, we discovered a novel panel of biomarkers for gauging the probability/severity of uremic VC based on miRNAs and their target proteins, which improved the diagnostic accuracy.

PO0422

Tope Olufadé,1 Lois Lamerato,2 Juan Jose Garcia Sanchez,3 Like Jiang,4 Joanna C. Huang,5 Stephen Nolan,2 AstraZeneca, Wilmington, NC; 3Henry Ford Health System, Detroit, MI.

Background: The DAPA-CKD Trial is the first SGLT-2i renal outcome trial to test the efficacy and safety of an SGLT-2i, dapagliflozin, in patients with diagnosed CKD with and without T2D. To appropriately evaluate future results and aid clinical interpretation of the DAPA-CKD trial, the present study assessed the renal and CV outcomes of a “DAPA-CKD-like population” (eGFR 25-75ml/min/1.73m2 and UACR 200-5000mg/g) in a contemporary US healthcare system.

Methods: Administrative data from the Henry Ford Health System was used to identify patients with CKD stages 2 through 4 between 2006 and 2016 based on eGFR lab reading (n=38,376). Exclusions included no confirmatory eGFR > 90 days from index date, death within 30 days, history of renal transplant, and evidence of renal replacement therapy, or progression to CKD stage 5 during the baseline period (6 months prior to post index date). Within that cohort, 17,742 had eGFR (25-75ml/min/1.73m2) and 9,177 had a UACR (0-5000 mg/g) within 12 months of index date. Additional exclusions were type 1 diabetes, lupus nephritis and polycystic kidney disease. Patients were followed through December 31, 2018.

Results: Of the 6,557 patients that met the eligibility criteria and were included in the study cohort, the mean age was 62.9 years and 46.2% were male. The population was stratified by UACR (0–30, 30–199, 200–5000mg/g). Across all outcomes assessed, incidences were highest in the DAPA-CKD-like cohort (UACR 200-5000mg/g) (HF 36.1%, CV 36.1%, Stroke 8.2% (ESKD 18.6%). Mortality 18.5% see Table 1). The greatest increase was observed for renal outcomes particularly ESKD, increasing from 0.9% (UACR 0–30mg/g) to 3.4% (UACR 30-199mg/g) to 18.6% (UACR 200-5000mg/g).

Conclusions: In a contemporary US healthcare system, there remains significant adverse renal, CV and mortality outcomes among patients fitting the DAPA-CKD study inclusion criteria. These results highlight the unmet need existing for additional therapies to delay disease progression and improve outcomes and survival in this high risk population.

Funding: Commercial Support - AstraZeneca

Table 1. 1-year CV, renal and mortality outcomes across the 3 UACR categories analyzed.

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<th>UACR 200-5000mg/g</th>
<th>Total 1-year incidence &amp; p-value</th>
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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
PO0423
NSAID Use Is Not Associated with Kidney Injury or Dysfunction in Ambulatory Older Adults
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Background: NSAIDs cause AKI and may worsen CKD, especially in vulnerable populations such as older adults. We hypothesized that NSAID use would be associated with markers of both tubular and glomerular damage in older adults.

Methods: In the multicenter Health ABC cohort of ambulatory older adults, prescription and OTC NSAID use was self-reported. Estimated GFR by cystatin C, and urine albumin (ACR), KIM-1, and IL-18 were measured in 2,999 participants; urine a1m, NGAL, P1NP, and UMOD were measured in a random subset of 500 participants. We evaluated cross-sectional associations between NSAID use and these biomarkers with separate linear regression models. The association between time-updated NSAID use and eGFR decline over 10 years was estimated with linear mixed models.

Results: Participants had a mean age of 74 years, 51% were female, and 41% African-American. No eGFR differences were detected between NSAID users (n=655) and non-users (n=2344) at baseline (72 mL/min/1.73m2 in both groups). Compared to non-users, NSAID users had 33% (95% CI: 11%-49%) lower adjusted odds of having ACR ≥30 mg/g and 11% (95% CI: 4%-18%) lower mean urine IL-18 concentration at baseline. No significant differences in baseline concentrations of the remaining urine biomarkers were detected. NSAID users and non-users did not differ significantly in the rate of eGFR decline (-2.2% vs. -2.3% per year).

Conclusions: Among ambulatory older adults, NSAID use was not associated with kidney dysfunction or damage upon eight markers of kidney health, and NSAIDs were associated with significantly lower urine albumin and IL-18 concentrations. These findings illustrate the potential for NSAID use without kidney harm, even in a presumably high-risk population.

PO0424
The Prevalence of CKD Among First-Degree Relatives of Saudi Hemodialysis Patients and Associated Factors
Dujanah Alhomrany,1 Imed Alharbi,1 Mohammed A. Alhomrany,1 Imed Helal,1 FayeZ F. Alhejaili,1 Diaverum Saudi Arabia Diaverum Renal Services Group, Riyadh, Saudi Arabia.

Background: In Saudi Arabia, there are currently over 20,000 patients on dialysis and 9810 patients followed up for functioning renal transplantation. The combined prevalence of renal replacement therapy (stage 5 CKD) in Saudi Arabia is estimated to 1294.3 PMP. There are no local data or registry about stages 1 to 4 CKD in the Kingdom. Objective: To assess the prevalence of CKD among first degree relatives of Saudi hemodialysis patients and evaluate the associated characteristics.

Methods: 1st degree relatives of all hemodialysis patients in Diaverum clinics in Saudi Arabia were screened for CKD. Demographic data were collected as well as history of hypertension or diabetes mellitus. Serum creatinine, urinalysis and a single Blood pressure reading were measured. eGFR was calculated using EPI formula. For the index cases, the cause of CKD, age and gender were recorded. The prevalence rates of CKD stages among relatives were calculated and the association between different variables and CKD stages assessed.

Results: Out of 4550 dialysis patients, 20258 1st degree relatives were approached of whom 5177 responded. The cause of CKD among the index cases was DM in 52.5% followed by hypertension (20.6%). The eGFR was < 90 ml/min in 39.6% and < 60 ml/min in 35% of the screened cases. Proteinuria was present in 8%, making the combined prevalence of CKD of 13.8%. In the screened group, the prevalences of glycosuria, hematuria and proteinuria were 9.5%, 17.9% and 26.5% respectively and systolic hypertension (≥130 mmHg) was observed in 28.1% and diastolic hypertension in 8.6%. Serum creatinine values in stage 4 were significantly younger than those in stages 2-5 (p<0.001). The relationship of the screened persons to the index patients among those in stages 2-5 were offspring (35.8%), sibling (41.6%) and parent (50.0%) (p=0.0005). The prevalences of the primary renal diseases in the index cases did not differ between screened relatives in CKD stages 0-1 and those in stage 2-5.

Conclusions: The overall prevalence of CKD was 13.8% and is highest in the Southern region of Saudi Arabia. The presence of CKD in the screened relatives was not associated with identifiable cause of CKD in the index cases or use of analgesics. Many relatives were discovered to have undiagnosed hypertension and undiagnosed diabetes.

Funding: Private Foundation Support

PO0425
Sex Differences in CKD Prevalence in Asia: A Systematic Review and Meta-Analysis
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Background: Individual studies reporting sex-specific chronic kidney disease (CKD) prevalence in Asia have shown inconsistent sex differences in CKD prevalence. We sought to synthesize available sex-disaggregated data to better define and compare CKD prevalence in women and men in Asia.

Methods: We systematically searched the literature for observational studies of a≥500 adults reporting sex-disaggregated CKD prevalence data in Asia. We calculated the women-to-men prevalence ratio (PR) for each study and pooled these using random-effects meta-analysis. Subgroup analyses were performed to explore potential sources of heterogeneity in the PR.

Results: Sex-disaggregated CKD prevalence data were available for 12 of the 26 Asian countries (109 studies; 1,452,308 women and 1,391,995 men). Most studies (83%) came from China, Taiwan, Japan and South Korea. Sex-specific CKD prevalence estimates varied substantially between studies (median [IQR] reported prevalence was 16% [9-35%] in women and 17% [8-28%] in men). Overall, CKD prevalence was higher in women compared to men (pooled PR 1.14; 95% CI 1.07-1.21), with evidence of significant heterogeneity (I²=99%). In subgroup analyses, prevalence was higher in women among studies with a younger mean age, a higher proportion of diabetes and that defined CKD using eGFR only (Table 1). The pooled PR varied considerably by country.

Conclusions: Existing sex-disaggregated data suggest a higher overall prevalence of CKD in women compared to men in Asia. However, adequate assessment of sex differences in CKD prevalence is limited by the absence of sex-disaggregated data for a large part of the region. Standardised reporting of sex-disaggregated CKD prevalence data in Asia is needed.

Table 1 Subgroup analyses of the pooled PR.

PO0426
Increased Circulating suPAR Levels in African Patients with HIV
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Background: Decline in kidney function associated with APOL1 risk alleles is dependent on circulating suPAR levels in African American (AA) patients. Yet, little is known among HIV infected persons in sub-Saharan Africa, and epidemiological data from

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
this region regarding APOL1 risk status is scarce. We aimed to determine APOL1 risk variants, plasma suPAR levels and estimate kidney function in HIV patients in Zambia.

Methods: We performed a cross-sectional study with 480 adult HIV infected persons on anti-retroviral treatment (ART) (women, 64.8%) in Lusaka, Zambia. APOL1 genotyping was done to determine the prevalence of the risk alleles; plasma suPAR levels were assayed and estimated GFR (eGFR) was calculated by CKD-EPI creatinine-based formula.

Results: Plasma suPAR levels were increased and were negatively correlated to eGFR, whether less than 60 or not (r=-0.15, p<0.001). Women while younger (42 vs 46 years old for men, p=0.0003), had higher suPAR than men (3.68 mg/ml vs 3.07 mg/ml, p<0.0001). Ten out of 480 patients (2.1%) had CKD, and their suPAR levels were higher than patients without CKD (5.6 mg/ml vs 3.44 mg/ml, p<0.0001). Fifty patients (10.4%) had 2 APOL1 risk alleles (35 for women vs 15 for men); among those, 3 (6%) developed CKD (p=0.07). No difference in suPAR levels or eGFR was observed between patients who carried 2 APOL1 risk alleles and those with 1 or 0 risk allele.

Conclusions: HIV infected persons in Zambia on ART have increased suPAR levels. The prevalence of two APOL1 risk alleles is similar as with AA HIV patients. A longitudinal study with a bigger cohort should reveal the relationship between suPAR, APOL1 risk alleles and kidney function.

Funding: NIDDK Support

PO0427
Kidney Tubular Injury and Dysfunction Relate to Frailty and Cognitive Function in Persons with CKD in SPRINT
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Background: The association of markers of kidney disease (eGFR and albuminuria) with frailty and cognition is well established. However, these markers do not specifically evaluate kidney tubule injury or dysfunction.

Methods: We measured 8 biomarkers of kidney tubule dysfunction and injury among 2,882 SPRINT participants with eGFR <60 and evaluated their association with frailty and cognitive function. Frailty was defined with a previously validated frailty index (FI), categorized as fit (FI < 0.10), less fit (0.10 < FI < 0.21), and frail (FI > 0.21). Global cognitive function was measured using the Montreal Cognitive Assessment (MoCA).

Models were adjusted for, demographic, behavioral, and clinical variables including urine creatinine, eGFR, and albuminuria.

Results: Higher urine concentrations of MCP-1 and cT1M were independently associated with frailty (Figure). These associations were independent of demographics, other CKD risk factors, eGFR and albuminuria, and were more strongly associated than associations of albuminuria with frailty (Figure). Higher urine cT1M was associated with lower cognitive function (β -0.09; 95% CI -0.17, -0.01), whereas albuminuria was not (β: -0.09; 95% CI -0.17, -0.01), among those, 3 (6%) developed CKD (p=0.07). No difference in suPAR levels or eGFR was observed between patients who carried 2 APOL1 risk alleles and those with 1 or 0 risk allele.

Conclusions: None of the urine tubule injury markers were associated with MSJE, whereas higher urine NGAL was associated with lower DSST scores. Lower concentrations of sHC03 were associated with lower scores of MSJE but not DSST (Table). These associations were independent of demographics, eGFR, and albuminuria.

Funding: NIDDK Support, Other NIH Support - NIA, NINDS, NHLBI, Veterans Affairs Support

Cross-sectional association between tubule injury markers of kidney dysfunction with cognitive function.

PO0428
Association of Kidney Tubule Injury and Dysfunction with Cognitive Function in the Health, Aging and Body Composition Study
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Background: The association of lower levels of eGFR and higher levels of albuminuria with poor cognition is well established. However, these markers do not specifically evaluate kidney tubule injury or dysfunction.

Methods: We measured 5 urinary biomarkers of kidney tubule injury and dysfunction (alpha-1 microglobulin [α1M], kidney injury molecule-1 [KIM-1], interleukin-18 [IL-18], uromodulin [Umod], and neutrophil gelatinase-associated lipocin [NGAL]) among a random sample of 502 participants, and serum bicarbonate [sHC03] among 2,288 community-living elders aged 70-79. We evaluated the cross-sectional associations with cognitive function using the Modified Mini-Mental State Exam (3MSE) and the Digit Symbol Substitution Test (DSST), where higher scores represent better cognitive function.

Results: None of the urine tubule injury markers were associated with MSJE, whereas higher urine NGAL was associated with lower DSST scores. Lower concentrations of sHC03 were associated with lower scores of MSJE but not DSST (Table). These associations were independent of demographics, eGFR, and albuminuria.

Conclusions: None of the urine tubule injury markers were associated with low cognition, only higher NGAL was associated with lower cognitive function testing by DSST. Similarly sHC03 was associated with worse cognitive function by MSJE independent of eGFR, albuminuria, or other risk factors.

Funding: NIDDK Support, Other NIH Support - This research was supported by National Institute on Aging (NIA) contracts #N01-AG-6-2101; N01-AG-6-2103; N01-AG-6-2106; NIA grant R01-AG028805; NINR grant R01-NR012459, Veterans Affairs Support

Cross-sectional association between biomarker of kidney tubule dysfunction with cognitive function.
Conclusions: We observed that elevated TG were associated with higher risk of pneumonia hospitalization in non-CKD and CKD stage 3A-3B patients, but this relationship was not observed in late-stage CKD patients. While use of statins and cholesterol levels have been studied in the context of pneumonia and lung function, future studies are warranted to also investigate the role of triglycerides in pneumonia risk especially among early stage CKD patients.

PO0430

The Reference Interval and Risk Factors of NT-ProBNP in CKD Patients Without Heart Failure

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Background: N-terminal pro-B-type natriuretic peptide (NT-proBNP), a diagnostic marker of heart failure (HF), as well as the specific and sensitive biomarker of HF is been demonstrated to be affected by renal failure. NT-proBNP is significantly associated with the severity of GFR loss. However, the reference interval (RI) of NT-proBNP in nondialysis chronic kidney disease (CKD) patients without HF remains unclear. The aim of our study was to establish the threshold value of NT-proBNP which could help to early recognition, prevention and treatment for HF.

Methods: All patients diagnosed with CKD aged more than 18 years old in our hospital from Jan 01, 2014 to Dec 31, 2019 were recruited into this study. Individuals who diagnosed with HF were excluded. The RI for NT-proBNP was defined by nonparametric method and risk factors were analyzed by linear regression analysis.

Results: A total of 1260 CKD patients without HF were included in this study. Of them, 588(46.67%) were female. NT-proBNP were increased with the advanced stage of kidney function in CKD patients without HF. The median level of NT-proBNP in CKD stage 5 (non-dialysis patients) without HF were the highest, as 610.25 pg/ml. The RIs for NT-proBNP in CKD patients without HF with respect to kidney function stage (ranges of stage 1, stage 2, stage 3, stage 4, stage 5 ND) were 8.15-536.32, 12.38-811.90, 16.62-1411.05, 33.14-2945.05, 88.58-5533.73 pg/ml. We also demonstrated that NT-proBNP was significantly correlated with the serum levels of Hb (β =-0.174, P<0.001), Ca (β =-0.214, P<0.001), P (β =-0.111, P<0.001), hs-CRP (β =-0.140, P<0.001), and eGFR(β =-0.243, P<0.001).

Conclusions: Our study proved that NT-proBNP was increased with the advanced stage of GFR in CKD patients without HF. The RI of NT-proBNP varied among the different stages of CKD without HF and multiple factors contributed to NT-proBNP, which could help clinicians to prevent and take actions against the occurrence of HF.

Funding: Government Support - Non-U.S.

PO0431

Soluble Urokinase Plasminogen Activation Receptor and Major Adverse Cardiac Event Morbidity in CKD Patients in the German Chronic Kidney Disease (GCKD) Cohort

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Background: Soluble urokinase plasminogen activation receptor (suPAR) is supposed as risk factor for both chronic kidney disease (CKD) and biomarker for major adverse cardiac events (MACE) disease. A long-term longitudinal analysis in a large cohort of patients suffering from both diseases simultaneously, CKD and cardiovascular (CV) disease including MACE criteria, to analyze suPAR as a predictive biomarker has not been performed, yet.

Methods: SuPAR was studied in the GCKD Study Group with a follow-up time of 4 years. Association of suPAR with CKD (estimated glomerular filtration rate, eGFR) and overall risk of all-cause death, CV death, and MACE (three-point MACE, MACE3; four-point MACE4) was estimated by Cox proportional hazards regression according to quintiles of suPAR.

Results: Altogether, 4994 participants were enrolled (60.1 ± 12.0 years; eGFR of 49.4 ±18.3 mL/min/1.73m²). Median suPAR concentration was 1771 pg/mL (25th-75th percentile, 1447-2254 pg/mL). Hazard ratio for CV mortality was 1.58 (95%CI 0.62-4.00) in the second, 2.15 (95%CI 0.87-5.26) in the third, 3.48 (95%CI 1.53-7.93) in the fourth, and 5.30 (95%CI 2.34-12.0) in the fifth quintile. If additionally adjusted for eGFR, UACR, NT-proBNP, hsCRP results were confirmed.

Conclusions: In the GCKD study cohort suPAR predicts all-cause death, cardiovascular death, and MACE independent of NT-proBNP, renal function and of markers of systemic inflammation.

PO0432

Incidence and Racial Disparities in Cardiovascular Disease and CKD Progression in Young Adults with CKD

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Background: Cardiovascular disease (CVD) is a major source of morbidity and mortality in adult CKD patients; yet is not well elucidated in young adults with CKD. Furthermore, racial and ethnic disparities in CVD and CKD progression has been found in research of pediatric and older-adult CKD populations, but has not been investigated specifically in young adults.

Methods: We studied 317 participants aged 21-40yrs of age with mild to moderate CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study, of whom, 174 were black or Hispanic. We calculated incidence rates for CV events (heart failure [HF], MI, stroke, and death) and CKD progression (50% decline in eGFR or ESRD) for all young adult participants and as stratified by race and ethnicity. Cox proportional hazards regression models were constructed to test the association between race/ethnicity and CV events and CKD progression, adjusting for age, sex, eGFR, UACr, baseline SBP, and APOL1 status.

Results: HF, mortality and CKD progression had the highest incidence rates amongst young adults with CKD (Figure 1). Rates of these events were higher among Black and Hispanic participants: HF (17.5 vs. 5.1/1000 person-years), all-cause mortality (15.2 vs. 7.1/1000 person-years), and CKD progression (125 vs. 59/1000 person-years). Lastly, in adjusted models, black or Hispanic status was significantly associated with higher risk of CV events (HR: 1.25, 95%CI: 1.12-1.41) and CKD progression (HR: 1.38, 95%CI: 1.21-1.57).

Conclusions: Young adults with CKD in the CRIC study experience high incidence rates of cardiovascular disease. The burden of disease is even higher for black and Hispanic participants with CKD. Further research is required to better understand the factors underlying racial disparities in young adults with CKD.

Funding: NIDDK Support

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Underline represents presenting author.
Trends in the Transition to ESRD Among Native Hawaiians and Pacific Islanders Across the United States

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Background: Census data indicate there are >1.5 million Native Hawaiians and other Pacific Islanders (NHOPIs) in the US. While growing data show NHOPIs have a high prevalence of kidney disease risk factors (diabetes, obesity, hypertension, limited healthcare access), there are major knowledge gaps regarding the burden of end-stage renal disease (ESRD) in this population. We examined trends in the transition to ESRD in NHOPIs.

Methods: Using United States Renal Data System (USRDS) and Census Bureau data, we compared annual incident ESRD rates among NHOPI, African Americans (AA), and other racial subgroups over 2010-16. Rates were calculated as the observed incident ESRD count divided by the race-specific Census population size of that year. Multiple race designations were considered by utilizing Census categorizations that incorporated primary race in combination with one or more other races (alone or combination). We estimated crude rates and rates standardized to the age-sex distribution of 2011 race-specific Census population data.

Results: Over 2010-16, NHOPIs and AAs demonstrated the highest crude incident ESRD rates over time (Fig 1A). A similar pattern was observed for standardized incident ESRD rates (Fig 1B): 918, 638, 308, and 226 incident ESRD patients per million (population/year) in 2016 for NHOPI, AA, Caucasian, Asian, and American Indian/Alaska Native subgroups, respectively. While standardized incident ESRD rates among AAs gradually declined, there was a steady rise in NHOPIs’ incident ESRD rates over time.

Conclusions: NHOPIs demonstrated the highest incident ESRD rates over time. Further studies are needed to determine sociodemographic, biologic/genetic, cultural, and health care related ESRD risk factors among NHOPIs to inform targeted interventions in this population.

Funding: NIDDK Support
PO0436
Defining the Excess Risk of Adverse Kidney Outcomes in CKD Patients with Type 2 Diabetes in the DISCOVER-CKD Cohort
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Background: Chronic Kidney Disease (CKD) patients with type 2 diabetes (T2D) are considered at a high risk of cardiovascular events. However, the excess risk of major kidney events in T2D patients compared to patients without T2D is unknown.

Methods: DISCOVER-CKD is an international observational study of patients with CKD that encompasses large retrospective electronic medical records (EMR) and claims data between 2008 and 2020. Preliminarily, data from US-based Limited Claims and Electronic Health Record (LCED) data (IBM Health, Armonk, NY) and TriNetx (healthcare-based EMR) were analysed. CKD patients (eGFR <60 mL/min/1.73 m²) aged ≥18 years with a 1-year record of urine albumin to creatinine ratio (UACR) were identified. T2D status was ascertained any time before the index date (2nd eGFR measurement). The risk of kidney outcomes (sustained ≥50% eGFR decline or end-stage kidney disease) was compared between patients with and without T2D at ≥5 years’ follow-up.

Results: Compared to non-T2D patients, T2D patients had a slightly higher incidence rate of adverse renal outcomes in LCED (2.7% versus 2.3% per year; TriNetX: 1.8% versus 1.2% per year). After adjusting for all confounding factors (Figure 1) we observed no increased risk of adverse renal outcomes in patients with T2D compared to non-T2D patients in LCED (hazard ratio (HR): 1.08; 95%CI 0.81-1.43) and a 34% increased risk in TriNetX database (HR:1.34; 95%CI 1.11-1.62).

Conclusions: There is an excess risk of renal adverse outcomes in CKD patient with T2D compared to those without T2D. This is explained in part by a large extent by conventional risk markers in LCED but not completely in TriNetX. Both groups (T2D and non-T2D) should be managed proactively to reduce the risk of poor clinical outcomes.

Funding: Commercial Support - AstraZeneca

ESRD (HR, 2.09 95%CI 1.43 to 3.07, I²=37%), all-cause mortality (HR, 1.53 95%CI 1.13 to 2.01, I²=77%) and hospitalization (HR, 1.28, I²=52).

Conclusions: Depressive symptoms in CKD are independent risk factors of poor clinical outcomes, including ESRD, all-cause death, and hospitalization. There is necessary to design high quality studies to assess the effects of treating depressive symptoms in patients with CKD.

PO0438
Association of the Creatinine-to-Cystatin C Ratio with Overall Survival with and Without CKD
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Background: Creatinine and Cystatin C are measured as glomerular filtration markers. Creatinine is highly correlated with skeletal muscle mass, whereas Cystatin C is not. We hypothesized that persons, in whom serum Cystatin C is lower than creatinine level, i.e., creatinine to Cystatin C ratio (CrCCR) >1.00 (regardless of measurement units) have incrementally greater survival chance, likely due to a larger muscle mass.

Methods: We examined a cohort of 7,849 Veterans with baseline measured Cystatin C and creatinine data between 2004-2015. Veterans were divided into 0.25 increments of CrCCR, i.e., <0.75, 0.75–<1.0,1.0–<1.25, ≥1.25. They were further stratified into groups based on normal vs. low eGFR (<60 vs. ≥60 mL/min/1.73 m²), and the associations of CrCCR with survival across two eGFR strata were examined.

Results: The mean age (±SD) in the Veterans’ cohort was 69±12 years. There were 4% female, 77% white, and 15% African American. The median (IQR range) for cystatin C was 1.28 (0.99,1.71) mg/L, for creatinine 1.24 (0.92,1.68) mg/dl, and for the CrCCR was 0.99 (0.81,1.17). Compared to the reference (CrCCR=1.25 and eGFR≥60 mL/ min/1.73 m²) the multivariable adjusted model showed that those with a lower CrCCR >0.75 (regarding lowest mortality strata) had the lowest mortality risk for both eGFR strata, with the normal eGFR group having higher death risk than the low eGFR group (HR=1.05; 1.05-1.32). The in the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the highest overall survival than those with low CrCCR (HR=0.65; 0.65-0.76), respectively. In the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the highest overall survival than those with low CrCCR (HR=0.65; 0.65-0.76), respectively. In the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the highest overall survival than those with low CrCCR (HR=0.65; 0.65-0.76), respectively. In the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the highest overall survival than those with low CrCCR (HR=0.65; 0.65-0.76), respectively. In the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the highest overall survival than those with low CrCCR (HR=0.65; 0.65-0.76), respectively.

Conclusions: A lower CrCCR indicating higher cystatin C relative to creatinine levels are strongly associated with worse overall survival in Veterans regardless of kidney function level. Future studies should examine the clinical utility of this potential surrogate of muscle mass and overall health over creatinine or Cystatin C alone in evaluating risk stratification in patients with and without kidney disease.

PO0437
Increased Risk of Progression to ESRD or Death in CKD Patients with Symptoms of Depression: A Systematic Review and Meta-Analysis of Cohort Studies
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Background: Comorbid symptoms of depression are common psychiatric disorder in patients with chronic kidney disease (CKD). It remains unclear whether it is an independent risk factor for progression of patients with CKD not requiring dialysis. We conducted a systematic review to assess the association of depressive symptoms with poor clinical outcomes in patients with CKD not requiring dialysis.

Methods: PubMed, Embase and CINAHL were searched (up to February 15th, 2020) for cohort studies assessing the association of depression with progression to end-stage renal disease (ESRD), defined as requiring maintenance dialysis, or all-cause mortality in patients with CKD not requiring maintenance dialysis. Two independent researchers extracted data, assessed risk of bias and evidence certainty.

Results: Seven cohort studies of 6145 patients were included. Methodological quality of studies was generally low risk of bias. Compared with non-depression or low depressive symptoms, high depressive symptoms increased the risk of progression to

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PO0439
CKD by Previous Diabetes or Hypertension: A Longitudinal Outcomes Study in Primary Care
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Background: To compare mortality and progression to end-stage-renal-disease (ESRD) in patients with new chronic kidney disease (CKD) by previous occurrence of type 2 diabetes (DM) and/or arterial hypertension (HT) in Catalonia

Methods: We designed a longitudinal retrospective study of adults with new CKD between 2007 and 2017 identified using electronic medical records from primary care
in Catalonia, Spain. New CKD was considered the index event and defined as a first occurrence of an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² or a urine albumin-to-creatinine ratio ≥ 30 mg/g or albuminuria a 20mcg for 90+ days, or a diagnostic code for CKD. Variables were extracted from the SIDIAP research database and the Spanish hospital basic minimum dataset. Patients were classified according to previous occurrence of HT, DM, both or none. The resulting mutually exclusive DM-CKD, HT-CKD, DM-HT/CKD and unspec-CKD, were followed until ESRD and death within the study period. We defined ESRD as an eGFR< 15 mL/min during 90+ days or renal replacement therapy. Fine and Grey regression models were used to assess competing risk of death and Cox regression among the four CKD groups, considering mortality as a competing risk and Cox regression for mortality. Both models were adjusted for multiple confounders.

**Results:** In total, 467,802 persons were included (median age 75 years; 46.8% men). At baseline, 51% had DM, 45% had HT, 33% had HT/DM-CKD and 12% had unspec-CKD. The DM-CKD group were the youngest in average, more likely to be men, had the highest proportion of persons with an eGFR below 60 mL/min/1.73m2 and the highest proportion of altered albuminuria. Comparing unspec-CKD, DM- and HT-CKD had lower risk of ESRD -adjusted subdistribution hazard ratio (SHR) and 95% confidence interval (CI): 0.98 (0.95-0.98) and 0.71 (0.65-0.79), respectively, but HT/DM-CKD had a higher risk: SHR(CI) 1.11 (1.06-1.15). In turn, the risk for death was higher in DM-CKD, HR (CI): 1.19 (1.11-1.27) and lowest in the HT-CKD group, 0.84 (0.79-0.88), as compared to unspec-CKD. For the group HT/DM-HT the HR(CI) was 0.92 (0.87-0.97).

**Conclusions:** According to these results, there are no differences in ESRD risk among CKD patients by prior DM or HT, but there is a synergic effect. Mortality is different in CKD patients with HT vs with DM.

**Funding:** Commercial Support - Bayer AG

PO0440 Elderly Patients Are Likely to Have Faster CKD Progression if Plasma Brain Natriuretic Peptide (BNP) Is Elevated

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**Background:** Elderly CKD patients have been mostly believed that they have slower decline in eGFR than younger individuals. However, this is not the case, especially when the patient has well-known factor(s) that accelerate(s) CKD progression, such as cardiac dysfunction. Plasma concentration of brain natriuretic peptide (BNP) is often elevated in patients with cardiac dysfunction and is known to be associated with higher mortality. This study was conducted to find out whether plasma BNP level can be used to predict future decline in eGFR.

**Methods:** A hospital-wide study with all the laboratory data for a period of 4 years and 2 months was performed. Non-diaryal CKD patients (median eGFR <60 mL/ min/1.73 m²) with an eGFR slope in whom the eGFR slope was obtained over 731 days or more with BNP measured at least three times were retrieved. An eGFR slope per each patient was calculated and its relationship with plasma BNP level and other factors was assessed. Statistical analysis was done with R 3.6.0 on Ubuntu.

**Results:** A total of 339 patients (M:F = 154:185, age 65-102 (median 84) years) were included whose initial BNP was 130.0±184.2 (0.164.1, median 75.76) pg/mL. A “random forest” analysis, one of the multivariate analyses, was performed using an R package (randomForest), in order to elucidate risk factors associated with faster decline in eGFR, i.e., with the highest change in eGFR. The following factors were found to be initial eGFR, initial BNP and variability of BNP. With linear regression analysis, the eGFR slope was significantly associated with initial eGFR and initial BNP (P<0.001). Patients with higher-than-average initial BNP (>130.0 pg/mL) and initial eGFR had lower rate of decline in eGFR than the rest of the population (3.83±4.62 vs 1.72±3.57, P<0.0001). A combination of initial eGFR and initial BNP correctly differentiated the fastest quartile from the rest in 72.9% of the population.

**Conclusions:** Elevated plasma BNP might predict faster decline in eGFR in the elderly CKD patients.

PO0441 Proton-Pump Inhibitors (PPIs) vs. H2 Blockers (H2B) Users and Overall Risk of CKD Progression

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**Background:** PPI use is associated with adverse kidney events. The relationship between PPI use and the development of acute interstitial nephritis (AIN) is well established. However, the relationship between PPI use and CKD progression is less clear. Notably, there is a lack of data concerning renal outcomes in established CKD. The aim of our study is to determine the risk of CKD progression among patients on PPI, H2B, or no anti-acid therapy.

**Methods:** Using our CKD registry, we evaluated the relationship between the use of PPI, H2B, and no treatment among patients with CKD stage 3 and 4 with at least 12 months of PPI visits in the year prior. We evaluated the relationship between medication group and overall mortality using a Cox proportional hazards model while adjusting for demographics and comorbidities, and the relationship between medication group and progression to eGFR<20 or ESKD with death as a competing risk using regression models as described by Fine and Gray.

**Results:** Among 3,930 patients, 1,374 were in PPI group, 119 were in H2 blocker group, and 2,347 had no medication. Average age was 72.8±11.1, and 42.5% male. Among PPI 28% had Coronary Artery Disease compared to 22% among H2B and 19% among no medication (P<0.001). Congestive Heart Failure was 13%, 8% and 7% for each group respectively (P<0.01). Overall mortality was not different amongst the three groups (PPI vs. none HR 0.94, 95% CI: 0.80, 1.10, and PPI vs. H2B HR 0.80, 95% CI: 0.52, 1.24). The cumulative incidence of ESKD/eGFR<20 with death as a competing risk was also not different across groups in univariate (Fig. 1) or adjusted models (PPI vs. none SHR 0.99, 95% CI: 0.74, 1.34, PPI vs. H2B SHR 1.82, 95% CI: 0.91, 3.63). Use of PPI in a CKD population was not associated with increased mortality or CKD progression to ESKD when compared to the use of H2 blockers and to no acid suppressing therapy.

**Conclusion:** Use of PPI in a CKD population was not associated with increased mortality or CKD progression to ESKD when compared to the use of H2 blockers and to no acid suppressing therapy.

PO0442 Renin-Angiotensin-Aldosterone System (RAAS) Blockade Does Not Affect Kidney Progression in Patients with CKD Without Diabetes and Without Proteinuria

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**Background:** Non-proteinuric CKD contributes to about 80% of end stage kidney disease and is poorly studied in terms of risk factors & pathogenesis. RAAS blockers such as an angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) have been shown to be renoprotective in CKD progression in patients with diabetes and proteinuria. There is a paucity of data on effect of ACEI/ARB in non-diabetic non-proteinuric CKD patients.

**Purpose:** This is a retrospective observational study of insurance claim database from 1/07 to 12/31/17 examining the effect of ACEI or ARB use on CKD progression. Inclusion criteria: adults at least 18 years of age, with CKD stage 3 or higher [based on at least 2 serum creatinine (SCr) values 90 days apart] with at least 2 urinalyses with dipstick urine protein with negative or trace, follow-up (FU) period of at least 3 yrs. Patients with diabetes or proteinuria were excluded. Primary outcomes were doubling of SCr, or reaching CKD stage 5. Mortality data was not available. Duration of ACEI/ARB exposure is defined as number of prescribed days. The eGFR was calculated based on CKD-EPI equation. Analysis are performed with 2 models: time varying Cox regression, and mixed model (which included time-period fixed effect and random effects). A greedy 1:1 propensity score matching scheme was applied.

**Results:** Of 20,000 CKD patients, there were 2,853 with CKD stage 3 or higher without proteinuria, with 301 on ACEI/ARB during mean FU 6 yrs. Percentage of patients with hypertension or CHF, mean age, gender, and eGFR did not differ between ACEI/ARB vs. non-ACEI/ARB groups. The eGFR decrease per year was not statistically different between those on ACEI/ARB vs. non-ACEI/ARB group (matched cox model, p = 0.2285; mixed model, p = 0.4546 respectively). Age and ACEI/ARB duration of exposure have no effect. ACEI/ARB patients had lower rate of developing diabetes during the study (OR 0.57, p = 0.0044), and higher rate of proteinuria at the end of study (OR 1.59, p = 0.0048), though these associations were not observed in the matched sample.

**Conclusions:** This study suggests ACEI/ARB does not affect CKD progression in non-diabetic non-proteinuric patients, irrespective of age. Further studies are needed to confirm those findings.

PO0443 Biomarkers of Immune Activation and ESKD: Results from AASK

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**Background:** Immune activation is fundamental to the pathogenesis of many kidney diseases, and innate immune molecules such as soluble urokinase-type plasminogen activator receptor (suPAR) have been linked to incidence and progression of CKD.

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

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Novel Fibrosis Biomarker Development and Validation in Human Kidney Disease

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Background: Biomarkers for non-invasive assessment of kidney fibrosis are not available. This study illustrates the characterization of five novel candidate biomarkers of kidney fibrosis—Cadherin-11 (CDH11), Sarcoplasmic reticulum calcium binding-2 (SMOC2), Pigment epithelium-derived factor (PEDF), Matrix-gla protein (MGP), and Thrombospondin-2 (THBS2)—which were selected from transcriptomic findings in animal models of fibrosis.

Methods: We developed Luminex-based assays and measured proteins in plasma and urine samples of two independent prospective cohort studies, the Boston Kidney Biopsy Cohort (BKBC, n=801), a cohort of individuals with biopsy-confirmed semi-quantitative assessment of kidney fibrosis, and the Seattle Kidney Study (SKS, n=252). Ordinal logistic regression and Cox proportional hazards models tested associations of biomarkers with interstitial fibrosis and tubular atrophy (IFTA) in the BKBC and progression to end-stage kidney disease (ESKD) in both cohorts, respectively. sRNA datasets of human kidneys assessed cell-specific gene expression profiles.

Results: In the BKBC, higher levels of urinary PEDF and plasma and urinary SMOC2 and CDH11 were independently associated with more severe IFTA (Figure 1). In both cohort studies, higher levels of plasma and urinary SMOC2 and urinary CDH11 associated with progression to ESKD (HR-range 1.27 to 1.89) after adjustment for age, sex, race, proteinuria, and eGFR. Higher levels of urinary PEDF were associated with ESKD in the SKS (HR=1.29, 95% CI 1.14 to 1.45), with consistent signals in the BKBC, although the latter narrowly missed statistical significance. sRNA-sequencing data demonstrated expression of all biomarkers in human fibroblasts.

Conclusions: Novel plasma and urine biomarkers of kidney fibrosis, developed from animal models, are associated with higher levels of human kidney fibrosis and subsequent progression to ESKD.

Funding: Private Foundation Support

PO0445

Urinary Fibrosis Markers and Risk for ESKD: The Chronic Renal Insufficiency Cohort (CRIC) Study

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Background: Connective tissue growth factor (CCN2) and amino-terminal peptide of procollagen type III (PIIINP) are both correlated with kidney fibrosis. However, it is unclear if these markers are independently associated with the risk for ESKD.

Methods: We measured CCN2 and PIIINP in baseline urine and standardized to urine creatinine (Cr) in a multi-center cohort study of men and women with chronic kidney disease (CKD), the CRIC Study (N=3727). ESKD was defined as initiation of kidney replacement therapy (N=1118 events). Cox proportional hazards models were adjusted hierarchically as indicated (Table).

Results: The mean age of the study population was 58 years; mean eGFR: 45 mL/ min/1.73 m2; and 48% had diabetes. After multivariable adjustment and median follow-up of 10 years, the highest quartiles of CCN2/Cr and PIIINP/Cr were associated with a 1.8-fold and 1.7-fold higher risk for ESKD compared to the lowest quartiles, respectively (Table). The association was no longer statistically significant after adjustment for proteinuria.

Conclusions: Urinary CCN2 and PIIINP are strongly associated with risk for ESKD, an association that may be mediated through proteinuria. Future studies should investigate if these markers add to the identification of those at highest risk for progression to ESKD.

Funding: NIDDK Support

PO0446

Urinary Retinol-Binding Protein Is Associated with the Risk of Kidney Replacement Therapy in CKD

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Background: Retinol-binding protein (RBP), a homolog of the retinol-binding protein (RBP), is used in clinical practice as a risk factor for CKD in tubular diseases, such as Dent’s disease and cystinosis, and in renal transplantation. However, its role as a biomarker of KD progression outside these conditions is less clear. The aim of our study was to evaluate the association of uRBP with the risk of mortality and kidney replacement therapy (KRT) in CKD of multiple etiologies.

Methods: The PROGREDIR cohort is composed of 454 older adults with CKD (predominantly G3 and G4) recruited from the outpatient services of a tertiary hospital in Sao Paulo, Brazil. Baseline uRBP was measured using an immunoenzymatic assay with monoclonal antibody and expressed as mg/g urinary creatinine, and those with missing values were excluded (n=22). Events of death (n=184) and KRT (n=60) were ascertained

Abbreviations: CI: confidence interval; HR: hazard ratio.

Model 1: unadjusted; Model 2: stratified by clinical site and adjusted for age, gender, race/ethnicity, education, BMI, SBP, Hgb, smoking, diabetes, and history of CVD; Model 3: Model 2 + urine Na, urine K, serum phosphate, FGF-23, serum bicarbonate, IL-10, IL-6, TGF-β, hs-TnT, hs-Troponin T, NTproBNP, urine NGAL, eGFR; Model 4: Model 3 + proteinuria.

Funding: NIDDK Support

PO0447

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

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Results: Mean age was 67 (12), y eGFR was 38 (15) mL/min/1.73 m², 64% were male and 58% were diabetic. Median (P25, P75) for uRBp were: 0.29 (0.08, 1.47) in all; 0.24 (0.06, 0.84) vs. 0.46 (0.10, 2.87) in those who remained alive vs. those who died (p = 0.001); and 0.26 (0.08, 0.90) vs. 2.98 (0.21, 17.5) in those without and with KRT, respectively (p = 0.0001). In Cox models, RBP was not related to mortality. However, competing models showed that uRBp was related to the risk of KRT, even after adjustments (Table). This association was also present when only normoalbuminuric participants (CKD A1) were included.

Conclusions: uRBp is significantly associated with the risk of KRT in the setting of CKD, and may be particularly useful as a biomarker in CKD patients with normoalbuminuria (CKD A1).

PO0447 Tubular Secretion of Creatinine and Risk of Kidney Failure: The Modification of Diet in Renal Disease Trial
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Background: Whether tubular secretion is associated with clinical outcomes beyond glomerular filtrate rate (GFR) or proteinuria is unknown. By using measured GFR and creatinine clearance, we evaluate the association of tubular secretion of creatinine with long-term kidney and mortality outcomes.

Methods: The Modification of Diet in Renal Disease (MDRD) Study was a randomized controlled trial conducted to examine the effects of strict blood pressure control and dietary protein restriction on progression of stages 3 to 4 CKD. This prospective analysis included 838 participants with baseline measures of iothalamate creatinine clearance (CICr), tubular secretion of creatinine (TS cr), and other potential confounding factors (Table). Higher TS cr was associated with a lower risk of ESKD (HR 0.74, 95% CI 0.66–0.84) after adjustments for mGFR, proteinuria, age, sex, body mass index, and GFR slope measurement period occurred in 301 subjects. The GFR slope of the cohort was -0.948 mL/min/1.73 m² per year (95% confidence interval [CI] -1.016, -0.880) in the linear mixed model and -0.982 mL/min/1.73 m² per year (95% CI -1.075, -0.889) according to least squares linear regression. Both calculated GFR slopes were significantly related to the HR of the composite hard endpoints. HR decreased by 0.85 (linear mixed model) and 0.9 (least squares linear regression) times in case of a reduction in slope of GFR decline by 0.75 mL/min/1.73 m² per year. Multiple regression analysis revealed strongly significant associations for GFR slope with urine protein and CKD stage and undetectable relationships for GFR slope with diabetes and age.

Conclusions: This study demonstrated the clinical significance of GFR slope as a surrogate marker for renal prognosis in Japanese CKD patients. In order to reduce slope of eGFR decline, active intervention for proteinuria before the progression to an advanced CKD stage appears to be effective.

PO0448 Clinical Significance and Related Factors of GFR Slope in a Large Multicenter Observational Study in Japan
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Background: Recently, GFR slope has attracted attention as an important surrogate marker for the prognosis of CKD, with a reduction in slope of GFR decline by 0.75 mL/min/1.73 m² per year reportedly having clinical significance. This investigation addresses the clinical significance of GFR slope and its related factors on Japanese CKD patients.

Methods: CKD patients in 15 general hospitals between January and March 2014 were surveyed using medical records. The selection criteria were age ≥20 years, eGFR <60 mL/min/1.73 m², and receiving medical treatment for CKD. Baseline patient characteristics, eGFR changes, and hard endpoints (death or ESKD requiring RRT) were analysed. We calculated GFR slope using eGFR data of 2 years by 2 calculation methods, the linear mixed model and least squares linear regression, and examined the relationship of GFR slope with the hazard ratio (HR) of the endpoints. The factors related to GFR slope were also assessed by multiple regression analysis.

Results: Among a total of 11233 patients, we analyzed the data of 7490 CKD G3 and G4 patients (60% male, mean age: 71 years, CKD G3a: 55%, G3b: 30%, G4: 15%, mean eGFR: 44 mL/min/1.73 m², urine protein positive: 51%, diabetes mellitus: 49%, use of RAS-I: 57%). The mean observation period was 1040 days. Hard endpoints after the GFR slope measurement period occurred in 301 subjects. The GFR slope of the cohort was -0.948 mL/min/1.73 m² per year (95% confidence interval [CI] -1.016, -0.880) in the linear mixed model and -0.982 mL/min/1.73 m² per year (95% CI -1.075, -0.889) according to least squares linear regression. Both calculated GFR slopes were significantly related to the HR of the composite hard endpoints. HR decreased by 0.85 (linear mixed model) and 0.9 (least squares linear regression) times in case of a reduction in slope of GFR decline by 0.75 mL/min/1.73 m² per year. Multiple regression analysis revealed strongly significant associations for GFR slope with urine protein and CKD stage and undetectable relationships for GFR slope with diabetes and age.

Conclusions: This study demonstrated the clinical significance of GFR slope as a surrogate marker for renal prognosis in Japanese CKD patients. In order to reduce slope of eGFR decline, active intervention for proteinuria before the progression to an advanced CKD stage appears to be effective.

PO0449 The Kidney Failure Risk Equation: Testing Previous eGFR Slopes, Clinical Variables, and Novel Populations
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Background: The 4-variable kidney failure risk equation (KFRE) is a well-validated tool that accurately predicts the 2- and 5-year risk of kidney failure in patients with eGFR <60 mL/min/1.73 m² using baseline eGFR, ACR, age, and sex. The aim of this study was two-fold: to assess whether KFRE can be improved using previous eGFR slope or other variables; and to evaluate whether the KFRE can be used in patients with eGFR ≥60 mL/min/1.73 m².

Methods: We used 36 cohorts in development and 17 cohorts in validation to accomplish these aims; all cohorts participate in the CKD-Prognosis Consortium and had data on the four variables, previous 2-year eGFR slope, and at least 25 ESKD events.

Results: There were 205,004 participants with eGFR <60 mL/min/1.73 m² (12,794 ESKD events) and 441,915 participants with eGFR ≥60 mL/min/1.73 m² (1,220 ESKD events). In the eGFR <60 group, previous 2-year eGFR loss >3 mL/min/1.73 m²/ year was associated with ESKD (meta-analyzed HR 1.36, 95% CI 1.19-1.56) with a small improvement over the 4-variable model (baseline c-statistic in validation cohorts, 0.87-0.89, meta-averaged difference in c-statistic in validation cohorts when adding slope, 0.001, 95% CI: 0.000-0.002). Using previous 5-year slope resulted in slightly better c-statistic compared to the model using 2-year slope (meta-analyzed difference in c-statistic in validation cohorts, 0.003, 95% CI: 0.001-0.005). Other approaches, such as using 1-year average eGFR or 1-year average ACR as inputs in the 4-variable KFRE, or incorporating black race, heart failure, or atrial fibrillation, did not result in meaningful improvements. The KFRE had poor discrimination and calibration in the eGFR ≥60 mL/min/1.73 m² population. In a model that instead predicted 40% decline in eGFR and included age, sex, ACR, diabetes, hypertension, heart failure, and coronary heart disease, previous eGFR loss >3 mL/min/1.73 m²/year over 2- and 5-years were associated with greater risk (HR, 1.43, 95%CI: 1.19-1.70; 1.84, 95%CI: 1.40-2.42).

Conclusions: In summary, the KFRE was improved only slightly by the inclusion of previous eGFR slope. For populations with eGFR >60, a more relevant and predictable outcome may be percent eGFR decline.

Funding: NIDDK Support, Private Foundation Support
Compared of Predicted Risk of Renal Replacement Therapy vs. eGFR for Arteriovenous Fistula Placement in CKD: A Retrospective Analysis

Background: The complexity in predicting which and when patients with chronic kidney disease (CKD) will progress to renal replacement therapy (RRT) contributes to 80% of patients starting hemodialysis without a functioning permanent access. Studies suggest AVF referral at eGFR of 15-20 ml/min increases the likelihood of starting dialysis with an AVF. We were interested in whether a prediction model developed at Kaiser Permanente Northwest better predicted progression to RRT at 1 year compared to eGFR.

Methods: We retrospectively followed 613 patients with stage 4 CKD between ages of 18 to 89 from May 2013 to May 2018 followed by nephrologists who had a nephrology visit with an eGFR and a calculable 2-year risk for RRT around 12 months before end of follow up (defined as death, initiation of RRT, or 2 years from initial enrollment date). We calculated sensitivity, specificity, and area under the curve (AUC) based on a range of 2-year risk for RRT (20%, 40%, 60%, and 80%) and compared them to eGFR threshold of 15 mL/min and 20 mL/min at the 12 month visit prior to end of follow up. We compared 2-year risk for eGFR vs. AVF.

Results: At end of follow up, 12% had died and 14% had progressed to RRT (69% hemodialysis, 22% peritoneal dialysis, 9% transplant). Compared to eGFR threshold of 20 mL/min, specificity and specificity was greater at 2-year risk of 40% (73% and 49% for eGFR threshold of 20 mL/min respectively compared to 83% and 54% respectively for 2-year risk threshold of 40%). Compared to eGFR threshold of 15 mL/min, sensitivity and specificity was greater at 2-year RRT risk of 80% (97% and 11% for eGFR threshold of 15 mL/min respectively compared to 98% and 18% respectively for 2-year RRT risk threshold of 80%). The AUC was greater between 2-year RRT of 20% to 40% (0.73 to 0.70) compared to eGFR between 15 mL/min to 20 mL/min (0.54-0.61). Decision curve analysis showed better net benefit using 2-year risk >40% compared to eGFR of 20 mL/min above a 1 year threshold of 25%.

Conclusions: In patients with CKD stage 4, 2-year risk for RRT better predicted progression to RRT at 1 year compared to eGFR alone. Our study suggests that use of prediction model for RRT may be an important tool for determining optimal timing for AVF referral.

Risk Factors of Renal Replacement Therapy in Hospitalized Patients with CKD Stage 4
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Background: Data on risk factors of renal replacement therapy (RRT) in hospitalized patients with CKD4 may help nephrologists to delay dialysis. The study was designed to describe the risk factors of RRT in CKD4 inpatients.

Methods: Medical records of CKD4 inpatients in Guangdong Provincial Hospital of Chinese medicine during January 2010 - January 2019 were collected. Risk factors such as demographic characteristics, laboratory and echocardiography test results, treatments, comorbidities and primary diseases were collected. Patients were followed up till they reached clinical outcomes (RRT) or the end of the study (January, 2020). Patients who withdrew from the study before 12 years were excluded. Descriptive statistics and survival analysis were performed by Cox regression, with 95% CI, considering a value of P<0.05 as statistically significant.

Results: 222 CKD4 inpatients [age, 60.00(47.75-72.25) years]; female, 55.9% were enrolled. In a multi-follow-up of 2.41 years, 199 inpatients (10.6%) started RRT. Among those patients, the median time progression to RRT was 2.10 (1.20-5.38) years. All patients were divided into two groups according to whether progressed to RRT within 2.41 years. For those received RRT within 2.41 years, they had heavier urine, urine occult blood and account for a higher proportion of inpatients with diabetes mellitus(63.6%), chronic heart failure (43.6%), diabetic kidney disease (55.5%). Their serum albumin and ejection fraction (EF) were lower (P<0.001). The multivariate Cox proportional hazards models showed that age, eGFR ratio (HR: 0.986; 95% confidence interval[CI]: 0.976-0.995); P=0.004, diabetic kidney disease (DKD) (HR: 1.727; 95%CI: (1.274-2.319), P=0.001), urinary protein (HR: 1.148; 95% CI: (1.094-1.205), P=0.001), serum albumin (HR: 0.971; 95% CI: (0.949-0.994), P=0.013), LVMi (HR: 1.010; 95% CI: (1.004-1.016), P=0.002), left ventricular dimension systolic(LVds) (HR: 0.948; 95% CI: (0.910-0.986), P=0.008) and EF (HR: 0.970; 95% CI: (0.950-0.990), P=0.004) were independently associated with factors for progression RRT in CKD4 inpatients.

Conclusions: DKD, urinary protein, LVMi were risk factors that were significantly associated with CKD4 progression to RRT in inpatients. Whereas, serum albumin, LVds, and EF are protective. The urinary protein, serum albumin and echocardiographic parameters need to be taken seriously for patients with CKD.
**PO0454**

Indexing Proteinuria to Renal Function Improves Prediction for Renal Events in Individuals with CKD

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**Background:** Identifying the optimal measurement of proteinuria in clinical settings has been challenging. To determine the potential consequence of varied measures of proteinuria, we contrasted their clinical significance primarily in relation to renal events and secondarily to cardiovascular (CVD) and mortality events.

**Methods:** We compared the predictive ability of four measures of proteinuria and albuminuria, among 3,992 CKD participants from the Chronic Renal Insufficiency Cohort (CRIC) Study, for incident renal events (halving of glomerular filtration rate [GFR] or end-stage renal disease), CVD events (myocardial infarction, congestive heart failure, stroke and peripheral arterial disease) and mortality over 5 years. The four measures included timed urinal albumin and protein excretion rates (AER, PER), albumin:creatinine ratios (ACR, PCR), albumin:protein: adjusted creatinine (accounting for creatinine production) ratios (eAER, ePER), and lastly albuminuria/proteinuria indexed to GFR (ACR-G, PCR-G), as an estimation of glomerular permeability. We used Harrell’s C-Statistics to measure model discrimination.

**Results:** Predictive performance for renal events was lowest for AER and PER. Results were generally similar for ACR vs eAER and PCR vs ePER. Notably, PCR-G showed significant improvement in predicting renal outcomes and performed better than albuminuria-based measures. C-Statistics for renal events were 0.831, 0.840, 0.841, 0.846 and 0.862 for AER, eAER, ACR, PCR and PCR-G, respectively. Trends were similar for CVD and mortality events, except that ACR performed better than PCR for CVD events, but not as well as PCR-G or ACR-G. Results were overall consistent across diabetes, gender and race strata, and were validated in an additional 1443 participants from the third phase of CRIC.

**Conclusions:** Indexing proteinuria to GFR is a simple and economical measure, compared to albuminuria, that significantly enhances the prediction of CKD progression and associated outcomes.

**Funding:** NIDDK Support

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**PO0455**

Evaluate Phosphate Intake and Excretion in CKD Patients

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**Phosphate (P) restriction is crucial in CKD patients. Classically, P intake has failed to correlate with 24-h phosphaturia. Organic or inorganic P have different intestinal absorption rates, which might explain the lack of correlation between P intake and phosphaturia. Thus, we aimed to evaluate if the source of dietary P rather than the total P ingested determines phosphaturia, and to what extent inorganic P intake modifies phosphaturia.**

**Methods:** A 3-day dietary survey was performed in 71 stages G2-3 CKD patients to estimate the amount and source of P intake. 24-h urine samples were collected. Total phosphaturia, the FeP(%), and P/UUN, which reflect intestinal absorption of P relative to different intestinal absorption rates, which might explain the lack of correlation between P intake and phosphaturia. Thus, we aimed to evaluate if the source of dietary P rather than the total P ingested determines phosphaturia, and to what extent inorganic P intake modifies phosphaturia.

**Results:** The P intake was 1086.5±361.3 mg/day. P intake was 64.0%, 22.1%, and 14.1% from animal, vegetables, and inorganic sources respectively. Total P intake did not correlate with urinary P (p=0.12), nor FeP. Patients ingesting more P ingested more inorganic P (Fig1). P intake correlated with P/UUN ratio (p=0.008). Patients in the upper P/UUN tertile showed the highest daily P intake (p=0.04) from inorganic sources (p=0.03), and the highest phosphaturia (p=0.04).

**Conclusions:** P/UUN reflects the total P intake and provides information about the amount of inorganic P, and could be used to guide the appropriate nutritional advice for CKD patients.

**Funding:** NIDDK Support

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**PO0456**

Hypophosphatemia as a Surrogate Marker of Renal Outcome in Chronic Hepatitis B Patients Receiving Antiviral Therapy

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**Background:** Antiviral therapy is crucial for the treatment of chronic hepatitis B (CHB). Although hypophosphatemia has been known to be an important adverse effect of antiviral agents, the clinical significance is yet to be revealed. In this study using a large cohort of CHB patients, the incidence and clinical significant of hypophosphatemia was investigated.

**Methods:** CHB patients who started antiviral therapy between 2005 and 2015, and had received at least one year of therapy, were included after excluding liver cirrhosis, diabetes mellitus, hypertension, concomitant administration of diuretics, and ESRD. Hypophosphatemia was defined as serum phosphorous level ≤ 2.5mg/dL. The primary outcome was changes in renal function. Secondary outcomes included the incidence of infection and changes in serum potassium, uric acid, and total carbon dioxide (tCO2).

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**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Results: Of the 4,335 patients, hypophosphatemia developed in 75 patients (1.7%). When patients were categorized depending on serum phosphate level, median phosphate level of 728 patients (16%) decreased by more than 0.5 mg/dL from the baseline. During the 2-year follow-up period, patients with hypophosphatemia showed lower eGFR compared to the control group. Also, patients whose serum phosphate level decreased by more than 0.5 mg/dL showed significantly lower eGFR compared to the control group at all time points. The incidence of infection and changes in serum potassium, uric acid, and CO2 were similar between groups.

Conclusions: Hypophosphatemia was associated with renal function decline in CHB patients receiving antiviral therapy. 50% of patients who took 12 months of antiviral therapy was relatively low, our results support the clinical significance of hypophosphatemia as a surrogate marker of adverse renal outcome in CHB patients.

PO0457
Dietary Phosphorus Restriction Improves Renal Function, Blood Pressure, FGF-23, and Klotho Levels in CKD Stages 1 and 2

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Background: To evaluate Impact of dietary education and intervention (phosphorus restriction) on creatinine, eGFR, FGF23, Klotho and blood pressure.

Methods: 105 subjects (CKD stages 1, 2 N 76, 3controls) evaluated for eGFR, creatinine, phosphorus, calcium, FGF-23, soluable o-Klotho iPTH FGF 23, blood pressure and 3 days dietary intake, using standard methodology on first visit, 6 and 12 months. CKD patients were grouped based on dietary phosphorus intake:Group 1 (n=42): phosphorous intake <1000mg/day and Group 2 (n=37; 17 in CKD 1; 20 CKD 2): high phosphorus intake (>1000mg/d). Patients in Group 2 were counselled for low phosphorus diet.

Results: Parameters of controls and CKD patients differed significantly. Dietary, serum and urinary phosphorus (0.001) had significant association. Systolic and diastolic BP, protein intake, dietary phosphorus, iPTH, FGF23 were significantly high (p<0.001) and Klotho significantly low (p<0.001) in Group 2 compared to Group 1. Impact of dietary intervention was seen at 6 and 12 months as reduction in protein intake from 0.64 ± 0.05 to 0.58±0.11 (CKD 1) and 0.71±0.04 to 0.64±0.05 (p<0.012 CKD 2); decline in creatinine from 1.13±0.14 to 1.07±0.14 (CKD 1) and 1.06±0.56 (p<0.009 CKD 1); serum phosphorus from 3.57±0.19 to 3.23±0.58 (CKD 1) and 4.32±0.42 to 3.35±0.85 mg/dL (p<0.001 CKD 2); FGF23 from 55.01±1.65, to 51.27±1.17 (CKD 1); 65.42±4.80 to 56.60±1.23 (p<0.010 CKD 2); systolic BP from 127.95±3.14 to 121.05±4.14 (CKD 1); 134.22±3.54 to 118.38±9.08 (p<0.001 CKD 2) and diastolic BP from 85.14±3.40 to 83.29±8.03 (CKD 1); 89.1±4.74 to 80.33±6.02 (p<0.003 CKD 2) and a significant increase in eGFR mL/min from 95.17±6.50 to 97.75±20.26 (CKD 1); 69.82±8.56 to 74.08±11.07 (p<0.019 CKD 2)) was observed. sKlotho increased from 700.79±27.82 to 879.39±168.37 (p<0.001 CKD 1); from 633.52±6.50 to 823.37±156.67 (p<0.001 CKD 2). Ca x P product declined from 36.10±8.44 to 29.48±7.63 (p<0.001). eGFR can predicted using dietary protein, creatinine systolic BP, haemoglobin, cholesterol (r 0.808).

Conclusions: Dietary counselling had significant effect on all the parameters in early CKD stages. Dietary intervention can prevent in FGF23, reduce blood pressure and prevent decline in renal function as demonstrated by significant increase in eGFR with phosphorus restriction in early stages of CKD.

PO0458
Baseline Serum Magnesium and Risk of CKD Progression in the Chronic Renal Insufficiency Cohort (CRIC) Study

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Background: Serum magnesium (sMg) concentration is regulated by intestinal absorption and renal handling which are impaired in CKD. While Mg has been implicated in absorption and renal handling which are impaired in CKD. While Mg has been implicated in absorp

PO0459
The Effects of Intermittent Fasting on the Progression of CKD

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Background: Intermittent fasting (IF) refers to the practice of restricting food intake to a short period of the day alternating with a prolonged period of fasting. Preclinical studies and clinical trials have shown that IF has broad-spectrum benefits for many health conditions, such as obesity, diabetes mellitus, cardiovascular disease, cancers, and neurologic disorders. There are currently few studies suggesting a decrease in the progression of chronic kidney disease (CKD) with IF.

Methods: Retrospective chart review was done on patients from outpatient nephrology clinic with CKD stage I to IV who were self-reported to practice intermittent fasting. Patients with ESRD on dialysis, hospital admission during the study period, and reported poor compliance with fasting regimens were excluded. The primary outcome was the change in eGFR at the end of the period of intermittent fasting.

Results: Here we report current findings from 16 patients practicing IF regimen with continued ongoing enrollment. 75% of these patients were diabetic. Duration of the IF regimen ranged from 4 months to 12 months. 50% of patients had completed 12 months of IF regimen. 62.5% of patients were found to have an improvement in eGFR at the end of the period of IF. The change in eGFR was found to range from 0.4 ml/min/1.73 m² to 38.8 ml/min/1.73 m² (1.4-76.5%). The median increase in eGFR was 6.5 ml/min/1.73 m² (18.1%) during an average period of 8 months of IF (p-value = 0.04). There was no significant correlation between change in eGFR and change in weight or hemoglobin A1C during this period.

Conclusions: A significant increase in eGFR was seen in a small population of patients with CKD practicing intermittent fasting for four months or more. Previous studies report an average annual decline in GFR of 1.5-2 ml/min/1.73 m² in the general CKD population, with a more rapid decline in certain subsets. Intermittent fasting as a preventive measure for the progression of CKD needs to be studied further.
The Association Between Dietary Fiber Intake and Clinical Outcomes in CKD: A Report from the Chronic Renal Insufficiency Cohort (CRIC)

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Background: Standard dietary interventions for individuals with chronic kidney disease (CKD) consist of reductions in salt, phosphorus, potassium, and protein intake, with no specific guidance regarding dietary fiber intake. In animal models of kidney disease, a diet high in amylose resistant starch has been found to trigger a reduction in inflammation and CKD progression. It is unclear whether low dietary fiber intake is associated with a higher risk of incident kidney disease progression, cardiovascular disease, and overall mortality in individuals with CKD.

Methods: A total of 3791 participants with chronic kidney disease and information on dietary fiber intake at the baseline visit in the Chronic Renal Insufficiency Cohort (CRIC) Study were included in the analyses. Cox proportional hazards models adjusted for sociodemographic, comorbidities, medications and laboratory data, including eGFR and proteinuria were used to analyze the association between dietary fiber intake and clinical outcomes.

Results: The mean age was 59±11 years, 46% were female, 47% had diabetes, and the average eGFR was 48±17 ml/min/1.73m². The average dietary fiber intake was 17.3±9.6 g. After a median follow-up of 8.8±4.5 years, there was an inverse association between crude death rates and baseline dietary fiber intake: increasing from 3.1 per 100 person-years (PY) for the highest to 3.4 per 100 PY for the lowest fiber tertile. After multivariable adjustments, individuals in the middle and low fiber tertiles were at greater risk of death compared to those in the highest fiber tertile (HR[95%CI], 1.18 [1.01, 1.38], p =0.04 and 1.10 (0.94, 1.29), 0.24, respectively). We found no significant association between dietary fiber intake at the baseline visit in the Chronic Renal Insufficiency Cohort (CRIC) Study with lower risk of ESRD (HR 0.94 [95%CI, 0.89-0.99] per 0.01 g/kg/day per year; p=0.025), but not with mortality risk (P=0.84), Non-linear regression models confirmed these findings (Figure). Compared to patients who had no change in DPI, the hazard ratio (95%CI) of death and ESRD in those with a change of -0.03 g/kg/day per year were 1.12 (0.95-1.47) and 0.71 (0.52-0.98), respectively.

Conclusions: In patients with CKD, DPI showed a relatively small intra-individual temporal variation, but decrease in DPI was significantly associated with lower risk of ESRD, without an association with mortality.
PO0463
Association of Plasma Selenium with Renal Function in Hypertensives: Modification by Folate
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Background: We aimed to investigate the association between plasma selenium (Se) and renal function decline in adults with hypertension and to explore the possible modification by folate.

Methods: This was a prospective study, including a total of 935 hypertensive adults from a folate-acid intervention trial (CSPPT) with baseline plasma Se measurements and renal outcome data available. The primary outcome was rapid decline in renal function, defined as an average decline in eGFR ≥5 mL/min/1.73 m^2 per year.

Results: Over a median follow-up of 4.4 years, the primary outcome occurred in 72 participants. After multivariate-adjusted, there was an inverse association between plasma Se and rapid decline in renal function (per 10-unit increment: OR, 0.85; 95% CI: 0.72, 0.99). Consistently, compared to the lowest tertile of baseline plasma Se (<74.5 μg/L), the highest tertile (89.4–150 μg/L) was significantly associated with a 60% (0.40; 0.21, 0.79) reduction in the odds of the outcome. A stronger inverse plasma Se-renal function decline association was observed in those received folic acid treatment (per 10-unit increment: OR, 0.70; 95% CI: 0.54, 0.90; P-interaction=0.036) or with a higher baseline folate concentration (a9 ng/mL: 0.59; 0.43, 0.82; P-interaction=0.004).

Conclusions: In China hypertensives with plasma Se <150 μg/L, there was an inverse relationship of plasma Se with the renal function decline, especially in those with folic-acid supplementation or a higher folate level.

Funding: Government Support - Non-U.S.

Association between plasma Se and the outcome

<table>
<thead>
<tr>
<th>Plasma selenium (μg/L)</th>
<th>Event (%)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per 10-unit increment</td>
<td>70 (10)</td>
<td>0.85 (0.72, 0.99)</td>
</tr>
<tr>
<td>Tertile 1 (34.5)</td>
<td>27 (11)</td>
<td>Ref (1)</td>
</tr>
<tr>
<td>Tertile 2 (45.5)</td>
<td>32 (17)</td>
<td>0.99 (0.81, 1.20)</td>
</tr>
<tr>
<td>Tertile 3 (55)</td>
<td>31 (16)</td>
<td>0.80 (0.61, 1.07)</td>
</tr>
</tbody>
</table>

Subgroup analyses on plasma Se (per 1-unit increment) and the outcome.

PO0465
Relationship of Serum Triglycerides with Incident Albuminuria Among 114,817 US Veterans
Melissa Soohoo,1 Jui-Ting Hsiung,1,2 Maria V. Marroquin,1,3 Csaba P. Kovedy,1 Kamyr Kalantar-Zadeh,1,2 Elani Streja,1,2 The University of Tennessee Health Science Center, Memphis, TN;1,2VA Long Beach Healthcare System, Long Beach, CA;1,2Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA;1,2Memphis VA Medical Center, Memphis, TN.

Background: The association of metabolic syndrome (MetS) components of impaired glucose, obesity, low high-density lipoprotein, hypertension, and serum triglycerides (TG), with renal endpoints such as incident chronic kidney disease (CKD) have been previously studied individually. Urine albumin to creatinine ratio (UACR) remains an integral part of CKD staging and incidence, yet it remains understudied. Thus, we sought to examine the relationship of TG with incident albuminuria among normal UACR patients with consideration for other MetS components.

Methods: Our cohort comprised 114,817 veterans with albuminuria stage A1 (<30 mg/g) and data on TG and MetS components. Incident albuminuria was defined as at least two UACR measurements of >30 mg/g at 90 days apart. We used Cox proportional hazards models to evaluate the association of TG with incident albuminuria, adjusted for case-mix characteristics, laboratory values and individual MetS components, as well as stratified by s2 and s3 MetS components.

Results: The means±SD age was 65±11, with a median[IQR] of TG, UACR and eGFR of 144[97, 214] mg/dL, 7[4, 13] mg/g, and 75[61, 89] mL/min/1.73 m^2 respectively, and 70% had at least 3 MetS components. We observed a linear association between TG and incident albuminuria, adjusted for case-mix characteristics, laboratory values and individual MetS components, as well as stratified by s2 and s3 MetS components.

Conclusions: Higher TG are associated with incident albuminuria independent of other components of MetS. Further study is needed to understand the drivers of this association, with a specific focus of how to best manage TG levels in addressing albuminuria development.

PO0464
Association Between CKD and New Onset of Dyslipidemia: Results from a Longitudinal Nationwide Survey
Takakii Kosugi,1 Masahiro Eriyuchi,1 Hisako Yoshida,2 Hikari Tasaki,1 Masatoshi Nishimoto,1 Masato Kasahara,3 Kunitoshi Iseki,1 Koichi Asahi,1 Kunihiro Yamagata,4 Tsuneo Konta,2 Shouichi Fujimoto,1 Ichiee Narita,5 Yugo Shiibagaki,10 Toshiki Moriyanma,11 Masahide Suruya,11 Kunihiro Shibagaki,12 Jui-Ting Hsiung,1,2 Maria V. Marroquin,1,3 Csaba P. Kovedy,1 Kamyr Kalantar-Zadeh,1,2 Elani Streja,1,2 Terasaki Institute, Los Angeles, CA;1,2VA Long Beach Healthcare System, Long Beach, CA;1,2Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA;1,2Memphis VA Medical Center, Memphis, TN.

Background: Dyslipidemia is a significant risk factor of CVD and seems to be associated with CKD onset and progression. On the contrary, CKD patients have associated with CKD onset and progression. On the contrary, CKD patients have dyslipidemia more frequently than non-CKD patients, but it is unclear whether CKD affects new onset of dyslipidemia.

Methods: This is a longitudinal study based on data obtained from the Japanese Society of Health Check and Guidance System. Among 664,926 individuals who participated in this program from 2008 to 2014, we excluded participants who met the following criteria: 1) health check only one time, 2) missing values for creatinine or proteinuria, 3) dyslipidemia at baseline, or 4) medication for dyslipidemia at any point. We evaluated new onset of dyslipidemia according to two factor; hypertriglyceridemia (High-TG), hyper-LDL cholesterolemia (High-LDL), or hypo-HDL cholesterolemia (Low-HDL), defined as triglycerides ≥150 mg/dL, LDL cholesterol ≥140 mg/dL, or HDL cholesterol ≤40 mg/dL, respectively, and compared between participants with and without CKD. These associations were analyzed using Kaplan-Meier methods and Cox regression analysis after adjustment for clinically relevant factors.

Results: During a median follow-up period of 3.1 years, the cumulative incidences of High-TG, High-LDL, and Low-HDL were 45,300, 51,940, and 13,313 participants, respectively, among 305,893 participants (non-CKD: 254,884; CKD: 51,009). In the univariable analyses, hazard ratios (HRs) [95% confidence intervals (CIs)] in CKD vs non-CKD participants were 1.31 [1.27-1.34], 1.02 [0.99-1.05], and 1.70 [1.63-1.77] for High-TG, High-LDL, and Low-HDL, respectively. After adjustment for clinically relevant confounders, adjusted HRs [95% CIs] in CKD participants were 1.10 [1.07-1.13], 0.99 [0.96-1.02], and 1.16 [1.11-1.22] for High-TG, High-LDL, and Low-HDL, respectively.

Conclusions: CKD was associated with new onset of High-TG and Low-HDL, but not High-LDL among general population in Japan.
PO0466

Short-Term Associations of Triglycerides with Atherosclerotic and Non-Atherosclerotic Cardiovascular Disease Alleviations Across CKD Stages

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Background: In chronic kidney disease (CKD) patients, we showed that the risk of atherosclerotic cardiovascular disease (ASCVD) and non-ASCVD events with high baseline triglycerides (TG) incrementally attenuated across worse CKD stages, where high TG was associated with lower risk of non-ASCVD events in late-stage CKD. TG levels can change with CKD progression, but associations of time-varying TG with ASCVD or non-ASCVD hospitalizations is unknown.

Methods: We examined time-varying TG with time to first ASCVD or non-ASCVD hospitalization in 2,963,176 US veterans who received care in 2004-2006 (baseline) and were followed to 2014. Events were classified by primary ICD-9 codes. Using time-varying Cox models, we evaluated associations of time-varying TG with first ASCVD or non-ASCVD events stratified by baseline CKD stage, for adjustment for demographics, and time-varying comorbidities and laboratory values.

Results: The cohort was 63±14 years old with a mean [IQR] TG [127, [87, 189]] mg/dL, and 23% had CKD 3A or higher at baseline. TG >80 mg/dL was associated with a lower risk of time to first ASCVD event (ref: TG 120-<160 mg/dL) for all baseline CKD stages (Fig A). There was a linear association between time-varying TG and ASCVD events. High TG (≥240 mg/dL) had the highest risks for ASCVD, for baseline non-CKD, and CKD 3A-3B. Among late-stage CKD patients, the association of high TG and ASCVD was null. We observed an inverse association between time-varying TG with time to first non-ASCVD event (Fig B). Patients with low TG had faster times to first non-ASCVD event for non-CKD and CKD 3A-4, while high TG were associated with slower times in all stages. CKD stage 5 at baseline renal disease patients with TG ≥240 mg/dL had the lowest risk of non-ASCVD event.

Conclusions: Short-term risk of higher TG with ASCVD or non-ASCVD events incrementally decreased across CKD stages, where risk was lower to null in late stage patients. High TG were associated with lower risks of non-ASCVD across all CKD stages. Investigation is needed to evaluate the pathways involving TG and cardiac events as CKD severity progresses in order to best manage health.

PO0467

Metabolic Acidosis and Progression to Renal Replacement Therapy

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Background: Metabolic acidosis is common in advanced chronic kidney disease (CKD) and is associated with its progression (Kraut J, Adv Chronic Kidney Dis. 2017). Methods: De-identified electronic health records (Optum® EHR), 2007 to 2017 were queried to identify patients with non-dialysis CKD Stages 3-5 with ≥1 and normal serum bicarbonate were established based on the index serum bicarbonate (> 22 mEq/L or 22-< 29 mEq/L). Progression to RRT was defined as initiation of dialysis or kidney transplantation, identified in EHR data by diagnosis or procedure codes, or (≤ 22 mEq/L or 22 - < 29 mEq/L). Patients (N = 136,067) were classified with non-dialysis CKD progression, but associations of time-varying TG with ASCVD or non-ASCVD hospitalizations is unknown.

Results: In pts with non-dialysis CKD Stages 3-5, 2 years of post-index data or death within 2 years, and grouped by baseline metabolic acidosis (12 to < 22 mEq/L) vs normal serum bicarbonate (22 to < 30 mEq/L). Patients (N = 136,067) were classified as Asian (N =1,328), Black (N =15,248), Hispanic (N =4,137), White (N=111,953) or Other (N=3,401). The primary endpoint was the composite outcome of death, kidney dialysis or transplant, or 40% decline in eGFR from baseline (DD40). Cox proportional hazards models examined the impact of serum bicarbonate on DD40 within each racial/ethnic group, adjusted for age, sex, eGFR, log albumin-to-creatinine ratio, diabetes, hypertension, heart failure, Charlson Comorbidity Score.

Conclusions: In a large community-dwelling US population, serum bicarbonate was independently associated with adverse kidney outcomes and death in Asians, Blacks, Hispanics and Whites with CKD. Since race and ethnicity are associated with other socioeconomic factors that affect health, further exploration of the potential reasons for the observed range of hazard ratios across groups is warranted.

Funding: Commercial Support - Tricida, Inc.

PO0468

Relationship Between Metabolic Acidosis and CKD Progression Is Evident Across US Racial and Ethnic Groups

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Background: Metabolic acidosis is a known risk factor for CKD progression, but little is known about the impact of race and ethnicity on this relationship. We used a large electronic medical record (EMR) database of >100 million patients from all 50 states and insurance types to evaluate the relationship between metabolic acidosis and adverse renal outcomes and death by race and ethnicity.

Methods: De-identified electronic medical records (Optum® EHR), 2007–2019 were queried to identify patients with non-dialysis CKD Stages 3-5, 2 years of post-index data or death within 2 years, and grouped by baseline metabolic acidosis (12 to < 22 mEq/L) vs normal serum bicarbonate (22 to < 30 mEq/L). Patients (N = 136,067) were classified as Asian (N =1,328), Black (N =15,248), Hispanic (N =4,137), White (N=111,953) or Other (N=3,401). The primary endpoint was the composite outcome of death, kidney dialysis or transplant, or 40% decline in eGFR from baseline (DD40). Cox proportional hazards models examined the impact of serum bicarbonate on DD40 within each racial/ethnic group, adjusted for age, sex, eGFR, log albumin-to-creatinine ratio, diabetes, hypertension, heart failure, Charlson Comorbidity Score.

Results: Overall, 47,032 patients (34.6%) experienced DD40 events within 2 years: Asian, 35%; Black, 44%; Hispanic, 48%; White, 32%; Other, 48%. Serum bicarbonate independent predicted DD40 in all racial/ethnic groups. Adjusted Hazard Ratios for DD40 per 1 mEq/L increase in serum bicarbonate (median 4.2 yrs, max 11.5 yrs follow-up) were as follows: Asian, 0.942 (CI: 0.917- 0.968); Black, 0.976 (CI: 0.969-0.983); Hispanic, 0.970 (CI: 0.956-0.984); White, 0.960 (CI: 0.957-0.963); Pc< 0.0001 for all groups.

Conclusions: In a large community-dwelling US population, serum bicarbonate was independently associated with adverse kidney outcomes and death in Asians, Blacks, Hispanics and Whites with CKD. Since race and ethnicity are associated with other socioeconomic factors that affect health, further exploration of the potential reasons for the observed range of hazard ratios across groups is warranted.

Funding: Commercial Support - Tricida, Inc.
Lower Urine Citrate Excretion Associated with Advanced CKD Stage Is Mediated by Reduced Plasma Citrate and Decreased Kidney Citrate Clearance

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Background: Lower urinary citrate excretion (UcitV) might be a biomarker of covert acid (H+) retention in patients with CKD but without metabolic acidosis and so mechanisms that mediate UcitV differences among patients with CKD would help assessment of its biomarker utility. Because longitudinal eGFR decreases in patients with CKD associated with decreasing UcitV (Goraya, et al. AJP 317:F502, 2019), we examined cross-sectional differences in UcitV across CKD stages and mechanisms that mediate such differences.

Methods: We measured 8-hour UcitV (8h UcitV), plasma citrate concentration (Pcit), and kidney citrate clearance citrate (UcitV/Pcit) in 52 patients with CKD 1 (eGFR=99.5±7.7 ml/min/1.73 m2), 2 (eGFR=73.4±6.1 ml/min/1.73 m2) and 52 with CKD 3 (eGFR=40.1±7.6 ml/min/1.73 m2) with macroalbuminuric, non-diabetic, hypertension-associated nephropathy. We assessed ongoing dietary H+ intake as potential renal acid load (PRAL) and steady-state acid-base status with plasma total CO2 (PTCO2) and H+ retention, the latter estimated by comparing observed to expected PTCO2, increase in response to retained HCO3 (administered minus UHCO3V) 2 hours after oral NaHCO3, bolus (0.5 mmol/kg bw), assuming 50% body weight HCO3, apparent space of distribution.

Results: Although PRAL was not different among CKD 1, CKD 2, and CKD 3 groups (62.4±11.9, 62.9±14.7, and 65.2±7.9 mmol/day, respectively, p=0.47), PTCO2, was progressively lower (26.4±0.7, 25.9±0.6, and 21.6±1.9 mM, respectively, p<0.01) and H+ retention progressively higher (3.9±12.9, 18.2±14.0, and 25.1±13.4 mM, respectively, p<0.01) with advancing CKD stage. 8h UcitV was progressively lower with advancing CKD stage (1.14±0.03, 1.06±0.25, and 0.86±0.10 mmol/1.73m2, respectively, p<0.01) as was Pcit (0.16 ± 0.01, 0.15 ± 0.02, and 0.14 ± 0.01 mM, respectively, p<0.01) and UcitV/Pcit (0.015 ± 0.001, 0.014 ± 0.003, and 0.013 ± 0.001 mmol/1.73 m2, respectively, p<0.01).

Conclusions: Cross-sectional advanced CKD stage was associated with greater H+ retention and lower UcitV, the latter mediated by lower Pcit and lower UcitV/Pcit. The data support that reduced UcitV associated with decreased eGFR reflects underlying H+ retention with reduced body citrate stores and increased citrate conservation through reduced kidney citrate clearance.

Urinary Calcium Excretion and Risk of CKD Progression: The CRIC Study

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Background: Hypercalciuria is implicated in nephrolithiasis and nephrocalcinosis, conditions associated with chronic kidney disease (CKD). We aimed to study the determinants of urinary calcium excretion (UCaE) and its association with adverse clinical outcomes in CKD.

Methods: 24-hour UCaE was measured in 3,768 Chronic Renal Insufficiency Cohort (CRIC) participants. We used multivariable linear regression models to determine independent predictors of UCaE in CKD 1-5. Weighted Cox regression analyses tested the associations of UCaE with incident end stage kidney disease (ESKD), CKD progression (50% eGFR decline or incident ESKD), atherosclerotic cardiovascular disease (ASCVD) events, and death.

Results: Estimated glomerular filtration rate (eGFR) correlated most strongly with UCaE (r=0.47, P<0.001). In both males and females, determinants of UCaE included eGFR, African American race, iPTH, 24-hour urine sodium and phosphate, serum albumin and the use of diuretics and angiotensin receptor blockers (Figure 1). Certain predictors of UCaE differed between sexes: systolic blood pressure and alcohol drinker were associated with UCaE in males, while serum calcium and vitamin D intakes were significantly associated with UCaE in females. Higher UCaE was significantly associated with lower risk of ESKD, CKD progression, death and ASCVD events in unadjusted models. These associations were attenuated after adjusting for baseline characteristics, and for most outcomes the associations became insignificant after adjusting for eGFR.

Conclusions: Predictors of UCaE in CKD differed between males and females. eGFR is extremely strongly associated with UCaE and greatly confounds the associations between UCaE and all the outcomes.
Methods: We utilized electronic health record (EHR) data of patients seen at a health care system in the 7-county metropolitan area in Minnesota and linked census tract data. Census tract measures (medium of owner occupied housing units (wealth), percentage of residents >25 years with a Bachelor's degree (education), and median household income (income)) and individual level insurance status (≥65 years: Medicare vs. other insurance; <65 years: Medicare vs. supplemental insurance plan) were obtained from the American Community Survey (2008-2012) and the EHR, respectively. A patient was considered to be living in low and high SES tracts if they belong to the first and fourth quartile of each SES measures. CKD prevalence was defined as having an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² or proteinuria. We used a multilevel Poisson regression with robust error variance with a random intercept at the census tract level to estimate the association between tract SES [low (first quartile) vs. high (fourth quartile)], insurance, and CKD.

Results: We included 185,269 patients. Tract SES (wealth and education) and insurance are independently associated with CKD prevalence. After adjusting for demographic and clinical characteristics, patients (<65 and ≥65 years) living in low vs. high SES tracts had higher CKD prevalence (Prevalence Ratio PR, 95%CI of low vs. high tract SES for education among patients <65 years: 1.11 [1.05, 1.18] and 1.08 [1.04, 1.12] for high vs. low SES for education among patients ≥65 years: 1.11 [1.05, 1.18] and 1.08 [1.04, 1.12]) for high vs. low SES for education among patients ≥65 years: 1.11 [1.05, 1.18] and 1.08 [1.04, 1.12]). After adjusting for insurance type, patients on supplemental insurance had higher CKD prevalence (PR, 95%CI: 1.51 [1.43, 1.60]). For patients ≥65 years, insurance type was not associated with prevalence of CKD in the fully adjusted model.

Conclusions: In conclusion, we found that patients from low SES tracts and Medicaid recipients (among patients <65 years) have greater rates of CKD compared to patients from high SES tracts and patients with other insurance. These may be two of several socioeconomic and individual factors influencing the complexity of identification, management, and treatment of CKD.

PO0474

Social Determinants of CKD in the Military Health System

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Background: A growing body of evidence suggests that negative social determinants of health—or social risks—contribute to socioeconomic and racial disparities in chronic kidney disease (CKD). One mechanism through which social risks appear to produce disease is by impeding access to healthcare. The Military Health System (MHS) provides an opportunity to assess CKD disparities in the context of universal healthcare.

Methods: We identified all MHS beneficiaries aged 18 to 64 who received care through the MHS from October 1, 2015 to September 30, 2018. CKD was identified by ICD-10 code and/or a validated laboratory value-based electronic phenotype for CKD. Directed acyclic graphs were developed to understand potential confounding or mediating roles of covariates. Multivariable logistic regression models were used to compare the prevalence of CKD by race, rank, zip code level median household income, and marital status, controlling separately for suspected confounders (age, sex, active duty status, service branch, and depression) and mediators (hypertension, diabetes, HIV and BMI). For family beneficiaries, the sponsor’s rank and zip code were used.

Conclusions: Racial and socioeconomic disparities persist in CKD under the context of universal healthcare coverage provided by the MHS. While racial disparities may result in part from underlying genetic differences, the presence of disparities by rank and area income suggest social factors remain pertinent despite access to universal healthcare coverage.

Funding: Other U.S. Government Support

PO0475

Low Documentation of Social Determinants of Health Among US Veterans and Medicare Patients with CKD

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Background: The implementation of ICD-10 codes in 2015 included new codes to identify social determinants of health (SDOH). We sought to identify differences in SDOH-related Z-code (SDOH-ZC) utilization in Veterans Health Administration (VHA) and Medicare patients identifying differences in SDOH-ZC utilization in those with and without chronic kidney disease (CKD).

Methods: We used 5% sample of Medicare claims data (2015-2018) and 100% VA health data (2015-2019). A list of SDOH-ZCs were grouped into 17 categories (education and literacy, employment status, occupational risk factors, housing, economic circumstances, lifestyle factors, etc.). Proportion of claims assigned a SDOH-ZC were measured quarterly across different healthcare encounters and described by patient characteristics including age, sex, race, and hypertension, diabetes, and CKD. Use of SDOH-ZC were compared between those with and without CKD.

Results: SDOH-ZCs appeared more frequently in the VA health system than in Medicare data (Fig 1.a-b). Tobacco use was the most common SDOH-ZC in both the VA and Medicare data. More SDOH-ZCs were evident in the VA employment, housing and economic, and family circumstances. Compared to those without CKD, use of SDOH-ZC was higher in individuals with CKD in outpatient settings but lower among those with inpatient visits, observation stays, and emergency department visits (Fig 1.c-d).

Conclusions: We observed lower recording of SDOH overall and among those with CKD in health care settings. Additional efforts might consider increasing SDOH documentation to help assess need for social services, which could potentially reduce disparities in health outcomes by socioeconomic status.

Funding: Other U.S. Government Support

PO0476

Association of Health-Related Social Needs with Kidney Protective Measures in an Urban Population

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Background: Health-related social needs are individual-level social determinants of health, such as food insecurity and housing insecurity. Maintaining blood pressure <130/80 mmHg, hemoglobin a1c ~7%, sodium intake <2 g/day, regular physical activity, BMI 20-25 kg/m², and smoking cessation reduce risk of CKD and CKD progression. We evaluated whether having unmet needs was associated with achieving kidney protective measures.

Methods: We performed a cross-sectional analysis of data from the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study (Baltimore, MD) during study visit 4. We used multivariable regression to quantify associations between having and least one unmet social need (food insecurity or housing insecurity), and the number of protective measures taken. Of the 3,330,893 MHS beneficiaries in this analysis, 105,504 (3.2%) had ≥65 years, insurance type was not associated with prevalence of CKD in the fully adjusted model.

Conclusions: In conclusion, we found that patients from low SES tracts and Medicare recipients (among patients <65 years) have greater rates of CKD compared to patients from high SES tracts and patients with other insurance. These may be two of several socioeconomic and individual factors influencing the complexity of identification, management, and treatment of CKD.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Association Between Unmet Health-related Social Needs and Kidney Protective Measures

Methods: Medical records from 1995 to 2019 were reviewed in order to obtain anthropometric measurements, occupation, past medical history and family history. Laboratory data included serum creatinine (Scr), albumin-creatinine ratio (ACR), 24 hour urinary protein-creatinine ratio (PCR), at baseline and at 1,3,5, and 10 years. Time zero kidney biopsies were obtained in a subset of the cohort. eGFR ACR and PCR were used as indicators of kidney function.

Results: 32 patients were included the mean age was 36 ± 10 y and mean eGFR at donation was 95.1 ± 15.5 mL/min. 35% worked in agriculture 50% in household 6% in construction 6% in a storage company 3% unemployed. The mean change in eGFR at 1, 3, 5, and 10 years was -1.82 ± 12.4, -7.5 ± 19.8, -6.9 ± 19.8, -8.1 ± 11.9 ml/min. There was a significant difference between agriculture and domestic workers in eGFR decrease at 5 and 10 years. 50% underwent zero time biopsy and 69% had some evidence of histological damage 62% showed glomerular abnormalities 40% had glomerular sclerosis, tubulointerstitial infiltrates 31% interstitial fibrosis 50% and either medial hypertrophy or intimal fibrosis 69%. These findings were not associated to occupation In multivariate analysis using a lineal model of repetitive measurements, working in agriculture was the most important risk factor associated to eGFR decline (p = .023).

Conclusions: Baseline histological changes were observed in the majority of the kidney donors, Agricultural work was the most important risk factors for eGFR decline.

Association Between Air Pollution and Renal Outcomes: A Systematic Review and Meta-Analysis

Methods: We searched EMBASE, Pubmed, Web of Science, Cochrane library, and CINAHL database, for relevant records using a combination of keywords related to the type of exposure (O3, CO, NO, NO2, SO2, PM10, PM2.5, and PM1) and outcome (CKD, end-stage renal disease -ESRD-, proteinuria/albuminuria, renal function, kidney transplant failure, nephrotic syndrome, and kidney cancer). Using random-effects meta-analyses, we pooled summary statistics (hazard ratios, odds ratios, or beta-coefficients with their respective 95% confidence intervals) associated with a standardized increased level of each pollutant and presented the results by air pollutant and outcome. Heterogeneity was interpreted with caution, due to significant between-studies heterogeneity and risks of methodological bias.

Conclusions: Chronic exposure to particulate matter and nitrite dioxide seems to be associated with poorer renal outcomes. Further studies are warranted to confirm these results.

Prevalence and Severity of Hyperkalemia in Patients Referred to Nephrology Consultation: Epidemiologic Data from 1106 Mexican Patients at a National Reference Hospital

Background: Hyperkalemia (HK, serum K > 5 mEq / L) is an electrolyte disorder that occurs frequently in patients with chronic kidney disease (CKD), heart failure. In CKD, the ability to excrete K+ is reduced, impairing quality of life and increasing morbidity and mortality.

Methods: Cross-sectional retrospective, observational study. Records of adult patients who attended an outpatient Nephrology consultation in the period from February 2019 to February 2020 were included, with laboratory reports from the last 15 days prior to the date of the medical consultation. Descriptive statistics were performed, with a 95% CI and a p-value ≤ 0.05.

Results: 1106 patient records were included. 51% (563) were women. The mean age was 55.8 ± 15.6 years. 47% of the population had Diabetes mellitus and / or hypertension as their main comorbidity and 61% were overweight or obese. HK was identified in 29% of the study population. Figure 1 shows the frequency of HK by stage of CKD. 13% of the patients who entered the study were on renal replacement therapy, of which 54% had HK. 54% of the subjects with HK were diabetic, 56% hypertensive, 25% consumed ACE inhibitors and 13% consumed NSAIDs on a regular basis and 48% had proteinuria.

Conclusions: The presence of HK is a risk factor that increases the risk for cardiovascular complications and accelerates the progression to more advanced stages of CKD. It is important to intentionally search for this alteration in all stages of CKD and implement measures that help correct and mitigate its impact on patients with CKD.

Poster

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Results: Out of the 3008 patients referred, 575 (19.1%) met the inclusion criteria (mean age: 70.4 years; 63.7% male and 94.0% white color). Mean follow-up was 4.1 ± 1.8 years. The prevalence of HK at first consultation was 8.7% and follow up incidence 21.7%. From this cohort, 164 (28.5%) had at least on episode of HK (Group B) and 101 (17.6%) died. During the follow up, RAAS inhibition was removed or not started in 200 (34.8%) and diuretic was initiated in 165 (28.7%). At least one HK episode was associated with Diabetes (65.9 vs 42.3%, p<0.001), Heart failure (36.6 vs 28.0%, p=0.007), Macroalbuminuria (34.1 v 21.2%, p=0.001), CKD progression (33.5 vs 16.3, p=0.001) higher frequency of diuretic initiation (38.4 vs 24.8%, p<0.001) and higher mortality (27.6 vs 13.7%, p<0.001). The independent predictors of mortality were: At least one HK episode (OR 1.82, 95% CI 1.08-3.34); Heart Failure (OR 1.97, 95% CI 1.16-3.35); Older age (OR per 1 year increase 1.04, 95% CI 1.02-1.07); CKD progression (OR 4.18, 95% CI 2.43-7.19); Patients who maintained RAAS inhibition during follow up (OR 0.50, 95% CI 0.26-0.96); Patients who started RAAS inhibition during follow up (OR 0.38, 95% CI 0.16-0.88).

Conclusions: Our study confirms that RAAS Inhibition had and protector and independent impact in mortality when prescribed in CKD early stages. Patients with at least one episode of HK have a higher risk of mortality. All efforts should be made to maintain these therapeutic agents, looking for other ways to control hyperkalemia rather than stop it.

PO0482
High Serum Alkaline Phosphatase Predicts CKD Progression: Effect Modification by GFR
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Background: In the post-hoc analyses of SUSTAIN/ASSURE trials, Apabetalone, an epigenetic modulator which lowers alkaline phosphatase (AlkPhos), stabilized the GFR in patients with CV disease and GFR <60 ml/min/1.73 m2. Analyzing the relationship between AlkPhos and renal outcomes in patients with CKD is useful to explore the biological hypothesis that AlkPhos is implicated in CKD progression.

Methods: We investigated the relationship between AlkPhos and the risk of a combined end-point (30% GFR loss or dialysis/renal transplantation) in 609 stage 3-5 CKD patients (mean GFR: 34.8±12.1 ml/min/1.73 m2).

Results: Median AlkPhos was 91 IU/L and in the majority of patients had values below 147 IU/L (the upper limit of the normal range). Over a median follow up of 3 yrs, 209 patients had the combined end-point. In an unadjusted analysis, 1 ln increase in AlkPhos entailed a 49% risk excess for the renal end-point (HR:1.49, 95% CI 1.11-2.01, P=0.008). Adjusting for age, gender, smoking, diabetes, cholesterol, BMI, systolic BP, CV comorbidities, hemoglobin, albumin, phosphate, and hs-CRP, did not modify this association (HR:1.48, 95% CI 1.08-2.02, P=0.016). In a fully adjusted analysis testing the GFR as an effect modifier of the AlkPhos - combined renal end point link showed a GFR-BP, CV comorbidities, hemoglobin, albumin, phosphate, and hs-CRP, did not modify this association. Adjusting for age, gender, smoking, diabetes, cholesterol, BMI, systolic BP, CV comorbidities, hemoglobin, albumin, phosphate, and hs-CRP, did not modify this association (HR:1.48, 95% CI 1.08-2.02, P=0.016). In a fully adjusted analysis testing the GFR as an effect modifier of the AlkPhos - combined renal end point link showed a GFR-

Conclusions: This study suggests that AlkPhos is predictive of CKD progression and may modulate CV risk. Further studies are needed to determine whether dietary factors may be a potential mechanistic link underlying these relationships.

Funding: Government Support - Non-U.S.
The Association Between Fibroblast Growth Factor 23 (FGF-23) and Pulse Pressure (PP) in CKD Stage G5 Patients

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Background: FGF23 is associated with increased cardiovascular events and mortality in CKD patients. Non-classical biological effects of FGF23, such as left ventricular hypertrophy and vascular remodeling, may potentially explain this association. Experimental models suggest that FGF23 stimulates renal tubular sodium reabsorption and volume overload. It is plausible that FGF23 also increases blood pressure. The linking of FGF23 increment with blood pressure control may help identify novel risk factors of mortality in CKD patients. Therefore, we aimed to evaluate the relationship between FGF23, blood pressure control, and indirect signs of arterial stiffness in subjects with CKD G5.

Methods: Clinical and analytical variables were analyzed in 159 CKD G5 patients immediately before starting kidney replacement therapy. The association between these variables and the levels of intact FGF23 (iFGF23) was evaluated with linear regression models. PP was used as an indirect surrogate of arterial stiffness. Statistics were performed using R v3.6.2.

Results: The mean SHP was 158.8±13.3 mmHg, whereas the mean DBP was 87.2±12.3 mmHg, and the mean PP was 76.6±12.3 mmHg. The median iFGF23 was 486.3 (268.8-904.9) pg/ml. iFGF23 was positively correlated with serum phosphate (p<0.001), plasma sodium (p=0.02), C-reactive protein (p<0.01), SBP (p<0.001), DBP (p<0.01) and PP (p=0.02). Linear multivariable analysis (Table 1) showed that iFGF23 was independently associated with the increase in SBP, DBP, and PP, suggesting that for each 10 pg/ml increase in iFGF23, the SBP increased 3.7 mmHg, the PAD increased 3.0 mmHg, and PP increased 2.1 mmHg. By every ten years of increment in age, PP increased 2.4 mmHg (p=0.01).

Conclusions: The increase in iFGF23 is associated with higher SBP, DBP, and PP. These data suggest that iFGF23 may increase the risk of cardiovascular events in patients with CKD G5 through increasing blood pressure and arterial stiffness.

Table 1. Determinants of SBP, DBP, and PP. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure. PP: Pulse Pressure. * Model adjusted by serum phosphate, serum calcium, parathyroid hormone, and C-reactive protein.

PO0483

PO0484

Pulse Mass Index and Pulse Mass Pressure Product in CKD Patients

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Background: Recent studies have conflicting findings on the association between obesity and the risk of chronic kidney disease (CKD). The body mass index (BMI) by itself is an imperfect marker of metabolically unhealthy obesity. The pulse mass index (PMI) and the pulse mass pressure product (PMPP) show strong correlations with the risk of cardiovascular disease and may reflect an individual’s metabolic energy state. However, it is still unclear whether PMI and PMPP can be useful parameters for the risk of CKD.

Methods: We retrospectively identified 51 subjects who underwent ambulatory blood pressure monitoring and kidney biopsy simultaneously at the Jikei University Hospital, Tokyo, from 2017 to 2019. All subjects were diagnosed as primary or secondary glomerular diseases or kidney biopsy. The BMI and the PMPP were calculated from the following formula: PMI = BMI × resting heart rate (RHR) /1730. PMPP = BMI × RHR × systolic blood pressure. We evaluated the clinicopathological findings associated with PMI and PMPP.

Results: Of 51 subjects, the age was 50.3 ± 16.1 years (mean ± standard deviation), and 60.8% were male. The eGFR was 44.4 ± 23.5 mL/min/1.73m². The median glomerulosclerosis index (GS) was 18.3 (interquartile range, 4.7-44.4) %, and the tubular injury level was 17.5 (5.0-36.3) %. The PMI was 0.94 ± 0.23, the PMPP was 21.6 ± 7.3 × 10⁶, and the BMI was 22.9 ± 4.7 kg/m². Both PMI and PMPP were positively associated with GS, HbA1c, and triglycerides, whereas negatively associated with eGFR (P = 0.02 and 0.004; respectively), CKD stages (P = 0.04 and 0.02; respectively) and HDL. Of note, each parameter such as BMI, RHR, and blood pressure was not correlated with either eGFR or CKD stages.

Conclusions: We observed correlations between both PMI and PMPP and kidney function. This study indicates that PMI and PMPP may be possible makers of the relative risk of unhealthy obesity with CKD.

PO0485

Thyroid Status and Mortality Among CKD Patients Transitioning to Dialysis

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Background: Hypothyroidism has been associated with higher death risk in non-dialysis dependent chronic kidney disease (NDD-CKD) and end-stage renal disease (ESRD) patients, presumably due to cardiovascular pathways. We examined whether pre-ESRD thyroid status is a predictor of survival in NDD-CKD patients transitioning to dialysis.

Methods: Among US Veterans with NDD-CKD transitioning to dialysis from 10/2007-3/2015, we examined the association of serum thyrotropin (TSH) levels (TSH) levels averaged over a three-year pre-ESRD transition period (“pre-ESRD prelude period”) with post-ESRD mortality. Patients were followed for the outcome for up to three-years, and HRS for all-cause mortality were estimated using expanded case-mix/laboratory adjusted Cox models. In sensitivity analyses, we examined varying pre-ESRD prelude and post-ESRD mortality intervals.

Results: Among 43,161 patients in the primary cohort (three-year pre-ESRD prelude cohort), increasingly higher TSH levels >3.0mIU/L were associated with incrementally higher mortality (ref: TSH 0.5-3.0mIU/L): adjusted HRs (95%CI): 1.04 (0.95-1.13), 1.04 (1.00-1.07), and 1.16 (1.11-1.22) for TSH levels of <0.5, 3.0-5.0, and >5.0mIU/L, respectively. A similar pattern of findings was observed for patients whose TSH levels were examined over one-year and two-year pre-ESRD prelude periods, with follow-up for the outcome of interest for up to one and two years, respectively.

Conclusions: There was a dose-dependent relationship between higher pre-ESRD TSH levels exceeding 3.0mIU/L and higher post-ESRD mortality in NDD-CKD patients transitioning to dialysis. Further studies are needed to determine the underlying determinants of thyroid dysfunction in CKD, and whether reduction of TSH levels with thyroid hormone supplementation ameliorates mortality in this population.

Funding: NIDDK Support
PO0486
Baseline Characteristics of Non-Dialysis CKD Patients with and Without Anemia: A Report from the Retrospective Cohort from DISCOVER CKD
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Background: Anemia is a frequent complication of chronic kidney disease (CKD), associated with adverse clinical outcomes and reduced quality of life. This analysis describes baseline characteristics of non-dialysis dependent (NDD) CKD patients with and without anemia in DISCOVER CKD.

Methods: The DISCOVER CKD retrospective cohort of patients in this analysis were extracted from the TruNet health research network, Japan Medical Data Vision (JMDV) and integrated Limited Claims and EHR (LCED) databases. Patients were aged >18 years with 2 estimated glomerular filtration rate (eGFR) measures <60 ml/min/1.73m2 at least 90 days apart between January 2008 and March 2020. The index date was the first Hb measure after the 2nd eGFR measure. Exclusion criteria included: <1-year registration/medical history prior to index, active bleeding, a Hb value (only) within 30 days from transfusion or bleeding and no Hb measure within a year after CKD diagnosis. Anemia was defined as <12 g/dl for females, <13 g/dl for males per WHO criteria. Baseline characteristics were summarized and stratified by presence of anemia.

Results: Preliminarly, of 799183 CKD patients meeting our I/E criteria, 67% were not anemic at baseline. In patients with anemia (33%): 191451 (81%) had a baseline Hb of 10-12 (female) 10-13 (male) g/dl, 36899 (16%) 8-10 g/dl and 9606 (3%) <8 g/dl. Compared to patients without anemia: patients with anemia were older, more likely to be female, to have more advanced CKD, and more likely to have comorbidities.

Conclusions: In routine clinical care, the presence and severity of anemia increases as CKD advances and is associated with a higher comorbidity burden.

PO0487
Incidence of and Risk Factors for Incident eGFR <60 in the Reasons for Geographic and Racial Differences in Stroke Study
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Background: Few contemporary US cohorts examined the incidence of and risk factors for developing a low estimated glomerular filtration rate (eGFR) or whether these factors vary by race, sex or region of US residence.

Methods: We studied 11,814 black or white participants with an eGFR> 60 ml/min/1.73m2 at baseline and who had 10-year follow-up eGFR. Low eGFR was defined as incident eGFR <60 ml/min/1.73m2 at the second visit and a 40% decline from baseline. Incidence rates were calculated overall and by age, sex and race groups. We used Poisson regression to calculate the risk of incident low eGFR, adjusting for demographics, socioeconomic status and clinical factors, and across race, sex and region strata.

Results: At baseline, mean age was 62 (±8.1) years, 54% were female, 36% black and 56% resided in the US stroke belt. The overall incidence of low eGFR was 9% and ranged from 4% in those aged 45-54 to 18% in those 75 years and older. Age, systolic blood pressure, diabetes, heart disease, BMI, smoking, lower income, higher education, and residence in the US stroke belt were independent risk factors for incident low eGFR. Blacks had higher risk, accounting for sociodemographic risk factors, but this was fully attenuated after adjusting for clinical factors. Low eGFR risk factors did not differ substantially by race, sex or region.

Conclusions: The higher incidence of low eGFR in black compared to white participants was accounted for by modifiable clinical risk factors. Residence in the US stroke belt was independently associated with incident low eGFR in REGARDS participants.

Funding: Other NIH Support - National Institute of Neurological Disorders and Stroke, National Institute on Aging

Risk factors for incident low eGFR (Relative risk and 95% confidence interval)

PO0488
High Prevalence of CKD Among Individuals Living with HIV in the United States
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Background: Chronic kidney disease (CKD) is an important comorbidity among people living longer with human immunodeficiency virus (HIV). We report the prevalence, trends and characteristics of individuals with HIV in the US, with the aim of better understanding this understudied, but important risk factor for CKD.

Methods: Data from 22,626 adults aged 20-59 who had consented for HIV testing in the National Health and Nutrition Examination Survey (NHANES; 1999-2014), were analyzed. Those with HIV+ vs. - serology were compared with respect to demographics, comorbidities, and social determinants of health in the full sample and those with CKD, as defined by either eGFR<60 ml/min/1.73m2 or urine albumin to creatinine ratio >30 mg/g. Logistic regression was used to assess the odds of CKD by HIV status. Comparisons were assessed using survey weights for all analyses.

Results: Prevalence of HIV+ remained stable, from 0.4% to 0.6% during this time period. Individuals HIV+ were older than those HIV- in both the full sample and among those with CKD. A higher proportion of HIV+ than HIV- individuals were black, current smokers, had < high school education, with income <$45k, and reported either Medicare or other government insurance (Table). Among individuals with CKD, those HIV+ had almost twice the prevalence of diabetes (30% vs. 19%, p<0.05) and over 4 times higher awareness of their CKD (28% vs. 6%, p<0.002) compared to HIV-. HIV+ vs. HIV- individuals had more than twice the prevalence of CKD (15.3% vs. 7.1%, p<0.002). CKD was associated with HIV+ status [unadjusted odds ratio (OR) = 2.37; 95% CI: 1.36-4.17]. Adjusting for other covariates, attenuated the association only slightly (adjusted OR=2.17; 95% CI: 1.21-3.89).

Conclusions: CKD was associated with HIV+ status among younger adults living with the disease in the United States. However, larger, longitudinal studies among individuals living with HIV and CKD are needed to increase awareness of this complication among survivors of the disease.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: We conducted a cross-sectional analysis using the data from the National Health and Nutrition Examination Survey between 2007 and 2018. We calculated the trend of self-reported illicit drug use (marijuana, cocaine, heroin, methamphetamine, and intravenous drug use) and defined current use if the last use was within 1 year of the survey. We then assessed whether the use of illicit drugs is associated with CKD (defined by estimated glomerular filtration rate ≤ 60 ml/min/1.73 m² and/or urine albumin-creatinine ratio (UACR) ≥ 30 mg/g), microalbuminuria (UACRs 30–300 mg/g) and macroalbuminuria (≥ 300 mg/g). Lastly, we assessed any predictors for drug use in CKD patients.

Results: Between 2007 to 2018, there were 22,214 adult patients between 18-59 years of age. Of these, 2,148 had CKD as defined above. CKD patients were significantly older, more likely to be female, obese, cigarette smoker, alcohol drinker, and to have diabetes, and hypertension. We found that prevalence of marijuana (21.9% vs 21.9%, p=0.23), cocaine (4.9 vs 3.6, p=0.95) and methamphetamine (1.5% vs 1.3%, p=0.52) did not differ between CKD and non-CKD. However, heroin use (0.2% vs 0.5%, p=0.02) were significantly lower in CKD compared to non-CKD. Interestingly, there is a significant trend towards increasing marijuana use in CKD patients overtime as prevalence increase from 17.3% in 2007-2010 to 21.7% in (2011-2014), and up to 26.5% in 2015-2018 (p trend 0.02). Recent illicit drug use was not associated with CKD, microalbuminuria or macroalbuminuria. Age, black race, current smoker and alcohol drinking were significant predictors of drug use within 1 year in CKD patients.

Conclusions: In a national sample, marijuana was the most common illicit drug use among CKD patients and the trend of marijuana use in CKD patients is increasing, likely due to marijuana legalization. Age, black race, current smoker and alcohol drinking increase the odds of illicit drug use in CKD patients.
Ideal cardiovascular health was defined as nonsmoker; body mass index (BMI) <25 kg/m²; ≤150 minutes/week of physical activity; healthy dietary pattern (high in fruits and vegetables, fish, and fiber-rich whole grains; low in sodium and sugar-sweetened beverages); total cholesterol <200 mg/dL; blood pressure <120/80 mm Hg; and fasting blood glucose <100 mg/dL.

At study entry, mean age was 57 years, 71% were male, and 57% had diabetes. The mean baseline eGFR was 47 ml/min/1.73m² and the median protein excretion 633 mg/24 hours. Nine percent met all seven criteria for ideal cardiovascular health. During a median follow-up of 2.9 years, there were 78 CKD progression events. In sex- and age-adjusted analysis, each point higher Life's Simple 7 score was associated with 13% lower risk of CKD progression (HR = 0.89; 95% CI = 0.78-0.96). This association attenuated after adjusting for baseline eGFR and proteinuria (HR = 0.94; 0.83-1.05).

Conclusions: In this cohort of adults with CKD in Mexico, the prevalence of ideal cardiovascular health as measured by Life’s Simple 7 was low. The protective effect of Life’s Simple 7 on CKD progression was explained by baseline kidney function.

Funding: NIDDK Support, Other NIH Support - Fogarty International Center, Private Foundation Support

PO0495
Patterns of Hospital Admissions Among Patients with CKD
Sarah S. Gray, Dena E. Cohen, Steven M. Brunelli. Davita Clinical Research, Minneapolis, MN.

Background: Although chronic kidney disease (CKD) is relatively common in the United States, an understanding of the frequency, causes, and costs of hospital admissions among patients with CKD at the national level is lacking.

Methods: Study data were derived from the Centers for Medicare & Medicaid Services 100% claims sample (2017-2018). Included patients were adults enrolled in Medicare Parts A and B who had a claim including a diagnosis code for CKD stage 3, 4, or 5 during 2017; exposure was ascribed as the most severe observed stage. Patients with evidence of commercial insurance, diagnosis of end-stage kidney disease, dialysis treatment, or death, prior to 31 Dec 2017 were excluded. Hospital admissions and paid for claims observed from January 1, 2017 through the first of 31 Dec 2018 or censoring for loss of Medicare Part A, dialysis initiation, or death. Hospitalization causes were ascribed on the basis of ICD-10 codes, grouped using Clinical Classification Software Level 1 categories.

Results: A total of 1,352,401 patients with CKD3, 208,963 patients with CKD4, and 16,159 patients with CKD5 met eligibility criteria. Annual hospitalization rates were 0.66, 0.87, and 0.77 admissions/patient-year among patients with each CKD stage, respectively. Across all 3 stages, admissions for “Diseases of the Circulatory System” accounted for approximately 25% of hospitalizations, with “hypertension with complications and secondary hypertension” contributing approximately half of the hospitalizations in this category. Considerable regional variation was observed with respect to annual hospitalization costs among this population, with the Southwest, Northeast, and Mid-Atlantic regions tending to have higher costs than other parts of the country.

Conclusions: Patients with CKD are frequently hospitalized, with associated costs that display marked regional variation. Clinically and regionally targeted programs may result in improved patient outcomes and lower health care costs.

Funding: NIDDK Support

PO0496
Critical Care Resource Use in CKD in the Safety-Net Setting
Jefferson L. Triozzi, Jingbo Niu, Sankar D. Navaneethan. Baylor College of Medicine, Houston, TX.

Background: Chronic kidney disease (CKD) is associated with adverse outcomes among patients with critical illness. There is limited data on the extent of critical care resource use among patients with CKD in safety-net settings.

Methods: We conducted a retrospective cohort study of patients in a safety-net healthcare system with non-dialysis-dependent CKD and critical illness, defined as admission or transfer to the intensive or intermediate care unit. Poison regression was used to identify risk factors for critical illness based on sociodemographic factors, comorbidities, and baseline stage of CKD. Critical care resource use was extracted from the medical record, including dialysis initiation, ventilatory support, blood products, and vasoactive medications. Baseline stage of CKD was included as a baseline stage of CKD.

Results: Out of 1,208 patients with CKD who were hospitalized during a three-year period (stage 3a-43%, stage 3b-35%, stage 4-22%), 495 patients required intermediate or intensive care. In the multi-adjusted model [IRR (95% CI)], critical illness was associated with stage of CKD [stage 3a-1 (referent), stage 3b-1.24 (1.10,1.40), stage 4-1.99 (1.72, 2.30)]. Hypertensive and non-Hypertensive black race, congestive heart failure, and moderate/severe anemia were also associated with risk of receiving critical care (Table 1).

Conclusions: We report a high burden of hospitalizations requiring critical care resources in a safety-net setting. Notably, a third of patients with CKD stage 4 and critical illness required hemodialysis initiation. Further research is needed to prevent critical illness and the need for critical care resources in patients with CKD.
Table 1. Critical care resource use and factors associated with outcomes in those with different stages of CKD. * Multi-adjusted model for baseline characteristics

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>Number of patients hospitalized, n</th>
<th>Risk of hospitalization with critical illness, IRR (95% CI)</th>
<th>Risk of hospitalization with critical illness, IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>594</td>
<td>0.67 (0.57, 0.78)</td>
<td>0.62 (0.53, 0.72)</td>
</tr>
<tr>
<td>3b</td>
<td>456</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>4</td>
<td>259</td>
<td>1.22 (1.12, 1.33)</td>
<td>1.22 (1.12, 1.33)</td>
</tr>
</tbody>
</table>

PO0497

Usual Source of Care and Clinical Outcomes in Adults with CKD: Findings from the Chronic Renal Insufficiency Cohort (CRIC) Study

Stephanie M. Toth-Manikowski,1 Jesse Y. Hsu,1 Michael J. Fischer,1 Jordana B. Cohen,2 Claudia M. Lora,1 Thida C. Tan,1 Jiang He,4 Raquel C. Greer,1 Matthew R. Weir,1 Sarah J. Schrauben,2 Mildra Saunders,2 Ana C. Ricardo,2 James P. Lash.1 1University of Pennsylvania, Philadelphia, PA; 2Kaiser Permanente Northern California, Oakland, CA; 3Tulane School of Public Health and Tropical Medicine, New Orleans, LA; 4Johns Hopkins Medicine, Baltimore, MD; 5University of Maryland School of Medicine, Baltimore, MD; 6University of Chicago, Chicago, IL.

Background: In general populations, having a usual source of care (USOC) increases use of preventive care and is associated with higher survival. However, there are limited data in adults with chronic kidney disease (CKD).

Methods: In the CRIC Study, we categorized participants’ self-reported USOC as follows: 1) clinic/doctor’s office, 2) emergency room (ER)/urgent care, and 3) other. Using multivariable regression analyses, we evaluated the association between USOC and incident end stage renal disease (ESRD), cardiovascular events (myocardial infarction, heart failure, stroke, and peripheral arterial disease), hospitalizations, and all-cause death.

Results: Among 3,140 participants, mean age was 65 years, 45% were non-Hispanic white, 43% non-Hispanic black, 9% Hispanic, and mean estimated glomerular filtration rate (eGFR) was 50 mL/min/1.73m². 90% identified clinic/doctor’s office as USOC, 9% ER/urgent care, and 8% other. Over a median follow-up time of 3.6 years, there were 288 deaths, 181 incident ESRD events, 444 cardiovascular events, and 7,957 hospitalizations. In multivariable analyses, compared to clinic/doctor’s office as USOC, ER/urgent care was associated with higher risk for death and hospitalizations (Table). No significant association was seen with incident ESRD or cardiovascular events.

Conclusions: ER/urgent care as USOC was associated with higher risk for adverse outcomes in this large and diverse adult cohort with CKD. Further studies are needed to identify barriers to accessing appropriate preventive care to reduce negative health outcomes in this population.

Funding: NIDDK Support

PO0498

Healthcare Resource Utilization and Costs of CKD According to the 2012 KDIGO CKD Classification: A Report from the DISCOVER CKD Retrospective Cohort

Juan Jose Garcia Sanchez,2 Juan J. Carrero,2 Supriya R. Kumar,2 Hiddo J. L Heesink,3 Glen James,1 Stephen Nolan,1 Lam S. Carolyn,4 Hungta (Tony) Chiolho,1 Alyshah Abdul Sultan,1 Carol A. Pollock,2 Roberto Dias-Filho,4 AstraZeneca, Cambridge, United Kingdom; 5Karolinska Institutet, Stockholm, Sweden; 6AstraZeneca, Gaithersburg, MD; 7Rijksuniversiteit Groningen, Groningen, Netherlands; 8National Heart Centre Singapore, Singapore, Singapore; 9Duke-NUS Medical School, Singapore, Singapore; 10Royal North Shore Hospital, St Leonards, NSW, Australia; 11Pontificia Universidade Catolica do Parana Escola de Medicina Campus Londrina, Londrina, Brazil; 12Arbor Research Collaborative for Health, Ann Arbor, MI.

Background: The DAPA-CKD trial finished early due to overwhelming efficacy. Real-world data reporting healthcare resource utilization (HCRU) and cost associated with CKD categorized according to the 2012 KDIGO recommendations are scarce. We assessed HCRU and costs in a “DAPA-CKD-like population” (eGFR 25-75/mL/min/1.73m² and UACR 200-5000mg/g) compared to patients categorized according to KDIGO 2012 recommendations.

Methods: DISCOVER CKD is an observational study in patients with CKD, data was extracted using the integrated Limited Claims and Electronic Health Record data. Patients were aged 18 years, with at least 90 days recorded at least 90 days apart between January 2008 and September 2018. Index date was 2nd eGFR. We calculated total and annualized number of encounters and estimated annualized per-patient and total costs. Incidence rates per 100 person-years (PY) were estimated for outpatient and hospitalization events.

Results: Preliminarily, 6270 patients met the KDIGO 2012 definition (mean±SD age 64.0(10.9) years, 51.0% female) and 383 patients met the DAPA-CKD-like criteria (mean±SD age 64.0(11.9) years, 38.9% female). The rate of hospitalizations almost doubled for the DAPA-CKD-like population vs the KDIGO 2012 defined population (Rate 100-PY[95CI] 59.0[53.7-64.8] vs 26.4[25.5-27.3]) and was also higher (Mean±SD 6.5[9.4] vs 5.4[6.6] days). The DAPA-CKD-like population incurred substantially higher annualized per patient hospitalization costs (Mean±SD USD39782[78572] vs USD25717[60019]); Figure 1.

Conclusions: This analysis demonstrated that the DAPA-CKD-like population is associated with a higher HCRU and cost burden. These results highlight the need for innovative therapies to improve patient outcomes in this population.

Funding: Commercial Support - AstraZeneca

PO0499


Tope Oyekanmi,1 Louis Lamerato,2 Juan Jose Garcia Sanchez,2 Like Jiang,1 Joanna C. Huang,1 Stephen Nolan.1 AstraZeneca, Wilmington, NC; 2AstraZeneca UK Ltd, Cambridge, United Kingdom; 1Henry Ford Health System, Detroit, MI.

Background: The DAPA-CKD Trial is the first SGLT-2i renal outcome trial to test the efficacy and safety of an SGLT-2i, dapagliflozin, in patients with diagnosed CKD with and without T2D. The objective of this study is to assess the healthcare resource utilization and cost in a “DAPA-CKD-like population” (eGFR 25-75/mL/min/1.73m² and UACR 200-5000mg/g) using a contemporary US healthcare system.

Methods: Data from the Henry Ford Health System (HFHS) were used to identify patients with CKD stages 2 through 4 between 2006 and 2016 (based on eGFR labs) and patients were followed through 2018. Patients with no confirmatory eGFR > 90 days from index date, death within 30 days, history of renal transplant, and evidence of renal replacement therapy, or progression to CKD stage 5 during the baseline period (6 months pre or post index date) were excluded. Cumulative primary and secondary utilization was evaluated for all patients during the follow-up time. Annual utilization rates are the total observed utilization divided by follow-up time. Billings records with HFHS were used to estimate costs.

Results: 6,557 patients (mean age 62.9 years, 46.2% male) met the eligibility criteria and are included in the study cohort. The population was stratified by UACR (0-<30, 30–189, 190–5,000mg/g) and the DAPA-CKD-like population (200-5000mg/g) was associated with significantly higher annualized per-patient healthcare costs, $39,222/yr (UACR 200-5000mg/g vs UACR 0-<30mg/g).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Understanding Patterns of Medical Spend Informs Design of Upstream Intervention in CKD

**Title**

**University Hospitals, Cleveland, OH.**

**Background:** Despite ease of diagnosis based on laboratory testing, CKD is often unrecognized and comorbid decompensation results in delayed diagnosis in acute care settings. The purpose of our inquiry was to inform the design of systems of care that would prevent escalation of total cost of care (TCOC) of CKD through minimization of acute care spend.

**Methods:** Unrecognized CKD was defined as CKD that was evident by laboratory data in the EHR but not captured by an ICD10 code or DRG for chronic kidney disease. Recognized CKD or ESRD had both ICD10 and DRG data and laboratory evidence of CKD. We then compared inpatient and total medical spends as well as the density of preventive measures such as wellness visits among these groups. The data repository was built on the MS Power BI platform and machine learning and high throughput analyses were conducted using Alteryx utilities.

**Results:** A total of 217,125 patients were included that had eGFR and spend data in 2019. Annual wellness visits occurred on average among 38 percent (n=142,373) of those with unrecognized CKD and only 20.5 %, and 24.3 % of those with undiagnosed CKD stage 3b-5 vs. 46.9 percent of those with recognized CKD/ESRD (p<.0001). A diagnosis of CHF was recorded in 13.1 %, and 10 among those with recognized CKD or ESRD (n= 52,242; P < 0.001). No statistical difference was observed in 2019. Annual wellness visits occurred on average among 38 percent (n=142,373) of those with unrecognized CKD and only 20.5 %, and 24.3 % of those with undiagnosed CKD stage 3b-5 vs. 46.9 percent of those with recognized CKD/ESRD (Chi square for trend <0.001).

**Conclusions:** Our high proportion of time on therapy for key pharmacological treatments during the follow-up period. However, it is well established that a substantial residual risk and unmet need exists with current standard of care.

**Funding:** Commercial Revenue Support - AstraZeneca

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**Abstract Withdrawn**

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**Treatment Pathways of CKD Patients Defined by the 2012 KDIGO CKD Classification: A Report from the DISCOVER CKD Retrospective Cohort**

**Juan Jose Garcia Sanchez, 1 Juan J. Carrero, 2 Supriya R. Kumar, 3 Roberto Pecoits-Filho, 4,5 Glen James, 6 Hiddo J. Heerspink, 7 Lam S. Carolyn, 8,9 Hungta (tony) Chen, 2 Eiichiro Kanda, 2 Alyshah Abdul Sultan, 2 Naoki Kashihara, 6 Mikhail Kostoborod, 7 David C. Wheeler, 11 Carol A. Pollock, 12 AstraZeneca, Cambridge, United Kingdom; 7 Karolinska Instituteet, Stockholm, Sweden; 8 AstraZeneca, Gaithersburg, MD; 4 Arbor Research Collaborative for Health, Ann Arbor, MI; 1 Pontificia Universidade Catolica do Parana Escola de Medicina Campus Londrina, Londrina, Brazil; 10 Rijksuniversiteit Groningen, Groningen, Netherlands; 11 National Heart Centre Singapore, Singapore, Singapore; 12 Duke-NUS Medical School, Singapore, Singapore; 9 Kawasaki Ika Daigaku, Kurashiki, Japan; 12 Saint Luke’s Mid America Heart Institute, Kansas City, MO; 13 University College London, London, United Kingdom; 12 Royal North Shore Hospital, St Leonards, NSW, Australia.

**Background:** Treatment strategies to delay the progression of CKD focus on use of RAASI, anti-hypertensive and, for patients with type 2 diabetes, anti-diabetic therapy. Data describing treatment pathways in patients defined according to the 2012 KDIGO classification are scarce.

**Methods:** The DISCOVER CKD retrospective cohort of patients was extracted using the integrated Limited Claims and EHR data. Patients were aged ≥18 years, with ≥1 UACR measure and two measures of eGFR 0-75 mL/min/1.73 m² recorded at least 90 days apart between 2008-2018. Sankey Plots were used to visualize chronological treatment pathways (1st-3rd line) post-index, of key treatments commonly prescribed to these CKD patients including: RAASI, anti-diabetic therapy, beta-blockers and anticoagulants. We also describe median time to 1st line therapy initiation.

**Results:** Preliminarily, 4283 patients were prescribed key treatments during follow-up with anti-hyperglycaemic therapy and RAASI therapy being the most common 1st line therapy. Figure 1. Median time to 1st-line therapy initiation was: 34 days for anti-diabetic therapy, 45 days for beta-blockers, 49 days for RAASI therapy and 50 days for anticoagulants. Anti-diabetic therapy and RAASI therapy accounted for the highest proportion of time in which treated patients remained on therapy during follow-up (68% and 63%, respectively).

**Conclusions:** We observed a high proportion of time on therapy for key pharmacological treatments during the follow-up period. However, it is well established that a substantial residual risk and unmet need exists with current standard of care.

**Funding:** Commercial Support - AstraZeneca

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**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

**Underline represents presenting author.**

**202**
PO0503
Treatment Pathways of Patients with CKD: A Report from the DIS-COVER CKD Retrospective Cohort
Glen James,1 Juan J. Carrero,2 Supriya R. Kumar,3 Steven Fishbane,4 Carol P. Moreno Quinn,4 Hildo J. L. Heerspink,3 Eric T. Wittbrodt,5 Eiichiro Kanda,6 Katarina Hedman,7 Naoki Kashihara,8 Hangta (tony) Chen,9 Mikhail Kosioborod,10 Lam S. Carolyn,11,12 Carol A. Pollock,12 Peter Stenwinkel,13 Roberto Petoecios-Filho,11,12 David C. Wheeler,13 AstraZeneca UK Ltd, Cambridge, United Kingdom; Karolinska Institutet, Stockholm, Sweden; AstraZeneca, Gaithersburg, MD; Northwell, Manhasset, NY; University of Groningen, Groningen, Netherlands; Kawasaki Medical School, Kurashiki, Japan; AstraZeneca, Gothenburg, Sweden; Saint Luke’s Hospital of Kansas City Health Sciences Library, Kansas City, MO; University of Sydney, Sydney, NSW, Australia; Karolinska Universitetssjukhuset, Stockholm, Sweden; Pontificia Universidade Catolica do Parana, Curitiba, Brazil; Arbor Research Collaborative for Health, Ann Arbor, MI; University College London, London, United Kingdom; National Heart Centre Singapore, Singapore, Singapore; Duke-NUS Medical School, Singapore, Singapore.

Background: Chronic kidney disease (CKD) is a global health problem associated with clinical complications. Gaps exist in real-world data to understand treatment pathways of CKD patients. We describe treatment pathways of key medications prescribed to CKD patients in DISCOVER CKD.

Methods: The DISCOVER CKD retrospective cohort of patients were extracted using Japan Medical Data Vision (JMDV) and integrated Limited Claims and EHR (LCED) data. The study included patients aged ≥18 years with a diagnostic CKD code (stage 3A through end stage renal disease or renal replacement therapy) or 2 estimate glomerular filtration rate (eGFR) measures ≥75 mL/min/1.73m2 at least 90 days apart between January 2008 and October 2018. The index date was the date of first diagnostic code or 2nd eGFR. Sankey Plots were used to visualize chronological treatment pathways (1st to 3rd line) post-index of key treatments (including combinations) commonly prescribed at least to 50% CKD patients including: RAAS, statins, diuretics and anti-hypertensives. We also describe median time to first line therapy initiation.

Results: Preliminarily, in the study cohort (N=159849) anti-hypertensives were the most common first-line therapy prescribed. Median time to first-line therapy initiation for LCED and JMDV was: 48 days and 168 days for anti-hypertensives, 39 days and 89 days for diuretics, 51 days and 259 days for RAAS and 56 days and 133 days for statins, respectively. In both databases patients remained on anti-hypertensives the most (33.7%) during treatment.

Conclusions: Patients with CKD have high therapy burden, with varying time to initiation of therapies.

Figure 1 – Treatment Pathways of Key Treatments

PO0504
Increased Urinary Albumin Creatinine Testing in CKD Stage 3 and Effect on Quality Metrics

Background: One of the goals of Advancing American Kidney Health Initiative is “reducing the number of Americans developing End Stage Renal disease by 25% by 2030.” An important part in achieving this goal is increased use of interventions backed by high quality evidence including use of ACE inhibitors or ARBs, control of hypertension, and diabetes (DM) control. Albuminuria has been clearly linked to CKD progression, with cardiovascular and all-cause mortality, dual testing remains limited. We sought to characterize trends in dual testing in all veterans and those seen by nephrologists.

Methods: We used Veterans Health Administration (VA) data (2009–18). VA patients with any inpatient or outpatient visit in a given calendar year were included. Time trend of dual testing and patient characteristics including age, sex, race, hypertension, diabetes, CKD, and cardiovascular diseases (CVD) were noted.

Results: There were 10,335 patients in the CKD registry on 12/5/2017 and 10,315 on 12/5/2019. Average age was 73, 81% had hypertension, 38% had DM, and 44% were male. Automated ACR testing in patients with stage 3 CKD was implemented on 5/23/2018. One and half years after implementation of ACR testing, ACR testing increased from 26% to 61% (p < 0.001). ACE inhibitor or ARB use among patients with renal indication did not increase significantly (79% vs. 81%, p = 0.08). Control of DM increased (78% vs. 81%, p < 0.001) while control of hypertension worsened (76% vs. 74%, p = 0.001). In conclusion: In patients with stage 3 CKD, increased albuminuria testing via automated testing linked with EHR alerts did not result in an overall improvement in CKD quality metrics. However, our study was limited by the cross-sectional design as well as the short follow up.

PO0505
Albuminuria Testing and Prevalence and Incidence of Elevated Albuminuria
Jung-Im Shin, Alex R. Chang, Yingying Sang, Ron T. Gansevoort. CKD Prognosis Consortium CKD Prognosis Consortium, Baltimore, MD.

Background: Guidelines recommend an annual evaluation of urine albumin creatinine ratio (ACR) in patients with diabetes (DM) or hypertension (HTN) for early identification and close monitoring of kidney damage. The aim of this study was to inform ACR testing strategies by 1) evaluating the frequency of ACR testing, 2) determining the prevalence and incidence of ACR≥30 mg/g, and 3) developing and validating a risk prediction model for incident ACR≥30 mg/g.

Methods: We analyzed 28 cohorts from the CKD Prognosis Consortium including 1,909,350 persons with DM or HTN from 5 countries. Analysis was performed separately for persons with DM and those with HTN but without DM. We selected a two-year baseline period for administrative cohorts and used the baseline visit for research cohorts to assess frequency of testing and prevalence of a single ACR≥30 mg/g. Confirmed incident ACR≥30 mg/g (elevated twiced 5 years) assessed 5 years after baseline in those with baseline ACR<30 mg/g. Development of prediction models for incident ACR≥30 mg/g used logistic regression and age, sex, baseline systolic blood pressure, HTN and DM medication use, coronary heart disease, heart failure, BMI, A1c, and eGFR as covariates. Models were validated in 5 DM cohorts and 4 HTN only cohorts.

Results: The median frequency of ACR testing across administrative cohorts was ≥48.8% (95% CI: 32.5-58.3%) and ≥4.3% (95% CI: 3.2-7.1%) in DM and HTN only. Among those tested at baseline, the median prevalence of ACR≥30 mg/g was 32.7% (95% CI: 28.4-37.0%) and 21.9% (95% CI: 18.6-29.6%) in DM and HTN only. Among 107,754 persons with DM and 15,676 persons with HTN only who had baseline ACR≥30 mg/g, the incidence median of ACR≥30 mg/g was 32.7% (95% CI: 28.4-37.0%) at least 5 years was 23.3% (95% CI: 18.6-28.5%) and 21.7% (95% CI: 15.7-26.3%) in DM and HTN only. Risk prediction models for 5 year incidence of ACR≥30 mg/g had only modest accuracy in DM (median C statistic: development cohorts 0.629, IQI: 0.600-0.655, validation cohorts 0.635, IQI: 0.619-0.641) and in HTN only (median C statistic: development cohorts 0.649, IQI: 0.621-0.695; validation cohorts 0.663, IQI: 0.635-0.671).

Conclusions: ACR testing in DM or HTN is low in clinical practice. The risk prediction models for incident ACR≥30 mg/g performed only modestly, suggesting future efforts based on risk stratifications may not improve the table strategy. Universal albuminuria testing for individuals with DM or HTN is likely necessary.

Funding: NIDDK Support, Private Foundation Support

PO0506
Urine Albumin and Serum Creatinine Dual Testing in US Veterans: Trends and Associations with Subspecialty Care
Nicolë M. Bhaye,1,2,3,4,5 Yoon Ha,1 Diane Steffick,2 Jennifer L. Bragg-Gresham,1 Kara Zivin,1,2 Nilka Rios Burrows,2 Meda E. Pavkovich,2 Delphine S. Tuot,2,3,4 Neil R. Powe,4,5 Rajiv Saran,6 University of Michigan, Ann Arbor, MI; US Department of Veterans Affairs, Ann Arbor, MI; Centers for Disease Control and Prevention, Atlanta, GA; University of California San Francisco, San Francisco, CA; Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, CA.

Background: Urine albumin and serum creatinine (SCr) help define chronic kidney disease (CKD). Despite the fact that urine albumin and SCr are multiplexed with cardiovascular and all-cause mortality, dual testing remains limited. We sought to characterize trends in dual testing in all veterans and those seen by nephrologists.

Methods: We used Veterans Health Administration (VA) data (2009-18). VA patients with any inpatient or outpatient visit in a given calendar year were included. Time trend of dual testing and patient characteristics including age, sex, race, hypertension, diabetes, CKD, and cardiovascular diseases (CVD) were noted.

Results: Among those tested at baseline, the median prevalence of ACR≥30 mg/g was 32.7% (95% CI: 28.4-37.0%) and 21.9% (95% CI: 18.6-29.6%) in DM and HTN only. Among those tested at baseline, the median prevalence of ACR≥30 mg/g was 32.7% (95% CI: 28.4-37.0%) and 21.9% (95% CI: 18.6-29.6%) in DM and HTN only. Risk prediction models for 5 year incidence of ACR≥30 mg/g had only modest accuracy in DM (median C statistic: development cohorts 0.629, IQI: 0.600-0.655, validation cohorts 0.635, IQI: 0.619-0.641) and in HTN only (median C statistic: development cohorts 0.649, IQI: 0.621-0.695; validation cohorts 0.663, IQI: 0.635-0.671).

Conclusions: ACR testing in DM or HTN is low in clinical practice. The risk prediction models for incident ACR≥30 mg/g performed only modestly, suggesting future efforts based on risk stratifications may not improve the table strategy. Universal albuminuria testing for individuals with DM or HTN is likely necessary.

Funding: NIDDK Support, Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: The study population included 58,508,942 patients (90.3% male). Overall, 12.5% of VA patients had both Scr and urine albumin testing in 2009 as compared with 18.6% in 2018 (Fig A, p<0.001). Among patients seen by nephrologists, 30% had both Scr and urine albumin testing in 2009, increasing to 43.3% in 2018 (Fig B, p<0.001). Compared to VA patients with Scr testing only, those with both Scr and urine albumin testing were older, more likely to be male, and more likely to have diabetes, hypertension, and CKD, but less likely to have CVD (p<0.001).

Conclusions: Dual Scr and urine albumin testing among VA nephrology patients is more common than among all VA patients and has increased over time. However, in a given year, less than half of nephrology patients undergo dual testing. Efforts to encourage screening for albuminuria among patients at high risk for CKD and CVD might be considered.

Funding: Other U.S. Government Support

PO0508

Prevalence of Coded and Uncoded CKD in the Military Health System
Jenna M. Norton, Lindsay Gruenwald, Cara H. Olsen, Eric S. Marks, Tracey L. Koehlmoo. Uniformed Services University of the Health Sciences, Bethesda, MD.

Background: Despite the substantial human and financial costs associated with chronic kidney disease (CKD) and its high prevalence in the general population, little is known about rates of CKD in the nearly 9.5 million beneficiaries of the Military Health System (MHS). Diagnostic codes lack adequate sensitivity and validity for identifying CKD using health system data. Using laboratory-data may enable a more accurate assessment of the burden of CKD in the MHS.

Methods: We identified all MHS beneficiaries aged 18 to 64 who received care through the MHS from October 1, 2015 to September 30, 2018. CKD was identified by ICD-10 code and/or a validated laboratory value-based electronic phenotype for CKD. CKD was considered coded if an ICD-10 code was present and uncoded if no ICD-10 code was present. Characteristics of the coded and uncoded CKD populations were compared using two-tailed t tests (continuous variables) and Pearson’s Chi Square test for independence (categorical variables).

Results: The total study population included 3,330,893 MHS beneficiaries. Of those, 105,504 (3.2%) were identified as having CKD. Of those with CKD, only 37% had an ICD-10 code for CKD. Compared to individuals with coded CKD, those with uncoded CKD had a younger average age (average age 45 vs 52), more likely to be female, and more likely to be active duty, but less likely to be of Black race, to have diabetes or to have hypertension (p<0.0001). Among those with test results recorded in the MHS, those with coded CKD had greater numbers of urine albumin, urine albumin-to-creatinine ratio, urine protein-to-creatinine ratio, serum creatinine, and eGFR results (p<0.0001).

Conclusions: Many MHS beneficiaries with laboratory values indicative of CKD were not coded for CKD, suggesting they may not be receiving appropriate management for this progressive and burdensome disease. Individuals with commonly recognized risk factors for CKD (e.g., older age, male sex, black race, diagnosed diabetes, diagnosed hypertension) were more likely to be coded for CKD, suggesting clinicians may be missing CKD in traditionally lower risk groups—despite available laboratory data to assess disease status.

Funding: Other U.S. Government Support

PO0509

Factors Associated with Screening and Recognition of CKD in the VA Healthcare System
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Background: The successful implementation of interventions to improve kidney disease outcomes requires early identification of CKD which involves screening at-risk population as well as recognizing CKD. We have reported suboptimal detection of proteinuria and documentation of CKD previously and now aim to identify factors associated with these rates.

Methods: We interrogated VISN-17 database for at-risk Veterans with hypertension (HTN) and diabetes seen regularly in primary clinics during 2012-19. The final cohort (N=270,170) charts were analysed for serum creatinine/eGFR, urine protein/albumin, ICD codes for CKD, and nephropathy referral. CKD was defined as eGFR<60ml/min at least twice 90 days apart and/or urine albumin creatinine ratio (uACR) >30 mg/g. Factors were examined which could be associated with screening and recognition.

Results: As shown in table, 94.3% patients had one or other screening procedures done. Urine protein/albumin was present in 56.4% charts, the least in patients with HTN only (40%). CKD by lab evidence was present in 42%; however, only 40% of these had documented ICD-codes for CKD or nephropathy referral. There was no clinically significant difference between screened vs. unscreened or recognized vs. unrecognized groups in age, sex, and BMI. Hispanic race association with decrease screening procedures but no difference in CKD recognition. Patients were more likely to have screening procedures as well documented CKD, if they had heart disease, stroke, lowered frequency of specialty care visits, hospitalizations or ER visits; or elective procedures as vascular and cardiac catheterizations. There was no difference in BP control in screened vs. unscreened group but more patients with documented CKD had BP<140/90mmHg.

Funding: Other U.S. Government Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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Conclusions: Proteinuria was detected and CKD was recognized in half of the at-risk Veterans. Co-morbidities and health care visits other than primary care associated with increased screening and recognition suggest utility of initiatives at primary care level to educate the need for CKD detection and awareness.

Funding: Veterans Affairs Support

PO0510
Spatial Distribution of Newly Detected CKD Among US Veterans, 2009-2018
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Background: While the rate of new end stage renal disease (ESRD) cases has slowed in recent years, less is known about trends in the incidence of pre-ESRD CKD. Using national data from the Veterans Health Administration (VHA) we examined the rates and spatial distribution of newly detected cases of CKD using laboratory measures.

Methods: Using data from 8.5+ million US Veterans over a decade (2009-18), in the VHA system during the previous 3 years with no indication of kidney disease, rates of newly detected kidney disease were calculated by year. Three measures of kidney disease were assessed by laboratory reports: 1) eGFR < 60 mL/min/1.73m², 2) albuminuria, and 3) either low eGFR or albuminuria. Spatial maps contain 3-year incidence rates (2016-18) by county, based on patient residence.

Results: Rates of newly detected low eGFR were steady from 2011 forward (~30/1,000 PY), after a drop from 55 to 31 cases between 2009 and 2011, a time when standardization of creatinine calibration to IDMS became mandatory and may explain the change in rates. Rates of newly detected albuminuria showed little variability (~10/1,000 PY). Areas of high incidence of low eGFR were present in northern Michigan, northern Indiana, central Illinois, and western North Carolina. Newly detected albuminuria was highest in coastal North Carolina, northern Idaho, northeastern Indiana, and on the border of Washington and Oregon.

Conclusions: Rates of newly detected disease reflect a combination of the true incidence rate as it presents to a health system, but is also influenced by the rate of testing for the disease in question. Despite this limitation, these findings are important for both individual and population health management, early detection, management and prevention.

Funding: Veterans Affairs Support

PO0511
Defining Criteria for CKD Stage 3 Patients Nephrology Referral: An Analysis Focused on CKD Progression and Mortality Risk
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Background: The high prevalence of CKD and its increasing awareness by primary care clinicians. While the referral of CKD stage 4 and 5 to a nephrology clinic is undisputable, the need for stage 3 patients referral is still subject to debate. Our objective was to investigate baseline characteristics of CKD stage 3 patients associated with subsequent CKD progression, in order to help determine which patients should be referred at this stage.

Methods: Retrospective analysis of all patients referred to a nephrology clinic over 6 years. We included CKD stage 3 patients with at least 36 months of follow-up or 24 of follow up with more than 3 serum creatinine determinations. CKD progression was defined by one of the following: 1) an eGFR decline superior to 5mL/min/year; 2) creatinine duplication; 3) The need for chronic RRT. Baseline covariates included demographics, comorbid conditions and laboratory values. Univariate and multivariate analysis were employed to determine independent predictors of CKD progression and mortality.

Results: Out of the 3008 patients 594 (19.8%) met the inclusion criteria (median age: 71.9 years; 63.8% male). Median follow-up was 4.9 years (IQR 2.2). 133 (22.4%) met the criteria for CKD progression and 110 (18.6%) died. CKD progression was associated with higher proteinuria (405.7 vs 65.5mg/gr, p<0.001), Diabetes (60.9 vs 45.3%, p=0.002), CHF (40.6 vs 28.7%, p=0.009), Anemia (68.0 vs 44.7%, p<0.001), higher diuretic use (48.9 vs 34.1%, p=0.002) and mortality (40.9 vs 12.2%, p=0.001) Albuminuria over 300 mg/gr [Odds ratio (OR) 3.57, 95% CI 2.20 - 5.80] and Anemia (OR 1.97, 95% CI 1.20 – 3.22) were associated with CKD progression. The independent predictors of mortality were: CKD progression (OR 4.49, 95% CI 2.69-7.50), Older age (OR per 1 year increase 1.03, 95% CI 1.01-1.05), presence of CHF (OR 1.75, 95% CI 1.03-2.98), presence of Hyperkalemia at first consultation (OR 2.12, 95% CI 1.00 – 4.52) and Anemia (OR 1.93, 95% CI 1.03 - 3.62).

Conclusions: Patients with macroalbuminuria and anemia at first consultation are at increased risk for rapid CKD stage 3 progression. In this group, patients with CHF, anemia and hyperkalemia (even at first consultation) have a higher risk of mortality. This study may be useful and help us in guiding which CKD stage 3 patients should be referred to a nephrology clinic.
PO0512

Laboratory-Based Potential Indications vs. Risk-Based Triage for Nephrology Referrals in the Veterans Affairs Health System

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Background: Clinical decision support tools may facilitate identification of chronic kidney disease (CKD) and timely nephrology referral. Little is known about the potential effects they might have on the volume of nephrology referrals. We sought to estimate how the implementation of a CKD decision support tool could affect potential nephrology referral volume based on U.S. Veterans Affairs Health System (VA)/Department of Defense (DoD) guidelines, and the risk profile of referred patients.

Methods: In a retrospective cohort study of 434,735 patients with CKD, we determined the number of patients who met laboratory-based potential indications for nephrology referral based on VA/DoD guidelines. We used the Kidney Failure Risk Equation to estimate end-stage kidney disease (ESKD) risk and to determine how incorporating ESKD risk thresholds would modify referral volume.

Results: Among 70,972 patients meeting potential indications for referral who had not visited a nephrologist in 2013, 12,008 (16.9%) were referred in 2014. The two-year risk of ESKD was low in both groups, 2.9% [9.8-8.6%] in the referred group, compared to 1.3% [0.3-3.9%] in the unreferred group (P < 0.001). The number of patients meeting potential indications for referral was approximately equivalent to the number of patients with a two-year risk of ESKD exceeding 1%, or N=81,132. Among potential indications for referral, rapid eGFR decline accounted for 37.6% of eligible unreferred patients and was associated with the lowest two-year ESKD risk.

Conclusions: Laboratory-based potential indications for referral identify a large number of patients at low risk of ESKD. Further study is needed to determine the value of nephrology care for these populations.

Funding: Veterans Affairs Support

PO0513

Variation in Kidney Failure Risk Across Health Organizations Among Adults with CKD in Nephrology Ambulatory Care

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Background: Since most adults with chronic kidney disease (CKD) have low risk for end-stage kidney disease (ESKD) progression, sub specialty nephrology care should focus on patients at highest risk of progression. To optimize utilization of nephrology care, a threshold of 3% risk of ESKD at 5 years based on the Kidney Failure Risk Equation (KFRE) has been proposed for nephrology referral. To understand how application of this threshold in practice could impact CKD care delivery and subspecialty referral, we examined variation in 5-year ESKD risk distributions of patients in nephrology ambulatory care across U.S. healthcare organizations.

Methods: In 22 healthcare organizations, we identified patients age ≥65 years, with eGFR < 60 ml/min/m² and concurrently measured urine albumin/creatinine ratio, who had an ambulatory encounter with a nephrologist from 1/1/2017-12/31/2018 using the OptumLabs® Data Warehouse, a longitudinal, real-world data asset with de-identified administrative claims and electronic health record data. We compared the distribution of patient-derived KFRE 5-year risk across healthcare organizations with ≥500 patients in nephrology care.

Results: Among 45,145 patients with CKD in nephrology care, the overall median 5-year ESKD risk was 2.4%. However, between organizations, the median 5-year ESKD risk varied widely, ranging from 0.8% to 6.7% (Figure). 54.3% of patients were below the 3% recommended referral threshold risk of ESKD.

Conclusions: There is substantial heterogeneity of ESKD risk across healthcare organizations in the population receiving ambulatory nephrology care. A greater understanding of the patient population and delivery system characteristics is needed to explain this heterogeneity, and associated health outcomes could inform recommended risk thresholds for referral and ongoing nephrology care.

Funding: NIDDK Support

PO0514

Prevalence of Comorbid Conditions at CKD Onset Among US Veterans

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Background: Comorbid conditions such as hypertension (HTN) and diabetes increase risk of adverse outcomes among patients with CKD. It is less clear whether such conditions develop prior to CKD onset or subsequently emerge as the disease progresses. Using a newly constructed national incident CKD cohort, we examined the prevalence of major comorbidities at the time of CKD onset by demographic groups.

Methods: The cohort included 1,074,238 subjects with new-onset CKD between 2002 and 2017 in the U.S. Veterans Health Administration (VHA). CKD onset was defined as the first time when estimated GFR (eGFR; CKD-EPI equation) decreased to a value <60 mL/min/1.73 m² for >3 months. We excluded subjects in VHA for <2 years prior to first eGFR <60, or with CKD stage 4 or 5, or end-stage kidney disease (ESKD) when first identified. Thus, the first time identified was close to the onset of CKD stage 3. Comorbidities at CKD onset were ascertained from ICD-9/ICD-10 codes during any time before onset and through 6 months after onset.

Results: All subgroups (age, gender, race and ethnicity) had similar mean eGFRs at onset (51 ml/min/1.73m²). The percentage with age at onset ≥65 years was greater in males (74%) than females (43%), greater in Black (48%) than in American Indian or Alaska Native (39%), Asian or Pacific Islander (33%), and Hispanic (30%), which in turn were greater than Whites (23%). At CKD onset, HTN was highly prevalent, varying from 83% in females to 96% in Blacks; diabetes ranged from 36% in females to 61% in Hispanics; more than two-thirds had cardiovascular disease (CVD); and 19-28% had cancer across subgroups (Table).

Conclusions: This finding suggests that many veterans at the time of CKD onset had already developed some major comorbidities, which could make them particularly susceptible to death before ESKD.

Funding: NIDDK Support, Other U.S. Government Support

Percentages of patients with the individual comorbidity at CKD onset

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Classification of Cause of CKD Using ICD-9 and ICD-10 Codes

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Background: Current KDIGO guidelines classify CKD using three parameters: glomerular filtration rate (GFR), albuminuria, and cause of disease. While prognosis based on estimated GFR and albuminuria have been studied, less is known about the prevalence of disease etiology in CKD patients. We sought to classify various causes of CKD using billing codes for better assessment of the prevalence and risk implications of disease etiology in CKD staging.

Methods: We categorized cause of CKD with 18 potential etiologies and assigned relevant Internal Classification of Diseases (ICD) 9th and 10th revision Clinical Modification codes pertaining to each etiology. We applied the algorithm to two study populations, Johns Hopkins Medicine and Geisinger Health, to assess the prevalence of different etiologies of CKD in large health systems. To validate our CKD classification system, we determined CKD cause among 101 outpatients treated within Johns Hopkins Medicine through internal chart reviews and compared our findings to the classification algorithm generated CKD etiology.

Results: 43.3% and 26.4% of patients with eGFR <60 ml/min/1.73 m² in 2016 in the Geisinger and Johns Hopkins study population, respectively, had a billing code used in our classification algorithm. The most prevalent etiologies of CKD in patients with available billing codes at Geisinger were hypertensive nephrosclerosis (27%), diabetic nephropathy (14.3%), and neoplasm (9.2%). In contrast, the most common causes of CKD in the Johns Hopkins cohort were miscellaneous (12%), obstructive nephropathy (6.3%), and non-PKD hereditary disease (3.2%). Chart review revealed 56% concordance between cause of CKD determined by chart review and that classification algorithm. The most prevalent etiologies of CKD in patients with available billing codes at Johns Hopkins Medicine through internal chart reviews and compared our findings to the classification algorithm generated CKD etiology.

Conclusions: We developed an algorithm for classifying CKD cause by ICD-9 and ICD-10 codes using electronic medical record data; however, validation suggests varying degrees of accuracy across different CKD etiologies.

Epidemiology of Patients with High-Risk CKD: A Demographic Evaluation of Patients Who Had Indications for SGLT2 Inhibitors and GLP-1

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Background: The emerging evidence of the favorable effects of sodium-glucose co-transporter-2 inhibitors (SGLT2is) and glucagon-like peptide 1 receptor agonists (GLP-1) on renal function has brought hope and excitement to the nephrology communities in the US. However, patients with high risk, CKD and indications for SGLT2is and GLP-1 were not on their medication. We would like to identify the features of these patients and their primary care providers to offer targeted recommendations regarding concerns for initiating SGLT2is and GLP-1.

Methods: This is a preliminary analysis of data obtained from the Kidney Coordinated Health Management Partnership (K-CHAMP) study (NCT03832595), an ongoing, NIH funded pragmatic randomized control trial testing an electronic health record-based registries enable population-based examination of care across racial groups.

Results: Of 2225 African-American patients, 743 (33.4%) would hypothetically be reclassified to a more severe CKD stage if the race multiplier were removed from the eGFR equation. Similarly, 167 of 687 (24.3%) would be reclassified from stage 3B to stage 4. Finally, 64 of 2069 patients (3.1%) would be reassigned from eGFR > 20 ml/min/1.73m² to eGFR ≤ 20 ml/min/1.73m², meeting the criterion for accumulating kidney transplant priority. Zero of 64 African-American patients with an eGFR <20 ml/min/1.73m² after the race multiplier was removed were referred, evaluated or waitlisted for kidney transplant, compared to 19.2% of African-American patients with eGFR<20 ml/min/1.73m² with default CKD-EPI equation.

Conclusions: Our study reveals a meaningful impact of race-adjusted eGFR on the care provided to the African-American CKD patient population.

Disparities in CKD Progression by Medicare Advantage Enrolees

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Background: The prevalence of chronic kidney disease (CKD) in Medicare beneficiaries has quadrupled in the past two decades, but little is known about risk factors affecting the progression of CKD. This abstract aims to understand the progression of CKD up to five years after study entry in a large cohort of Medicare Advantage (MA) enrollees and whether it differs by provider recognition of CKD, race and ethnicity, or geographic location.

Methods: In a cohort of 1,002,388 MA enrollees with CKD stages 1-4 based on 2013-2018 labs, progression was estimated using a mixed-effects model that adjusted for demographics, urbanicity, comorbidity, urine albumin-to-creatinine ratio, clinical recognition via diagnosis of CKD, and time fixed effects. Race and ethnicity, geographic location, or clinical recognition of CKD were interacted with time in three separate regression models.

Results: Mean (median) follow-up was 3.1 (3.0) years. At study entry, Black and Hispanic MA enrollees had greater kidney function at study entry than other beneficiaries, but their kidney function declined faster compared to non-Hispanic Whites. At study entry, MA enrollees with clinically recognized CKD had estimated glomerular filtration rate levels that were 18.6 units (95% confidence interval (CI): 18.5-18.7) lower than those of unrecognized patients, but kidney function declined more slowly in enrollees with clinical recognition of CKD. There were no differences in CKD progression by metropolitan or non-metropolitan areas.

Conclusions: These results suggest that patients with clinically recognized CKD and racial and ethnic minorities merit closer surveillance and management to reduce their risk of faster progression.

Impact of the Race Multiplier in the Estimated Glomerular Filtration Rate Equation on Care Delivery Among African-American CKD Patients

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Background: African-American patients with chronic kidney disease (CKD) have poorer outcomes, including in dialysis access placement and transplantation. Estimated glomerular filtration rate (eGFR) equations, which assign higher eGFR values to African-American patients, may be an inadvertent mechanism for inequitable outcomes. Electronic health record-based registries enable population-based examination of care across racial groups.

Methods: Cross-sectional study at two large academic medical centers and affiliated community primary care and specialty practices.

Results: Of 2225 African-American patients, 743 (33.4%) would hypothetically be reclassified to a more severe CKD stage if the race multiplier were removed from the eGFR equation. Similarly, 167 of 687 (24.3%) would be reclassified from stage 3B to stage 4. Finally, 64 of 2069 patients (3.1%) would be reassigned from eGFR > 20 ml/min/1.73m² to eGFR ≤ 20 ml/min/1.73m², meeting the criterion for accumulating kidney transplant priority. Zero of 64 African-American patients with an eGFR <20 ml/min/1.73m² after the race multiplier was removed were referred, evaluated or waitlisted for kidney transplant, compared to 19.2% of African-American patients with eGFR<20 ml/min/1.73m² with default CKD-EPI equation.

Conclusions: Our study reveals a meaningful impact of race-adjusted eGFR on the care provided to the African-American CKD patient population.

Private Foundation Support
PO0519
Prevalence of Diabetes, Hypertension, Anemia, and Hyperkalemia as Frequent Comorbidities in Patients with CKD Regardless of their KDIGO Staging
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Background: Chronic kidney disease (CKD) is a worldwide public health problem. Currently in Mexico, the prevalence of CKD is only an estimate, based primarily on records of advanced stages of the disease. It is necessary to identify comorbidities and thus establish strategies to delay its progression and reduce morbimortality associated with CKD. Objective: To know the prevalence of comorbidities associated with CKD at different stages in an outpatient population who attended a 3rd level hospital.

Methods: This is a cross-sectional retrospective study. Records of adult patients who attended an outpatient nephrology consultation in the period from February 2019 to February 2020 were included, with laboratory reports from 15 days prior to the inclusion date. Descriptive statistics were performed, with a 95% CI and a value of p<0.05.

Results: 1772 patient records were included. 51% (907) were women, the mean age was 42 ± 24.2 years. 12% were on renal replacement therapy, 11% hemodialysis and 1% peritoneal dialysis. 87% (1546) lacked family history of CKD; 11% (192) were smokers. Regarding body mass index, 2% (32) presented low weight, 37% (562) normal weight, 53% (804) overweight and 8% (122) obesity. Figure 1 shows the distribution by CKD stage and main comorbidities. The prevalence of proteinuria was 39% (893), 53% (826) had anemia. The prevalence of hyperkalemia (HK; K>5) was 29% (325). The prevalence of serum albumin <3.5 was 26%; 44% of the population had glucose > 200 mg/dL; 53% with triglyceride >150 mg/dL and 29% with total cholesterol <3.5 was 26%; 44% of the population had glucose >100 mg/dL; 53% had total cholesterol ≥200 mg/dL.

Conclusions: A high prevalence of CKD comorbid risk factors such as diabetes, hypertension, anemia and HK were identified regardless of CKD staging, increasing in proportion in later stages.

Funding: Commercial Support - AstraZeneca

Figure 1. Distribution by CKD stage and presence of type 2 diabetes(left) and hypertension(right)

PO0520
Cystatin C Use in Clinical Practice
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Background: Cystatin C is a filtration biomarker that can be used as an alternative for serum creatinine. The 2012 KDIGO guidelines advocate for the use of cystatin C to confirm the diagnosis of chronic kidney disease (CKD), but 9 years later it is not clear how this test is being used in clinical practice.

Methods: We examined 87,803 cystatin C levels obtained among 55,360 participants between 11/2011-6/2018 in the database of Laboratory Corporation of America Holdings (LabCorp®). The CKD-EPI cystatin equation was used to calculate the estimated GFR for each level. Descriptive analyses of patient age, sex, and ordering provider were conducted, and relationships between serum cystatin C and creatinine levels were examined with correlation analysis and linear regression.

Results: The mean age was 58 ±17.50% were women. Frequency of orders increased over time, from 6,323 tests in 2012, to 17,822 tests in 2017. Providers ordering cystatin C included: Internal/Family Medicine MDs (64%), radiologists (9%), mid-levels (4%), and 9% unknown. Cystatin C was ordered on patients with a wide range of estimated GFR values (Figure). Linear regression showed that 75% of the variation in cystatin C could be modeled if age, sex, BUN, and creatinine were known. Dispersion between actual and predicted cystatin was minimal at cystatin C levels ≤ 0.5yr and that of eGFR slope 1.5yr (p<0.001 and p=0.001, respectively). In stratified analysis, eGFR slope ≥ 1.5yr had significantly greater C-statistics than that of eGFR slope ≤1yr. eGFR slope ≥1yr had higher prognostic ability of renal events in patients with versus without diabetes, advanced CKD and proteinuria. C-statistics of renal events when considering baseline eGFR alone was 0.853 but combination use of baseline eGFR and eGFR slope ≥1yr significantly increased C-statistics, to 0.913 (p<0.01).

Conclusions: Cystatin C use has increased in recent years and growing evidence has shown the prognostic utility of eGFR slope for the risk of ESRD. Previous observational studies have assessed the association between renal events and eGFR slopes estimated by two measurements of eGFR but had great differences in the interval between two eGFR measurements. In this study, we thus aimed to determine the appropriate interval between two eGFR measurements to evaluate the association of eGFR slope with incidence of renal events.

PO0521
Appropriate Interval Between Two eGFR Measurements for the Evaluation of the Association of eGFR Slope with Incidence of Renal Events
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Background: In recent years, growing evidence has shown the prognostic utility of eGFR slope for the risk of ESRD. Previous observational studies have assessed the association between renal events and eGFR slopes estimated by two measurements of eGFR but had great differences in the interval between two eGFR measurements. In this study, we thus aimed to determine the appropriate interval between two eGFR measurements to evaluate the association of eGFR slope with incidence of renal events.

Methods: This is a retrospective cohort study in 203 CKD patients who visited Nara Prefecture General Medical Center, Japan between 1 January 2013 and 31 December 2016 and in whom two or more than two measurements of eGFR levels were confirmed in medical records. eGFR slopes were estimated by using two measurements of eGFR at baseline and 3, 6, 1.5, 2, or 3 years. We excluded patients with acute kidney injury, urologic malignancies, nephritic syndrome with steroid treatment or collagen diseases. Outcome was renal events defined as a composite of ESRD and eGFR decline of ≥ 30%. C statistics were used to evaluate the association between eGFR slope and incidence of renal events.

Results: The median age of study participants was 67 (56-77) years and 71 (37%) were male. The median levels of baseline eGFR were 34 (21-48) mL/min/1.73m² and diabetes was present in 80 (39%) participants. During the median follow-up period of 38 months, renal events occurred in 52 participants. Median levels of eGFR slopes0.5yr, 1yr, 1.5yr, 2yr and 3yr were -7.8, -3.6, -2.9, -0.9, -1.5 mL/min/1.73m², respectively. C-statistics of eGFR slope ≥0.5yr for renal events were 0.622, 0.691, 0.797, 0.858, 0.806, respectively, and that of eGFR slope ≥1yr was significantly higher than that of eGFR slope ≤0.5yr and eGFR slope ≥1yr (p<0.001 and p=0.001, respectively). In stratified analysis, eGFR slope ≥1yr had higher prognostic ability of renal events in patients with versus without diabetes, advanced CKD and proteinuria. C-statistics of renal events when considering baseline eGFR alone was 0.853 but combination use of baseline eGFR and eGFR slope ≥1yr significantly increased C-statistics, to 0.913 (p<0.01).

Conclusions: eGFR slope for high prognostic ability of renal events may be needed to be calculated by at least 1.5-year interval between two eGFR measurements.

PO0522
Rates of Clinical Events in Patients with CKD: A UK Population-Based Cohort Study
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Background: Epidemiological evidence of clinical event rates in patients with chronic kidney disease (CKD) is limited and can impede the ability of dialysis organizations, government agencies, other institutions, and payers to counsel patients and assess quality of care.

Methods: The Clinical Practice Research Datalink (CPRD) is a large, longitudinal UK-based primary care database that covers 6% (~4 million people) of the population. CPRD is linked to Hospital Episode Statistics (HES), which contains information on all hospital admissions in England. We identified CKD patients with eGFR <60 ml/min/1.73m² in CPRD between 2004 and 2017. Adverse clinical events were identified using ICD-10 and READ codes. Non-dialysis dependent (NDD) patients were staged by eGFR. Dialysis dependent (DD) patients were identified using Classification of Interventions and Procedures (OPCS) and READ codes. Clinical events were identified by ICD10 and READ codes. Incidence rates per 100 person-years (PY) were calculated for selected adverse event stratified by dialysis status and CKD stage.
Results: We identified 310362 NDD and 5248 DD patients with a mean (standard deviation [SD]) age of 75.5 (10.2) years and a median (interquartile range [IQR]) follow-up of 87.5 (46.5-130.9) months. Among NDD patients 96%, 3%, and 1% of patient-years came from CKD 4, and 2, 5, and 5, respectively. Most event rates were consistently higher in DD CKD patients, compared to NDD CKD patients; and higher among CKD 4-5 compared to CKD 1-3 patients (Table 1).

Conclusions: Our results help establish baseline rates of specific clinical events and provide additional evidence of increased morbidity for DD vs. NDD patients, and for NDD patients with more severe vs. less severe kidney disease.

Funding: Commercial Support - AstraZeneca

Table 1: Incidence rates of adverse clinical events per 100 PY

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>NDD CKD 3 Rate</th>
<th>NDD CKD 4/5 Rate</th>
<th>DD Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>0.5</td>
<td>1.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Allergic anaphylaxis</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>2.5</td>
<td>3.2</td>
<td>5.8</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>0.7</td>
<td>2.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1.3</td>
<td>2.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0.1</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7.8</td>
<td>12.2</td>
<td>15.2</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>0.1</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>0.1</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Seizure</td>
<td>0.4</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>UCI</td>
<td>7.1</td>
<td>12.6</td>
<td>9.8</td>
</tr>
</tbody>
</table>

PO0524

Estimating the Future Burden of CKD Through Microsimulation Methods

Lise Retal,1 Michael Xu,1 Laura Webber,1 Claudia S. Cabrera,2 Elisabeth Strastudis,2 Stephen Nolan,2 Juan Jose Garcia Sanchez,2 HealthLamens, London, United Kingdom; 1AstraZeneca AB, Sodertalje, Sweden; 2AstraZeneca PLC, Cambridge, United Kingdom.

Background: Chronic kidney disease (CKD) is a debilitating and costly condition, impacting over 10% of people globally. Early diagnosis and proactive management could potentially mitigate the rates of progression to end stage renal disease. Understanding the future trajectory of CKD prevalence, progression, outcomes and the related economic burden are important considerations for public health and policy planning. This study explores the epidemiological and cost burden of CKD with an emphasis on high-risk populations with macroalbuminuria, type 2 diabetes (T2D) and/or heart failure (HF), from 2020 to 2025.

Methods: A patient-level microsimulation was developed to estimate the epidemiological and economic burden of CKD in the UK. KDIGO 2012 recommendations were used to categorise patients according to eGFR and albuminuria using the Health Survey of England extrapolated to the UK population. The future prevalence and healthcare costs for the CKD population, as well as for subpopulations – macroalbuminuria, T2D, HF were estimated. Finally, “current practice” management scenario was compared to an early detection and proactive scenario.

Results: By 2025, CKD prevalence in the UK is expected to grow by 11% from ~9.1M to 10.2M corresponding to a £4B (18%) increase in annual cost from £18B, of which, £0.58B is incurred due to macroalbuminuria where prevalence is projected to reach 860,000 by 2025. Within the macroalbuminuria population, costs were comparable between patients with (390,000; £0.31B) and without (465,000; £0.27B) T2D. However, costs for patients with macroalbuminuria were 3-times higher than for CKD patients with HF (£0.11B, 140,000). Early identification and proactive management of patients with CKD and macroalbuminuria resulted in a cumulative £0.65B direct healthcare cost saving by 2025.

Conclusions: This model predicts that CKD poses a serious public health threat. The overall epidemiological burden for patients with macroalbuminuria was comparable with patients with and without T2D. Early detection along with proactive treatment may reduce CKD progression and more directly improve patients’ quality of life while also reducing the long-term economic burden of CKD.

Funding: Commercial Support - AstraZeneca

PO0525

Identifying and Clustering CKD Progression Trajectories Using Machine Learning

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Background: There is evidence suggesting that estimated glomerular filtration rate (eGFR) slope can be used as a surrogate clinical endpoint in renal clinical trials. However, there are limited data on the characteristics of fast and slow progressors based on eGFR slope from large population-based studies.

Methods: We identified CKD patients (based on two consecutive eGFRs of ≥75ml/min/1.73m2 recorded more than 90 days apart) aged ≥18 years from the UK Clinical Practice Research Datalink (CPRD) between 2004 and 2019. Estimated GFR measurements over a 5-year observation period post-index date (date of 2nd eGFR measurement) were extracted from their eGFR trajectories using statistical (linear mixed effect models (LMM)) and machine learning techniques (unsupervised machine learning and Bayesian approaches). Association between trajectory clusters and all-cause mortality was assessed using Cox regression analysis.

Results: Preliminary, 407,108 patients with 1.8 million eGFR measurement (median 4 (IQR: 2-6) eGFR measurements per patient) were identified. Using LMM, we found 5% of patients declined rapidly with an average rate of eGFR change per year ~4.78 (95%CI: -9.40 to -3.28) whereas the majority (95%) remain stable or progressed slowly. A distinct fast progressing cluster was also detected using unsupervised machine learning and Bayesian methods which showed broadly linear patterns. Overall, there was an agreement between all three clustering approaches. These findings were replicated in the validation dataset showing consistent findings. Compared to stable/slow progressors, fast progressors were 3 times more likely (HR=2.82; 95%CI 2.75-2.90) to die following the 3-year observation period.

Conclusions: A clear fast progressing cluster was identified with an average eGFR decline of ≥3 ml/min/1.73m2 per year with a higher risk of all-cause mortality compared to other clusters. Whilst Bayesian and unsupervised machine learning methods can detect non-linear patterns, we found broadly linear trajectories.

Funding: Commercial Support - AstraZeneca

Figure 1: A) Number of patients with at least one endpoint and B) number of events

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Underline represents presenting author.
PO0526

Using Autoencoders for Imputing Missing Data in eGFR Decline Trajectories of Patients with CKD

Davina J. Zamanizadeh,1 Panayiotis Petousis,1 Tyler A. Davis,1 Anders O. Garlid,2 Xiaoyan Wang,1 Keith C. Norris,1 Obidighwu Duru,1 Katherine R. Tuttle,2 Alex Bui,1 Susanne B. Nicholas.1 CURE-CKD Registry Study Team1 University of California Los Angeles, Los Angeles, CA;2 Providence St Joseph Health, Spokane, WA.

**Background:** Using machine learning (ML) approaches to impute missing data has not been explored in CKD progression. We investigated the utility of a data-driven imputation to improve downstream classifier prediction of rapid eGFR decline in the CURE-CKD registry.

**Methods:** We analyzed CKD patients at UCLA (N=13,206) over a 2-year period. We used: 1) the dataset with missing data; and 2) a censored subset with no missing data. We introduced 33% and 66% missingness by removing values by replacing missing values either missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR). We included: eGFR, hemoglobin (HbA1c), systolic blood pressure (SBP), number of ambulatory and inpatient visits, age, sex, ethnicity, rurality status, diagnosis of hypertension, diabetes mellitus (DM), pre-DM, and use of renin angiotensin aldosterone system inhibitors. We introduced missingness on SBP and HbA1c to mirror the original dataset. We imputed missing values using an autoencoder ML model. To predict a 40% eGFR decline over 2 years, we developed random forest models using the full and resultant imputed datasets.

**Results:** On the full subset, the MNAR imputation method achieved a root mean squared error (RMSE) of 0.9. The MAR method achieved RMSE of 3.8 at 33% missingness and 5.4 at 66%. MCAR achieved RMSE of 38.5 at 33% missingness and 56.4 at 66%. Using the random forest model to predict rapid decline on the fully observed subset without removing and imputing data achieved a receiver operating characteristic (ROC) area under the curve (AUC) mean of 80.8±1.1 and precision/recall (PR)-AUC mean of 23.9±1.5; the same as our methodology on MNAR, which is explained by the RMSE of 0, shown in Table 1.

**Conclusions:** Our method accurately imputes clinical data values while accounting for uncertainty caused by missing values.

**Funding:** Other NIH Support - NIMHD

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean ROC-AUC</th>
<th>Mean PR-AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAR</td>
<td>80.8±1.1</td>
<td>23.9±1.5</td>
</tr>
<tr>
<td>MCAR</td>
<td>38.5±3.8</td>
<td>56.4±6.6</td>
</tr>
<tr>
<td>MNAR</td>
<td>0±0</td>
<td>0±0</td>
</tr>
</tbody>
</table>

PO0527

Machine Learning Prediction of ESKD and Death in CKD Patients: Electronic Medical Record-Based Cohort Study


**Background:** Chronic kidney disease (CKD) is a risk factor for end-stage kidney disease (ESKD) and death. An accurate prediction of those risks is required to improve their prognosis. We developed the new machine learning models for the prediction of CKD progression and death using the electronic-medical-record-based CKD-patient big database in Japan (n=3,714, 66,981 claim data).

**Methods:** We developed 20 risk prediction models with 45 variables for the classification of the patients on the basis of their outcomes (ESKD and death) over 1 to 3 years using random forest (RF), Gradient Boosting Decision Tree (GB), Extreme Gradient Boosting (XG), support vector machine, and multivariate logistic regression models using validation datasets including baseline or time-series datasets. The performance characteristics of the models were compared with those of the laboratory indices, and the kidney failure risk equation (KFRE) using the area under the prediction curves (AUCs) by bootstrapping 1000 times.

**Results:** 53.1% were male; age, 60.1±17.6 years; eGFR, 54.2±30.7 mL/min/1.73 m²; diabetes mellitus, 23.1%. In the validation dataset, 14 models showed statistically significantly higher AUCs for the prediction of outcomes than KFRE 0.782 (0.682, 0.881), and the RF, GB, and XG models based on time-series data showed the highest AUCs: 0.924 (95% CI 0.895, 0.953) (Fig. A). These three models also demonstrated the highest performance in the subgroup analysis that considers eGFR, DM, gender, and age. Moreover, the models' sensitivities were 0.971 (95% CI 0.914, 1.0). Cox proportional hazards models revealed that the probabilities predicted by these models represented the risk of the outcome (p<0.0001) (Fig. B).

**Conclusions:** The machine learning models exhibit better performance than pre-existing models in identifying patients at an increased risk of CKD progression and death. They will enable us to implement effective measures to improve patient's prognosis.

**Funding:** Government Support - Non-U.S.

PO0528

Predicting Rapid eGFR Decline Using Electronic Health Record (EHR) Data Despite High Missingness in the CURE-CKD Registry

Tyler A. Davis,1 Panayiotis Petousis,1 Davina J. Zamanizadeh,1 Xiaoyan Wang,1 Keith C. Norris,1 Obidighwu Duru,1 Katherine R. Tuttle,2 Alex Bui,1 Susanne B. Nicholas.1 CURE-CKD Registry Study Team1 University of California Los Angeles, Los Angeles, CA;2 Providence St Joseph Health, Spokane, WA.

**Background:** Patients with rapid eGFR decline tend to progress to kidney failure. Automated tools can identify individuals at risk of severe renal functional decline and facilitate disease mitigation. We describe a deep neural network (DNN) for predicting the risk of rapid eGFR decline (~40% decrease in eGFR over 2 years) and identified populations at higher risk of rapid decline using the CURE-CKD Registry.

**Methods:** Variables include: age, sex, race/ethnicity, ACE inhibitor/ARB use, eGFR, systolic blood pressure (SBP), hemoglobin A1c, and the diagnosis of hypertension, type 2 diabetes (DM), pre-DM or chronic kidney disease (CKD) based on EHR data. We trained and validated our models on patients with CKD (N=93,567) and at-risk for CKD (N=913,289) with eGFR ≥15ml/min/1.73m² over 2 years. We trained and validated a 5-layer DNN, a logistic regression (LR) model, and a gradient boosted tree (GBT) model using a 60/20/20 train/test/validation split. We computed the risk distribution of all 25,475 subpopulations, based on all possible expert defined combinations of the above variables, and compared this risk distribution against the whole population’s risk distribution using the Kolmogorov-Smirnov (KS) test. Subgroups with the highest risk of decline were identified using the KS test (p<0.05) on our highest performing model.

**Results:** The DNN achieved an area under the receiver operating curve (AUC-ROC) of 0.75 on the test set. The LR and GBT achieved an AUC-ROC of 0.72 and 0.73, respectively. The subpopulations with significantly highest average predicted risk across training, validation, and testing were 17,734. We identified the most frequent predictors of rapid eGFR decline across the highest risk populations. Of the top 100 significantly higher risk subpopulations the following variables were the most frequent: CKD (100%), SBP >140 mmHg (72%), age 45-66 years (56%), DM (52%), and AIC >8 (50%).

**Conclusions:** We developed a methodology that uses a risk model for rapid eGFR decline using big data and used its predictions, along with the KS test, to identify subpopulations with significantly high risk for rapid eGFR decline.

**Funding:** Other NIH Support - NIMHD

PO0529

A Machine Learning-Based Prediction Model for Trajectory of GFR in CKD Patients with Rapid Decline of GFR by Using a Big Database

Daisho Inaguma,1 Akimitsu Kitagawa,1 Ryosuke Yanagiya,1 Akira Koski,2 Takayoshi Furumori,2 Michiharu Kudo,1 Shogo Fukuma,1 Naotake Tsuibo,1 Yukio Yuzawa,1 Fujita Health University School of Medicine, Department of Nephrology, Toyoake, Japan;1 IBM Research, Tokyo, Japan;2 Fujita Health University Bantane Hospital, Department of Nephrology, Nagoya, Japan;2 Fujita Health University, Division of Medical Information System, Toyoake, Japan;3Kyoto University Graduate School of Medicine, Human Health Sciences, Kyoto, Japan.

**Background:** There are various patterns of GFR trajectories in patients with chronic kidney disease (CKD), even among those with rapid declines in GFR. We sought to create a machine learning-based predictive model for extremely rapid decline of GFR in patients with CKD using a single hospital database.

**Methods:** We used a database, which included the electronic medical records of 286,494 patients. We selected patients with CKD and rapid decline in kidney function, which was defined as an estimated GFR (eGFR) decline of 30% or more within two years. We used longitudinal statistics using data extracted from baseline, 90-, 180-, and 360-day windows prior to baseline and exponentially weighted averages (ESAs) where the weight was calculated as 0.9^n (days/decay parameter). The random forest algorithm and python code for the scikit-learn library (https://scikit-learn.org/) were used for model creation.

**Results:** Patients were automatically classified, using machine learning, into three groups according to eGFR at baseline (G1; high GFR, G2; intermediate GFR, G3; low GFR) and nine subgroups according to the slope of eGFR decline. The subgroup with the lowest eGFR decline had the highest risk of declining eGFR.

**Funding:** Other NIH Support - NIMHD

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Underline represents presenting author.

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fastest GFR decline exhibited the steepest slope (Figure 1). The area under the curves for predicting the steepest (fastest) GFR decline by random forest model among the G1, G2, and G3 were 0.68, 0.72 and 0.81, respectively. Regarding feature importance, in the G1 group, hemoglobin of the 7-day ESAs and measures obtained 90 days prior to baseline ranked within the top five. Meanwhile, serum albumin and CRP at baseline ranked within the top seven in the G3 group.

Conclusions: The random forest model identified patients with extremely rapid GFR decline. Anemia in patients with higher eGFR, and nutritional status in patients with lower eGFR, emerged as strong risk factors.

PO0530

Automation of Renal Blood Flow Analysis from Dynamic Phase-Contrast MRI with Deep Learning

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Background: Phase-contrast magnetic resonance imaging (PC-MRI) allows to assess renal blood flow (RBF), an important parameter in the development of chronic kidney disease (CKD). RBF assessments require time-consuming and observer-dependent delineations of the renal arteries. Thus, we have developed and evaluated a fully-automated deep learning model for renal artery segmentation.

Methods: PC-MRI data came from 131 subjects, four studies, three MRI vendors and a range of velocity encodings. The deep learning model (DL) was a deep-supervised attention U-Net with residuals with the result re-introduced in a second iteration. Flow was estimated by integrating the flow values in the segmentations. Segmentation and flow results were compared for cross-validation (CV, 73 subjects) against manual delineations and reference flow measurements from external software. The remaining data (Extra) only had reference flow measurements, being only evaluated for flow.

Results: In 4-fold CV, a segmentation accuracy of Dice 0.71 ± 0.21 was obtained. Although most segmentations were relatively accurate, the model failed in ten out of 144 arteries. Flow measurements were relatively highly correlated in CV with no significant deviation from the reference: (r=0.84, DL: 5.8±3.0 ml/s vs Ref: 5.8±3.0 ml/s, p=0.98). The Extra set provided a high correlation and no significant deviation (r=0.94, DL: 6.4±2.8 ml/s vs Ref: 6.7±2.9 ml/s, p=0.11).

Conclusions: The method showed promise to support RBF measurements from PC-MRI. It may save analysis time and increase objectivity in the future. More high quality and representative training data are likely to improve accuracy and generalizability.

Funding: Government Support - Non-U.S.

PO0531

Healthcare Engineering to Predict Time and Resource Impact of Integrating a CKD Education Intervention into Primary Care Practice

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Background: This study describes the novel use and application of healthcare engineering and Discrete Event Simulation (DES) to study the impact of adding a physician-led chronic kidney disease (CKD) education review for patients in two primary care settings.

Methods: We developed a computer model to simulate a General Internal Medicine and Family Medicine practice and used it to examine the impact of adding a physician-led CKD education review into routine primary care appointments. To create the computer models we gathered data using real-time process mapping and information from the electronic health record (EHR). The physician-led education review included physicians reviewing a one-page education information sheet, tailored to individual patients. Computer models of each clinic were developed to test the effect on patient flow and time through clinic appointments using different proportions of patients with CKD for which a physician would review the CKD education. We also tested varying amounts of time it would take for physicians to review CKD education within the model.

Results: Adding the physician-led review of CKD education into clinic visits did not significantly increase patient flow or time through clinic. Incrementally increasing potential times for the CKD education review, up to 10 minutes with 50% of all patients, did not reduce patient flow significantly. The estimated resource utilization of physicians increased by about 5%. Similar results were found for Family Medicine.

Conclusions: This research allowed us to perform a "what-if" analysis on the effect of introducing physician-led CKD patient education into routine primary care practice. Results show that it is possible to introduce patient education and support without major disruptions in clinic flow nor patient time through clinic.

Funding: NIDDK Support
or death. Progressive CKD was defined as kidney failure or ≥40% decline in eGFR from the baseline (4 months after surgery). Models were unadjusted, adjusted for %IFTA, and adjusted for %TI.

Results: At surgery mean age was 64 years, 64% male, 66% hypertensive, and 13% diabetic. Samples contained a mean of 349 glomeruli and mean baseline eGFR was 48 ml/min/1.73m². After a mean follow-up of 6.4 years there were 117 CKD progression events and 299 deaths. %IFTA and %TI predicted progressive CKD independent of each other (Table). %TI non-IFTA (not %IFTA) contributed to this risk. After %IFTA adjustment, smaller mean IFTA focus area associated with a higher risk of CKD progression. These findings persisted with adjustment for clinical characteristics including eGFR and proteinuria.

Conclusions: Both total %IFTA and %TI (particularly %I-non IFTA) are important predictors of progressive CKD. At the same %IFTA, a greater number of small IFTA foci are more predictive of progressive CKD than fewer large foci of IFTA.

PO0533

Modification of the Association Between Dipstick Hematuria and Decline in Kidney Function by Proteinuria: Results from a Longitudinal Nationwide Survey

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Background: We hypothesize that proteinuria has a modification effect on the association of hematuria with decline in kidney function.

Methods: Participants were recruited who have undergone multiple nationwide specific health checks between 2008 and 2014 and have been observed for ≥2 years. We divided the participants into two and three categories according to hematuria and proteinuria, respectively. Using analysis of covariance, changes in eGFR over time (delta-eGFR) were examined in hematuria category stratified by proteinuria category.

Results: Among 253,679 participants, median delta-eGFR was -0.36 mL/min/1.73m² per year (IQR: -2.25-0.54) during a median observation period of 4.0 years (IQR: 3.1-6.4). Among general population, delta-eGFR levels with and without hematuria were comparable in the absence of proteinuria, but proteinuria levels had a gradually increased as the proteinuria category progressed (P for interaction <0.001).

Conclusions: Among general population, delta-eGFR levels with and without hematuria were comparable in the absence of proteinuria, but proteinuria levels had a synergistic effect on eGFR decline rate associated with hematuria.
PO0535

Impact of Variability in Estimated Glomerular Filtration Rate on Major Clinical Outcomes: A Nationwide Population-Based Study

Soojin Lee,1 Yeonhee Lee,1 Schoon Park,1 Yae-rit Kim,2 Min woo Kang,1 Semin Cho,1 Yong Chul Kim,3 Kwon Wook Joo,1 Chun Soo Lim,1 Yon Su Kim,1 Dong Ki Kim.1 1Seoul National University College of Medicine, Seoul, Republic of Korea; 2Keimyung University, Daegu, Republic of Korea; 3Seoul National University Seoul Metropolitan Government Boramae Medical Center, Dongjak-gu, Seoul, Republic of Korea.

Background: The estimated glomerular filtration rate (eGFR), commonly estimated using the serum creatinine value, often fluctuates throughout the serial measurement. The clinical significance of GFR variation among the general population with normal renal function has not yet been demonstrated. Thus, we explored the impact of GFR variability on adverse clinical outcomes.

Methods: A nationwide retrospective cohort study using the Korean National Health Insurance System database was performed. National health screening examinees who underwent creatinine measurement at least three times between 2012 and 2016 were considered. Those with eGFR under 60 mL/min/1.73m² were excluded. The fluctuation of eGFR was represented with variability independent of the mean (ViM), which was calculated by the standard deviation divided by the exponent of the regression coefficient of the mean. Then, the risks of myocardial infarction (MI), stroke, and death were assessed according to the quartiles of the ViM.

Results: Of total 3,538,500 participants, 0.29% of myocardial infarction (MI), 0.14% of stroke, and 0.36% of deaths were observed during the median follow-up of 3.27 years. Participants with the highest ViM index, which represents the highest eGFR variability, were significantly associated with an increased risk of MI (hazard ratio [HR]; 1.10, 95% confidence interval [95% CI]; 1.04-1.16), stroke (HR; 1.16; 95% CI 1.09-1.23), and death (HR; 1.18; 95% CI 1.12-1.24). (Figure 1)

Conclusions: Increased eGFR variability exhibited an association with major clinical outcomes, indicating that monitoring eGFR variability might be a useful parameter for predicting the adverse outcomes.

Figure 1

PO0536

Development and Internal Validation of a Mortality Risk Prediction Model in Older Adults with Advanced Non-Dialysis-Dependent CKD

David Y. Li,1 Heather L. Prigmore,2 Thomas G. Stewart,2 Khaled Abdel-Kader,1 Vanderbilt University Medical Center, Nashville, TN; 1Vanderbilt University, Nashville, TN.

Background: Older adults with CKD expect practitioners to share prognostic estimates to inform decision-making regarding future care. The availability of useful mortality prediction models in NDD-CKD could reduce prognostic uncertainty and aid in identifying patients who would benefit from advance care planning (independent of dialysis initiation).

Methods: 699 patients with NDD-CKD stages 4-5 and age ≥60 were enrolled and followed between 2014 and 2019. Cox proportional hazards regression was used to model the risk of 1-year mortality. Candidate predictor variables included age, gender, race, Charlson Comorbidity Index (CCI), common labs and the provider’s response to the Surprise Question (“Would you be surprised if this patient died in the next 12 months?”), SQ, recorded using binary and 5-point Likert response scales). Optimism-corrected measures of model performance were calculated with bootstrap resampling. Model calibration was assessed visually.

Results: In the derivation cohort, age, CCI, hemoglobin levels and the provider’s Likert scale response to the SQ were predictive of 1-year mortality (Table 1). The C-statistic in the derivation sample was 0.76 and the optimism corrected C-statistic obtained by bootstrap resampling was 0.73. Visual examination of model calibration demonstrated good calibration.

Conclusions: A 1-year mortality risk prediction model in older adults with advanced NDD-CKD performed reasonably well and was well calibrated. Studies are needed to understand how to best leverage information on mortality risk to enhance patient-provider communication and ensure that future care delivered to patients is aligned with their priorities.

Table 1

1-year Mortality Hazard Ratios

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 years)</td>
</tr>
<tr>
<td>CCI (per 2-point increase)</td>
</tr>
<tr>
<td>Multigener generation by 2-point increase</td>
</tr>
<tr>
<td>eGFR &lt; 30 mL/min/1.73 m²</td>
</tr>
<tr>
<td>Not surprised:</td>
</tr>
<tr>
<td>Surprised:</td>
</tr>
</tbody>
</table>

Table 1

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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PO0538
Association of eGFR Index Category and Annual Slope with Adverse Clinical Outcomes in Japan
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Background: The relationship between the slope of eGFR with adverse clinical events has not been evaluated extensively. The objective of the study was to assess the association between eGFR and clinical outcomes.

Methods: The study population included persons with 3 or more eGFR values in the MDV database between January 1, 2014 and September 30, 2019. Patients were stratified into 5 index eGFR categories (TABLE). Least square regression model was used to examine the association between eGFR and its slope vs. study outcomes. Patients were stratified into 5 index eGFR categories (TABLE). Least square regression model was used to calculate the annual rate of eGFR change to stratify into 6 categories. Cox proportional hazard model was applied to examine the association between eGFR and its slope vs. study outcomes.

Results: 57,692 patients met the study criteria, and were grouped by index eGFR and its slope (TABLE). The mean age ranged from 56.69 to 74.21 in the index eGFR and from 65.3 to 67.2 in the slope categories. The risk of all-cause mortality or hospitalization, CV death, and any CV or renal outcomes were higher among the low and high index eGFR compared to the reference groups (grade 3 eGFR and -1~+1 slope), as well as those with rapidly declining or increasing eGFR.

Conclusions: Our study showed that those with the highest or lowest categories in index eGFR and eGFR slope had a higher risk for adverse clinical outcomes. Further studies are needed to confirm the findings and explore potential reasons why high eGFR and rapid increase are associated with mortality, CV and renal events.

Funding: Private Foundation Support

Hazard Ratio of clinical events with eGFR and slope categories

![Hazard Ratio](image)

* eGFR = 194 x Cr-1.094 x Age-0.287
** stroke, CHF, MI,
***ESRD, dialysis, acute kidney failure, renal transplant.

PO0539
Sex-Specific Differences in Clinical Outcomes Among Patients with CKD: Results from CKDopps
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Background: Women have more chronic kidney disease (CKD) than men, but are under-represented in the dialysis population. We aimed to assess sex-specific differences in clinical outcomes among CKD Outcomes and Practice Patterns Study (CKDopps) participants.

Methods: Using data of 5682 CKDopps stage 3-5 patients from Brazil, Germany and the US, we reported cumulative incidence of pre-dialysis death, dialysis, and transplantation, by sex and CKD stage at CKDopps entry. We used Fine & Gray models to assess the effect of sex on the time to events, stratified by CKD stage. Models were adjusted for age and race, and then for eGFR slope in the first 6 months after enrolment, but not for case mix variables as men and women are biologically different.

Results: There were more men than women at baseline (54 vs 46%). Men were more likely on the transplant waitlist (13 vs 10%) and had higher median eGFR at dialysis initiation (11.2 vs 10.6 mL/min/1.73m²). Over a median follow-up of 1.75 years, the crude cumulative incidence of dialysis was higher in men while that of death was similar (Figure). The age- and race-adjusted hazard ratio (HR) (95% CI) between men vs women was 1.59 (1.40-1.82) for dialysis, 1.24 (1.04-1.49) for death and 1.80 (0.83-3.80) for transplantation. After adjustment for eGFR slope, the HR for dialysis was 1.72 (1.46-2.01), but the HR for the other two outcomes remained similar.

Conclusions: Despite higher CKD prevalence in women, more men received treatment at nephrologist-run clinics in our study. Men had a higher chance of commencing dialysis before death, unexplained by CKD progression. This finding helps interpret the preponderance of men in the dialysis population.

PO0540
Predictive Value of Urine Osmolal Gap and Urine Anion Gap in CKD Progression
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Background: Metabolic acidosis is the major complication of chronic kidney disease (CKD) and associated with poor clinical outcome. Impaired renal ammonium excretion in CKD lead to metabolic acidosis. The urinary anion gap (UAG) and urinary osmolal gap (UOG) have been used to estimate urinary ammonium excretion because of the limitation of clinical application of direct ammonium measurement. We sought to determine whether UAG and UOG predict progression of CKD.

Methods: 185 patients with Stage II-V CKD were prospectively followed up at Catholic Medical College Multicenter Native Kidney Biopsy Cohort. 24-hour urine chemistry was measured at baseline. Routine laboratory test results were obtained at baseline and 1 year after enrollment. UAG and UOG were calculated using 24-hour urine chemistry results. Estimated GFR was calculated with CKD-EPI equation.

Results: Baseline characteristics are shown in Table 1. Positive association between UOG and decline of renal function was observed (Figure 1). The line indicates the regression line for the relation between decline of renal function and urine osmolal gap; R = 0.035, P = 0.003 (P = 0.011).

Conclusions: UAG and UOG predict decline in renal function in CKD patients. Further study is required to determine the direct correlation between UAG and UOG and urinary ammonium excretion.
The overall model fit was excellent ($\chi^2$ = 119.6, p < 0.000). Seven comorbidities were significantly associated with bleeding. Obesity, age, hypertension were not significantly associated with bleeding.

Conclusions: Our results indicate that renal failure, female gender, coagulopathy, and anemia are risk factors for bleeding after renal biopsy, whereas obesity and hypertension are not. A strength of this study is the large sample size. It also suggests that peripheral anemia are risk factors for bleeding, whereas obesity and hypertension were not significantly associated with bleeding.

PO0542
Evaluation of Thromboelastometry and Multiple Electrode Aggregometry in ESRD
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Background: Bleeding and thrombosis rates are paradoxically increased in chronic kidney disease (CKD), but risk assessment for both is not possible with routine laboratory tests. We aimed to evaluate haemostatic changes in CKD stage 5 patients with modern techniques; using thromboelastometry (TEM), multiple electrode aggregometry (MEA), markers of thrombogenesis, fibrinolysis and endothelial activation.

Methods: TEM, MEA, thrombin anti-thrombin (TAT), alpha-2 antiplasmin, d-dimer and Interferon Adhesion Molecule-1 (ICAM-1) were quantified in 50 CKD Stage 5 patients (including 20 haemodialysis patients) and 30 healthy controls. Patients taking antiplatelet agents were excluded from MEA analysis.

Results: TEM parameters showed hypercoagulability, with increased maximal clot firmness (MCF) & shorter clot formation time (CFT); and D-dimer, TAT and ICAM-concentrations were also increased in CKD Stage 5 patients compared to HC (Table 1). Platelet dysfunction was evident in CKD Stage 5 with lower aggregation in ADPtest and TRAPtest compared to HC.

Conclusions: Our study shows that the prothrombotic changes in CKD Stage 5 are due to increased coagulation and endothelial activation. Bleeding tendency may relate to platelet dysfunction and possibly increased fibrinolytic activation.

Table 1: Comparison of TEM, MEA, alpha-2 Antiplasmin, D-dimer, Thrombin Antithrombin and ICAM-1 between Healthy Controls and CKD Stage 5 (Median and Interquartile Range (IQR))

|$p$-value

PO0543
During P2Y12 Antiplatelet Therapy, Treatment of Anemia Was More Frequent Among Peripheral Artery Disease Patients with Lower eGFR: The EUCLID Trial
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Background: Anemia independently predicts amputation and mortality among patients with peripheral artery disease (PAD). In the EUCLID trial, minor bleeding was more frequent among PAD patients with baseline eGFR<60 ml/min/1.73m2 (adjusted HR 1.51, 95% CI 1.07-2.15; p=0.02 for TIMI minor bleeding; HR 1.21, 95% CI 0.89-1.64; p=0.22 for TIMI major bleeding). We evaluated the impact of eGFR on hemoglobin (Hb) levels and anemia treatment.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: EUCLID (NCT01732822) randomized symptomatic PAD patients to monotherapy with ticagrelor or clopidogrel for 30 months (median); treatment groups were combined for analysis. Independent predictors of Hb change from baseline were evaluated in a multivariable model including baseline Hb and eGFR, sex, age, and post-randomization revascularization procedures, myocardial infarction and anemia treatment.

Results: At baseline, 9025, 1870 and 1000 patients had eGFR ≥60, 45-59 and <45 ml/min/1.73m², respectively. Patients with lower eGFR were older, more often male and had higher prevalence of diabetes and hypertension. Mean Hb at baseline was 14.2, 13.5 and 12.7 g/dl for the 3 eGFR categories. Mean fall in Hb during the trial was 0.5±1.7 g/dL and did not differ by baseline eGFR category. On-study treatment with iron, erythropoietin and/or red blood cell transfusion was reported for 479 (5.3%), 163 (8.8%) and 129 (12.9%) patients, respectively (Figure, p < 0.0001 across eGFR categories). In multivariable analysis, even after adjustment for baseline and post-randomization effects, baseline Hb was a significant independent predictor of Hb fall; anemia treatment was a significant independent predictor of Hb rise.

Conclusions: Among patients with PAD taking antiplatelet therapy in the EUCLID trial, those with lower eGFR were more often treated for anemia.

Funding: Commercial Support - AstraZeneca

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PO0544

The Ratio and Difference of Urine Protein-to-Creatinine Ratio and Albumin-to-Creatinine Ratio Facilitate Risk Prediction of All-Cause Mortality: A Retrospective Cohort Study

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Background: The difference and ratio of albuminuria (defined by urine albumin-to-creatinine ratio, uACR) and proteinuria (defined by urine protein-to-creatinine ratio, uPCR) has not been systematically evaluated with relevant clinical outcomes. We aimed to assess the prognostic performance between the difference and ratio of uACR and uPCR with all-cause mortality.

Methods: This retrospective cohort study identified 2904 adult patients with concurrently measured uACR and uPCR from the same urine specimen in a tertiary medical center in Central Taiwan between January 2003 and June 2017. Urinary albumin-to-protein ratio (uAPR) was derived by dividing uACR by uPCR. Urinary non-albumin protein (uNAP) was calculated by subtracting uACR from uPCR. Conventional severity categories of uACR and uPCR were used to develop a risk matrix. We evaluated all-cause mortality based on uAPR and uNAP on a continuous scale using the multivariable Cox proportional hazards model.

Results: For each doubling increase in uPCR, uACR, and uNAP, the adjusted hazard ratios (aHRs) of all-cause mortality were 1.29 (95% confidence interval [CI]: 1.24-1.35), 1.12 (1.09-1.16), and 1.41 (1.34-1.49), respectively. Linear dose-response association with all-cause mortality was only observed with uPCR and uNAP. The 3 x 3 risk matrices revealed that patients with severe proteinuria and minimal albuminuria had the highest risk of all-cause mortality (aHR 5.25, 95% CI: 1.88, 14.63). uNAP significantly improved the discriminative performance compared to that of uPCR (c-statistics: 0.834 vs. 0.828, p < 0.05).

Conclusions: uNAP provides better mortality prognostic assessment than uPCR and uACR.

Funding: Private Foundation Support, Government Support - Non-U.S.

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PO0545

Metformin and the Risk of Lactic Acidosis in Patients with CKD Stage 3


Background: Metformin has become the first-line therapy for the treatment of diabetes in patients with CKD stage 3. The use of metformin in CKD has been debated due to safety concerns related to lactic acidosis.

Methods: We assessed the safety of metformin in a double-blinded trial (NCT02252081). Fifty patients with CKD Stage 3 and metabolic syndrome and/or prediabetes were randomized to either metformin or placebo for 16 weeks. Metformin was started at 500 mg and titrated in 1-2 weeks up to 1500 mg/day in CKD 3a and 1000 mg/day in CKD 3b. Lactic acid (LA) levels were measured at weeks 2, 4, 8, 12, and 16. We compared the effect of metformin on LA between groups and over time using a mixed model and on plasma HCO3 and anion GAP (AG) using ANCOVA of change analysis.

Results: The mean age was 65 ± 10 years old, 80% were male, BMI was 31.4 ± 5.1 kg/m², 16% of patients were CKD Stage 3b. LA levels slightly increased with metformin, but in most patients remained within normal limits (≤ 2.5 mEq/L) [Figure 1, p = 0.05]. The association of metformin and LA remained non-significant in the multivariable-adjusted mixed model (β = 0.15, p = 0.07) and remained steady over time (β = -0.003, p = 0.54). Baseline eGFR had no effect on LA levels (β = 0.01, p = 0.35), whereas higher BMI was associated with higher LA levels (β = 0.02, p = 0.03). Only 3 patients developed LA levels > 3 mEq/L, but no drug discontinuation and 1 at week 12 which was transient. The changes in HCO3 levels and AG were not statistically significant ([HCO3 - Metformin baseline 27 ± 2.1 mEq/L, week 16 26.2 ± 2.8 mEq/L; placebo baseline 26.2 ± 2.1 mEq/L, week 16 26.7 ± 2.8 Eq/L; p = 0.21] (AG: Metformin baseline 10.1 ± 2.2 mEq/L, week 16 10.4 ± 2.1 mEq/L; placebo baseline AG 10.4 ± 2.2 mEq/L, week 16 10.2 ± 2.3 mEq/L, p = 0.42)).

Conclusions: Metformin use in patients with CKD stage 3 appears to be safe. LA levels mildly increased with metformin, but remained within normal limits and stable after week 2. Patients did not develop clinical or laboratory manifestations of acidosis based on HCO3 levels and AG.

Funding: Veterans Affairs Support

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0546
Magnetic Resonance Imaging-Based Renal Function Estimation Using a Machine Learning Approach
Daichi Fukuya, Tsutomu Inoue, Eito Kozawa, Masahiro Ishikawa, Yusuke Watanabe, Hiroaki Arano, Naoki Kobayashi, Mamoru Niitsu, Hirokazu Okada.

Background: In patients with deterioration of GFR with an unknown clinical course, it is quite difficult to determine whether the renal dysfunction is caused by a hematologic alteration or changes in the renal parenchyma, even when using kidney imaging. Therefore, to estimate renal function quantitatively based on the morphology of the renal parenchyma, we performed an advanced image analysis of renal magnetic resonance imaging (MRI) using machine learning (ML).

Methods: We used coronal Dixon water-dominant images obtained on a 3.0T MR device and a deep ML convolutional neural network (CNN) to evaluate renal function (eGFRcre). K-fold cross-validation (k = 5) was performed for the assessment of accuracy and generalization performance. The study protocol was approved by the IRB of our institute.

Results: A total of 196 patients (age, 57.9 ± 16.9 years; 128 males; CKD stage, G1 (n = 18), G2 (39), G3a (43), G3b (45), G4 (35), and G5 (16)) were included. After optimization of the CNN model, the accuracy, precision, recall, and f-score of the confusing matrix, as well as the AUC of the ROC curve at thresholds of eGFRcre of 60, 45, and 30 were 0.80, 0.83, 0.87, 0.90, 0.87, 0.86, 0.75, 0.71, 0.84, 0.77, 0.83, and 0.76, 0.80, 0.90, 0.85, 0.83, respectively. The output value of the CNN also showed a significant positive correlation with the normalized eGFRcre of the subjects (R² = 0.46, P < 0.01). When the difference in signal intensity between the renal cortex and medulla, as measured based on the region of interest method, was used as a diagnostic index, the accuracy was the same as that of ML if the threshold was eGFRcre 30 (AUC of the ROC curve, 0.84). Conversely, when the threshold was set at eGFRcre 45 or 60, the accuracy deteriorated gradually (AUC = 0.80 and 0.73, respectively).

Conclusions: Compared with the classical method, in which only the signal intensity is used, the ML approach was able to quantitatively evaluate differences in renal morphology regarding a wide range of renal functions. Our results may have clinical applications for assessing the cause of changes in kidney function in the conditions in which renal function and morphology diverge, e.g., in the early stages of acute kidney injury, renovascular hypertensive, and therapeutic interventions that cause hemodynamic alterations.

Funding: Government Support - Non-U.S.

PO0547
Inflammation Mediates the Association of Depression Severity with Selective Serotonin Reuptake Inhibitor Treatment Response in Patients with CKD
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Background: Patients with chronic kidney disease (CKD) are at high risk for depression, which is associated with inflammation in patients with chronic diseases. We investigated whether depression severity is associated with response to treatment with sertraline and whether inflammation mediates this relationship in CKD patients with major depression (MDD).

Methods: We conducted the CKD Antidepressant Sertraline Trial (CAST), a randomized double-blind trial of 193 participants with stage 3-5 CKD and MDD randomized to sertraline or placebo for 12 weeks. Depressive symptoms were assessed using the Quick Inventory of Depressive Symptomatology (QIDS). High sensitivity C-reactive protein (hsCRP) was measured at baseline. Logistic regression determined associations of QIDS and hsCRP with treatment response (≥50% decrease) or improvement (≥3-point decrease) in QIDS. Interaction P < 0.10 was considered significant.

Results: Fifty-nine (30%) participants achieved treatment response. Baseline depression severity by QIDS correlated positively with hsCRP, χ²(1) = 162, P < 0.05. Median (IQR) hsCRP was 5.0 (2.0, 14.6) mg/L in sertraline responders and 2.7 (0.8, 6.0) mg/L in non-responders, P = 0.03. Higher baseline QIDS was associated with increased odds of response in the sertraline group. OR (95% CI) per 1-point increase 1.26 (1.04, 1.53), but lower odds in the placebo group, 0.77 (0.61, 0.97), interaction P = 0.02 (Figure).

Conclusions: Higher depression severity was associated with improvement in depressive symptoms and response to treatment with sertraline in CKD patients. This may be mediated by elevated baseline inflammation. Future studies should test whether sertraline is more effective than placebo in CKD individuals with higher hsCRP.

Funding: NIDDK Support, Veterans Affairs Support

PO0548
Prospective Study of Patient-Reported Outcomes After Endovascular Renal Ablation in Individuals with Chronic Kidney Pain and Opiate Use
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Background: Endovascular renal ablation (ERA) may be useful for palliating and in some instances relieving refractory kidney pain (RKP) but is not widely available. We report our experience of ERA in 20 patients with RKP.

Methods: We conducted a prospective study of patient-reported outcomes pre and post ERA for RKP. Baseline & subsequent pain questionnaires (McGill Pain (MPQ), Brief Pain Inventory (BPI), Oral and Intravenous morphine milligrams equivalent (MMPE)) & QOL (LASA-6, PHQ-9 & SF-8) were obtained. The Wilcoxon test was used. ERA using an open epidural ablation catheter was performed in a spiral manner distal to proximal the renal arterial ostium. Power was titrated between 5-30 watts guided by change in impedance.

Results: We performed 24 ERA (3 bilateral, 21 unilateral; 4 redo) in 20 patients, 14 male; median age 47yr. 12 patients (60%) had low Pain Hematuria Syndrome (LPHS), 4 (20%) ADPKD, and others 4 (20%). 17 of 20 have completed the baseline questionnaires & 9 of 17 patients have 6mo data. All nine experienced variable or complete reductions in pain & QOL from baseline to 6mo (Table1). A median of 8mo pain relief was reported. After their first ERA, responders (pain relief >6mo) median 8.5mo (n=12) 60% while 4 (20%) reported pain relief <6mo (non-responders) median 2mo. 3 (15%) had no relief, and 1 was lost to FU. In the redo ERA, there was no relief in 2; in 1 pain relief lasted 4mo (non-responder), and in the other, relief was 8mo (responder). Following the first ERA, MME decreased by ≥30% in 6, increased in ≥7 (≥30% in 6:15% in 1:50% in 1). Pain was changed in 3, and no pain was noted in 13. All 17 of 17 patients who completed the procedure had ≥1 renal artery stenosis (5mo later) treated by percutaneous transluminal angioplasty but subsequent reduced kidney function.

Conclusions: Among patients with RKP undergoing ERA, half achieved objective improvement in pain & QOL at 6mo. Prospective randomized studies with careful patient selection are required to assess the role of ERA for palliation of pain.

Assessments of Pain & QOL

PO0549
Clinical Impact of Body Muscle Mass for Kidney Function Evaluation: New eGFR Formula Based on Serum Creatinine and Body Muscle Mass
Kazunori Goto, Yoshiharu Yasuda, Sawako Kato, Shoichi Maruyama, Nagoya University, Nagoya, Japan.

Background: Kidney function is globally evaluated by estimated glomerular filtration ratio (eGFR) based on serum creatinine (C). Since C is influenced by body muscle mass, there is serious concern of overestimation of eGFR among elderly people with low body volume due to frailty. In this study, eGFR based on C (eGFRc) and CxSy (eGFRcSy) were analyzed in association with psao muscle mass index (PMI) by CT image among CKD patients whose kidney function was accurately evaluated by measured GFR (mGFR) computed from inulin clearance (CIn).

Methods: Study design: single-center cross-sectional retrospective study. Study subjects were consecutive 158 CKD patients (123 males) at Nagoya university hospital whose C and abdominal CT were examined within 1 year between 2009 and 2013. New eGFR formula based on C and PMI (eGFRcSy-PMI) were developed in 122 patients and validated in 62 patients, which were randomly determined to each cohort. 20%
accuracy for Cin was analyzed by eGFRcreat and eGFRcrels calculated by eGFR formulae for Japanese. The performance of each eGFRcrel-PMI was assessed by means of bias (eGFRcrel-
mgFR), accuracy (percentage of estimates within 20% of mgFR), root mean squared error, and correlation coefficient. In PMI tertile subgroups and GFR(Cin) subgroups (<30, 30-60, >60%), the performance of each formulae was assessed.

Results: Patients’ characteristics (n=184, mean±SD) or median(IQR) were age: 62 [50, 70], eGFRcrel: 58.5 (25.5), eGFRcrels: 59.4 (25.9), Cin: 55.0 (25.0) and PMI: 7.29 [6.18, 9.11]. Log-PMI was significantly associated with age, gender, log-BMI, log-Cre and logCr in univariate analyses, and with age, gender and log-BMI in multivariate analysis. Next, GFR formula (eGFRcrel-PMI) was well correlated with Cin. 20% accuracy for Cin was the highest in eGFRcrel-PMI (74.5%), compared to eGFRcrels (67.9%) and eGFRcrel (68.5%), which was more prominent among low PMI tertile group (77.4% in eGFRcrel-PMI, 67.7% in eGFRcrels, and 71.0% in eGFRcrel) and high PMI tertile group (75.8% in eGFRcrel-PMI, 59.0% in eGFRcrels, and 67.7% in eGFRcrel).

Conclusions: Body muscle mass seriously influences accuracy of kidney function evaluation, and new GFR formula based on PMI and Cre would be useful for accurate evaluation of kidney function, especially among patients with low and high body muscle mass.

PO0551
Alterations of Gray Matter Volumes and Connectivity in Patients with CKD
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Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing due to the global epidemics of obesity and diabetes mellitus, which are commonly seen in CKD. We studied the incidence and predictors of NAFLD in those with CKD.

Methods: We conducted a retrospective cohort study of patients with incident CKD (eGFR <60mL/min/1.73 m^2) for 90 days) in the Veterans Health Administration from 2005-2016. Patients with no NAFLD at the time of CKD diagnosis were followed for a primary outcome of NAFLD, defined as development of sustained elevated alanine aminotransferase levels in the absence of hepatitis B or C virus infection or alcoholic liver disease, identified by laboratory values and diagnosis codes. We calculated incidence rates for NAFLD for the entire study population and by CKD stage. Predictors of NAFLD were evaluated using Cox proportional hazards regression, considering death and ESKD as competing risks.

Results: Of 1,155,901 veterans with CKD but no NAFLD, 51,584 (4.4%) developed NAFLD at a rate of 0.86 (0.85-0.87) per 100 person-years during 4.7 years follow-up. A total of 3.9% developed ESKD at a rate of 0.76 (0.75-0.77) per 100 person-years, and 33% died at a rate of 6.5 (6.5-6.5) per 100 person-years during the same time period. In a multivariable model, age >50 (vs. 40-49 years) (HR 0.72, 95% CI 0.67, 0.77), women, blacks and veterans with advanced CKD were less likely to develop NAFLD; however, presence of diabetes, higher BMI, anemia, CHF, and hypertension were associated with higher risk of developing NAFLD (Table).

Conclusions: Patients with CKD have a high incidence of NAFLD, which was associated with diabetes, BMI, and CHF. Future studies should determine if interventions targeting these factors may reduce NAFLD risk.

Factors associated with incident NAFLD in CKD

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**PO0554**

**Sensitivity of Urinary N-Terminal Osteopontin-to-Creatinine Ratio in Predicting Renal Function Loss**

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Metabolic Syndrome in Men (METSIM) UCLA, University of California Los Angeles, Los Angeles, CA; Xuzhou City Centre Hospital, Xuzhou, China.

**Background:** Osteopontin (OPN) is a multifunctional protein that gets cleaved to create N-terminal OPN (ntOPN). ntOPN has been reported in urine in kidney disease but little is known about the sensitivity of ntOPN to creatinine ratio (ntOCR) as a urinary biomarker compared to the urinary albumin-to-creatinine ratio (UACR). This study is aimed to explore the prognostic value of ntOCR regarding renal function loss in a subset of the metabolic syndrome in men (METSIM) study with a high incidence of diabetes mellitus.

**Methods:** The METSIM study recruited 10,197 Finnish men between 2005 and 2010 and reexamined participants at two 5-year follow-ups. We performed a prospective observational study of a METSIM cohort of 137 participants, 45-72 years old at entry, with available urine at baseline and the first follow-up period, after 3.8±1.4 year. Serum and urinary levels of the ntOPN were quantified by ELISA. Using estimated glomerular filtration rate (eGFR), UACR and urine albumin excretion (UAEC) of progressors and non-progressors, data were analyzed by paired t-test and Wilcoxon matched-pairs signed-rank test. The area under the receiver-operating characteristics (ROC) curve (AUC) was used to assess the sensitivity/specificity of variables in predicting the progression of CKD.

**Pearson correlation coefficient was performed to detect the relationships between the values of variables.**

**Results:** Compared to the CKD non-progressors, the progressors had significantly higher eGFR at baseline (96.95 vs. 87.75 mL/min/1.73 m², p=0.00) and lower eGFR at follow-up (86.11 vs. 91.40 mL/min/1.73 m², p=0.01). The baseline urine levels of ntOCR were higher in progressors than non-progressors (6.83 vs 3.68 pmol/mg, p=0.05). There were no differences in the UAE, UACR, or serum ntOPN between the two groups. However, baseline urinary ntOCR predicted renal function loss with an AUC of 0.60 (p=0.05), and the change between baseline and follow-up had a higher AUC value of 0.63 (p=0.01).

**Conclusions:** Our study suggests that urinary ntOCR might be a promising predictive biomarker for renal function loss in a population with high rates of metabolic syndrome and diabetes. Measurements at the second METSIM follow-up may confirm this observation. Further studies are needed in females, larger size populations, and long-term follow-up.

**Funding:** Other NIH Support - NCATS

**PO0555**

**Effect of Renin-Angiotensin System Blockade in Immunoglobulin A Nephropathy Only with Persistent Hematuria**

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**Background:** Recent guideline recommended that long-term renin-angiotensin system blockade (RASB) should be used in immunoglobulin A nephropathy (IgAN) when proteinuria > 1g/d. If proteinuria is 0.5–1g/d, RASB is also suggested. We tried to investigate whether IgAN patients only with persistent hematuria and without proteinuria can benefit from RASB.

**Methods:** IgAN patients only with persistent hematuria initially from January 2013 to December 2018 from four centers were included. We divided patients into treatment and untreated group according to the use of RASB. The primary outcome was the appearance of proteinuria, the secondary outcome was the decreased percentage of hematuria and the rate of estimated glomerular filtration rate (eGFR) decline. Effect of RASB on the outcomes was assessed by multivariate Cox regression models and a propensity score matching.

**Results:** 110 eligible patients were included and 44 (41.9%) received RASB. Patients in the treatment groups had higher diastolic pressure. The unadjusted primary outcome of RASB treated patients was better than the untreated individuals. The multivariate Cox regression revealed that RASB lowered the risk of primary outcome, besides, RASB decreased more percentage of hematuria. No obvious difference was found in the rate of eGFR decline between two groups.

**Conclusions:** RASB decreased the risk of proteinuria appearance and increased the remission of hematuria in IgAN only with persistent hematuria initially, but it did not obviously impact the blood pressure of patients without hypertension and the rate of eGFR decline.

**PO0556**

**Fibrates and CKD Patients: A Controversial Issue**

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**Background:** Fenofibates were not previously known to affect renal function tests until some reports indicated that these drugs may lead to a decrease in renal function. Likewise, the nephrotoxic effect of fibrates remains to be vague and unclear Fenofibrate’s safety in patients with renal insufficiency is an issue because it may increase plasma creatinine. Furthermore, guidelines regarding fenofibrate dosing in renal impairment vary internationally. We investigated fenofibates’ effects on cardiovascular and on advanced CKD, according to eGFR. The multiple incidents of elevated kidney function tests for patients on fibrates have led us to make this study to review our experience as well as literature on this matter.

**Methods:** A prospective cohort study over 6 months with a total of 80 patients on fibrates divided into 2 groups, 40 of which received statins and the other 40 continued on fibrates. All our patients were subjected to full history, clinical examination and complete baseline labs. The kidney function tests including serum creatinine and eGFR were measured at 0.1, 2 and 6 months’ intervals and lipid profile at 0.3,6 months serially in both groups.

**Results:** Out of the baseline values of the kidney function tests that were recorded on previous fibrate therapy, the statin group (n=40) showed a significant decrease in all kidney function values including serum creatinine by (0.9mg/dL, P<0.001) and an increase in the eGFR (8.9 mL/min/1.73 m², P<0.001). Whilst in the other 40 patients who continued to receive fibrates the kidney function tests continued to rise as serum creatinine showed a significant increase in their mean serum Cr levels (by 0.9 mg/dL or 20%, P=0.001), and a significant decrease in their mean eGFR values (by 8.2 mL/min/1.73 m² or 20.55%, P=0.001). On the other hand total and LDL Cholesterol were significantly lower in Statin group at all follow up intervals. Also triglycerides were significantly higher in Statin group at the end of month-6 from baseline.

**Conclusions:** In our study fibrates administration showed a short term state of renal insufficiency. The long term effects of fibrates versus variable renal derangement are yet to be identified. As to lipid profile, shifting from fibrates to statins led to a stastically significant rise in triglycerides but it’s clinical impact is yet to be investigated, so established guidelines might need a revision regarding clinical benefits of fibrates versus it’s renal injury.

**PO0557**

**Calciphylaxis: An Uncommon Skin Manifestation in Non-Dialysis CKD Patients**

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**Introduction:** Calciphylaxis is a rare but fatal skin disorder seen in 1-4% of dialysis patients. It is characterized by ischemia and necrosis of the skin tissue due to the deposition of calcium in the arterioles and subcutaneous tissues. The risk of infection is increased, and once ulceration develops, the mortality rate can be above 80%. Risk factors include diabetes, warfarin, vitamin D, obesity, female, white race and mineral-bone disorder. The skin findings ranging from livedo reticularis to nodules, plaques, or deep ulcerations. The treatment is focused on supportive care. To date, there is no strong studies to suggest that sodium thiosulfate (STS), bisphosphonates, or calcimimetics are curative. However, STS is commonly used despite the lack of strong supporting data.
Case Description: We report a case of a 76-year-old Caucasian woman with a history of stage G4/A3 chronic kidney disease, insulin-dependent diabetes, hypertension, secondary hyperparathyroidism, and obesity, who presented with severe pain and redness on both legs. The skin lesions had progressed to the painful ulcerations and eschars on both shins one month after the initial visit. A skin biopsy was performed and histopathology was consistent with calciphylaxis. She was started on STS 25 mg ivq(IV) twice a week and calcitram 30 mg by oral route (PO) thrice a week. The patient showed improvement within one month of the treatment.

Discussion: Calciphylaxis in non-dialysis patients is uncommon; however, it should be considered in those with predilection factors. The skin biopsy is crucial for the diagnosis, which can lead to proper management of such a rare yet lethal disease. STS is the most common drug used to treat calciphylaxis. It acts as a calcium chelator with some antioxidative and vasodilation properties leading to recovery.

PO0558
Calciphylaxis: Clinical Features, Therapeutic Options, and Outcomes
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Background: Calciphylaxis is characterized by microvascular disease with calcification of the middle layer of the arterioles, intimal hyperplasia and thrombotic occlusion, conditioning areas of ischemia and skin necrosis. Given the rarity of this pathology, there is a lack in literature regarding clinical presentation, diagnostic approach and therapeutic management. We performed a descriptive analysis of clinical, epidemiologic, laboratory characteristics, treatment options and outcomes in a population of patients with calciphylaxis.

Methods: Retrospective analysis of all calciphylaxis diagnosed in a single-center between January 2003 and December 2019.

Results: The diagnosis of calciphylaxis was made in 9 patients, 7 of whom were female, with a mean age of 63.4±10.9 years. Eight patients were on renal replacement therapy (hemodialysis) at the time of diagnosis, with a dialysis vintage of 66.4±22.4 months and one patient had no chronic kidney disease. Six patients were taking warfarin, with a mean of 46 months on anticoagulation. The mean pre-diagnostic serum calcium product was 42 mg2/dL2 with an average of 46 months on anticoagulation. The mean prediagnostic serum calcium product was 42 mg2/dL2 with an average of 46 months on anticoagulation. The mean prediagnostic serum calcium product was 42 mg2/dL2 with an average of 46 months on anticoagulation.

Conclusions: More than 60% of patients were under warfarin, reinforcing the role of vitamin K antagonists in the pathogenesis. Mean time on dialysis was highly variable, from the 1st to the 216th month since the beginning of the technique. The standard of treatment varied according to the drugs available and the clinical evidence that supported its use at the time of diagnosis. The registered deaths corresponded to patients diagnosed later in the course of the disease, reinforcing the importance of a high clinical suspicion regarding the appearance of trophic skin lesions in this population as a form of early diagnosis to prevent mortality.
Pegunigalsidase Alfa, PEGylated α-Galactosidase-A Enzyme in Development for the Treatment of Fabry Disease, Shows a Correlation Between Renal Gb3 Inclusion Clearance and Reduction of Plasma Lyso-Gb3

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Background: Fabry disease (FD) is caused by the loss of function of the lysosomal enzyme α-Galactosidase-A leading to the accumulation of globotriaosylceramide (Gb3). Reduction in histological Gb3 burden in renal peritubular capillaries (PTC) is considered an important and objective surrogate endpoint, likely to predict the clinical benefit of treatment in FD. Pegunigalsidase-alfa is a novel PEGylated enzyme in development for the treatment of FD with enhanced pharmacokinetics.

Methods: The phase I/Ii (NCT01678989) dose-ranging studies (0.2 mg/kg; 1 mg/kg; 2 mg/kg) were designed to evaluate the safety (primary objective), pharmacokinetics and efficacy (secondary objective) of pegunigalsidase-alfa administered IV every 2 weeks in adult symptomatic FD treatment naïve male and female patients. The Barisoni Lipid Inclusion Scoring System (BLISS) was adopted to quantitatively assess patients' renal biopsies taken at baseline and at 6 months of treatment. BLISS methodology consists of counting the number of Gb3 inclusions per peritubular capillary; a decrease in the score is indicative of clinical improvement.

Results: Renal biopsies were available and evaluated in 13 out of 16 patients allocated in the three dose groups. Mean BLISS score at baseline was 4.23, proving an important renal involvement, and was reduced to a mean of 0.83 after 6 months (-67.3% ± 3.3 %) with an 86.5% reduction in the 1 mg/kg dose cohort. From the total availability of biopsies (14, including one subject with an FD cardiac variant), 78.6% of patients reached a 50% reduction in BLISS score.

Conclusions: These results show a profound reduction in Gb3 inclusions in PTC after 6 months of pegunigalsidase-alfa treatment. A high correlation (r=0.80) between the reduction in plasma Lyso Gb3 and the reduction of kidney Gb3 inclusions in the kidney biopsies was observed, giving additional support to the potential effectiveness of pegunigalsidase-alfa in treating FD.

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Switching from Agalsidase Alfa to Pegunigalsidase Alfa for Treating Fabry Disease: One Year of Treatment Data from Bridge, a Phase 3 Open-Label Study

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Background: Pegunigalsidase-alfa is a novel, PEGylated α-Galactosidase-A enzyme in development for the treatment of Fabry disease (FD).

Methods: Bridge (PB-102-F30, NCT03018730) is a phase III, open-label, switch-over study, designed to assess the safety and efficacy of pegunigalsidase-alfa (1 mg/Kg EOW) in adult FD patients previously treated with agalsidase alfa for at least 2 years. Results: This is an interim report of 12-months on-treatment data generated from the first 16 patients (9 males and 7 females) out of the 22 adult patients enrolled. Baseline characteristics: age 24-60 years, the mean estimated Glomerular Filtration Rate (eGFR) 75.45 in males and 85.78 mL/min/1.73m² in females, annualized eGFR slope was -0.04 and -0.05 in males and females respectively, mean eGFR at 1.73m² was 90.07 mL/min and 91.57 mL/min, respectively, mean potassium was 3.3% and 3.3 mEq/L, respectively. After one year the mean annualized eGFR slope improved from -5.10 mL/min/1.73m²/year while on agalsidase alfa, to -0.23 mL/min/1.73m²/year on pegunigalsidase alfa. According to Wanner et al. 2018, FD patients with eGFR slope between -5 and -<3 mL/min/1.73m²/year are defined as kidney disease progressing and with eGFR slope < -3 mL/min/1.73m²/year are defined as fast progressing. The therapeutic goal is to reach eGFR slope > 3 mL/min/1.73m²/year for the progressing, and a >5 mL/min/1.73m²/year for the fast progressing. In this interim analysis, 100% of the progressing patients and 66.7% in the fast progressing group achieved the proposed therapeutic goals after switching to pegunigalsidase-alfa. The switch to pegunigalsidase-alfa was safe and well-tolerated. The majority of the patients completed the study fully and the study was well-tolerated.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
by 39.4% (P=0.0049). Triamterene reduced 24-hour urine protein by 33.7% (P=0.0113), UACR by 17.1% (P=0.004) and ACR by 28.6% (P=0.0294). The effect on the 24-hour urine protein is not significantly different between the two drugs. The average change on the eGFR is -2 and -9 ml/min/1.73m2 in the amiloride and triamterene groups, respectively. Average systolic blood pressure reduction is 11 and 3 in amiloride and triamterene groups, respectively. The average change in the weight is -0.5 and -0.7 kg in amiloride and triamterene groups, respectively. Three patients exited the study due to hyperkalemia.

Conclusions: Both amiloride and triamterene showed the effect of proteinuria reduction regardless of the underlying pathology. This effect appears to be independent of the RAAS, given that patients were all on RAAS blockade. Large scale trials are needed to evaluate the antiproteinuric and renoprotection effects of ENaC inhibitors.

PO0565
Comparison of Extended-Release Calcifediol (ERC), Immediate-Release Calcifediol, Cholecalciferol, and Paricalcitol for Treating Secondary Hyperparathyroidism (SHPT) in CKD

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Background: Serum total 25-hydroxyvitamin D (25D) levels above 50.8 ng/mL are required to produce meaningful and progressive reductions in plasma intact parathyroid hormone (iPTH) in patients with stages 3 or 4 CKD [Strugnell et al 2019]. The current study compared the abilities of four treatment regimens to increase serum 25D to this level and to reduce iPTH in this population.

Methods: Subjects with stage 3 or 4 CKD, SHPT (iPTH >85 and <500 pg/mL) and vitamin D insufficiency (25D <30 ng/mL) underwent an 8-week washout from previous vitamin D therapies and were randomized to 60 days of open-label treatment with: 1) ERC 60 mcg/day; 2) immediate-release calcifediol (IRC) 266 mcg/month; 3) high-dose cholecalciferol (HDC) 300,000 IU/month; or 4) paricalcitol plus low-dose cholecalciferol (PLDC) 0.5 mcg/day and 800 IU/day. Paricalcitol was increased to 2 mcg/day after 30 days if iPTH was not reduced by 30% and safety parameters allowed. Subjects were monitored for changes in serum 25D, calcium (Ca) and phosphorus (P), and plasma iPTH.

Results: Mean (SD) post-washout/pre-treatment baseline levels for 25D and iPTH in the per-protocol population were 20.6 (6.6) ng/mL and 145 (99) pg/mL, respectively. No differences were observed at baseline between treatment groups (14-17 subjects each). At the end of treatment, mean 25D (ng/mL) increased to 82.9 (17.0) with ERC (P<0.05), 30.8 (11.6) with HDC (P<0.05), 26.3 (6.8) with IRC and 24.2 (7.3) with PLDC. All subjects treated with ERC attained 25D levels ≥30 ng/mL vs. only 44% with HDC (P<0.001), 20% with IRC and 14% with PLDC. Most ERC subjects (94%) attained 25D levels ≥50.8 ng/mL. The proportion of subjects who achieved at least a 20% reduction in iPTH were 71% with ERC, 38% with HDC, 20% with IRC and 79% with PLDC. No changes from baseline were observed in mean Ca or P in any treatment group, but one instance of hypercalcemia (≥10.3 mg/dL) was observed with PLDC treatment.

Conclusions: ERC was safe and more effective at increasing serum 25D and decreasing plasma iPTH than IRC, HDC or PLDC in patients with SHPT, vitamin D insufficiency, and stage 3 or 4 CKD.

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PO0566
Renoprotective Effects of Febuxostat and Allopurinol in Patients with Hyperuricemia and CKD: A Meta-Analysis

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Background: Hyperuricemia is associated with rapid deterioration of renal function in patients with chronic kidney disease (CKD). The two most common urate-lowering drugs available are allopurinol and febuxostat. Randomized controlled trials and observational studies have shown that the individual drugs have potential to slow down deterioration of renal function in CKD patients. However, it is unclear which drug is more effective because of insufficient direct comparison between the two. Hence our study aims to perform a meta-analysis to assess the renoprotective and urate-lowering effects between the two drugs in patients with CKD and hyperuricemia.

Methods: A comprehensive literature search using PubMed was performed with the following search terms: febuxostat, allopurinol, chronic kidney disease, renoprotection. Five relevant studies were selected and analyzed using Cochrane Revman v5.3. Outcomes assessed were changes in estimated glomerular filtration rate, serum creatinine, level of proteinuria and/or albuminuria and change in serum uric acid levels.

Results: Five studies comprising 606 patients were selected – 304 treated with febuxostat and 302 with allopurinol. No significant differences were found in the changes in serum creatinine (mean difference (MD) -0.02; CI -0.07, 0.03; P = 0.39) and eGFR (MD 2.09; CI -0.67, 4.84; P = 0.14) from baseline to 3 months between the two groups. Significant difference in the change in eGFR favoring Febuxostat, was observed after 6 months (MD 4.94; CI 2.25, 7.64; P = 0.003). Significant decrease in proteinuria (MD -0.24; CI -0.42, -0.07; P = 0.007) and albuminuria (MD -80.47; CI -149.29, -11.64, P = 0.02) were observed more in the febuxostat group after 3 months; however these changes were not significant after 6 months. Serum uric acid levels were significantly more reduced in the febuxostat group both after 3 (MD -0.90; CI -1.14, -0.67, P = 0.00001) and 6-months (MD -1.50; CI -1.70, -1.30, P = 0.00001).

Conclusions: Our study showed that febuxostat might be more renoprotective (as measured by eGFR change in 6 months) and offers a better anti-proteinuric and urate-lowering effect. However, more studies are needed to assess its efficacy across the spectrum of CKD, including those requiring hemodialysis and post-transplant patients.

PO0567
CKD Is Associated with Attenuated Plasma Metabolome Response to Oral Glucose Tolerance Testing

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Background: Chronic kidney disease (CKD) is associated with decreased anabolic response to insulin contributing to protein-energy wasting. Targeted metabolic profiling of the response to oral glucose tolerance testing (OGTT) may help identify metabolic pathways contributing to disruption in incretin response.

Methods: Using targeted metabolic profiling, we examined the plasma metabolome in 58 moderate to severe non-diabetic CKD patients with estimated glomerular filtration rate (eGFR)-60ml/min per 1.73m2 and 37 healthy controls with normal eGFR before and after 2h of 75g oral glucose challenge. We used linear mixed effect models adjusting for potential confounders of age, sex, race, and body weight to determine the interaction of eGFR and change in metabolites in response to OGTT by CKD status. Pathway analyses were performed using Metaboanalyst.

Results: CKD patients had lower eGFR compared to healthy control (37.3 ± 12.5 Vs. 89.3 ± 17.1 ml/min per 1.73m2). Oral glucose challenge was associated with a marked reduction in a wide array of metabolites, predominantly amino acids, TCA cycle intermediates, and bile acids. CKD status was associated with attenuated OGTT induced prominent changes in pathways of tauurine metabolism, phenylalanine, tyrosine and tryptophan biosynthesis, nicotinamide metabolism, and TCA cycle (Figure 1).

Conclusions: Targeted plasma metabolic profiling in response to OGTT suggests a broad disruption of amino acid and mitochondridal energy metabolism in CKD patients. These findings motivate further investigation into incretin response in patients with CKD and the impact of incretin mimetics such as GLP-1 receptor agonist.

Funding: NIDDK Support

Figure 1: Pathway analysis of OGTT challenge in CKD vs control subjects.
The Effects of Allopurinol on the Progression of CKD According to Baseline Serum Urate Level: Results from Post Hoc Analyses of the CKD-FIX Trial


Background: Allopurinol did not slow decline in estimated glomerular filtration rate (eGFR) over 2 years in patients with chronic kidney disease (CKD) at risk of progression in the CKD-FIX trial. We assessed the effect of allopurinol on eGFR slope by baseline serum urate level.

Methods: In this trial, 369 adults with stage 3 or 4 CKD, without history of gout, and either baseline serum urate ≥265 mg/g or eGFR decrease ≥3.0 mL/min/1.73 m² in the preceding year, were randomized to allopurinol or placebo. The primary outcome was change in eGFR up to 104 weeks using the CKD-EPI creatinine equation. This post hoc subgroup analysis describes outcomes in 352 participants according to baseline serum urate level (normouricemic and hyperuricemic serum urate ≤6 mg/dL in women and >7 mg/dL in men), and tertiles of baseline serum urate level.

Results: At baseline, 65 (18.5%) and 287 (81.5%) participants had normouricemia and hyperuricemia, respectively. The mean serum urate level in the normouricemic group was 5.9 mg/dL (4.8 mg/dL for women, 6.1 mg/dL for men), and mean serum urate in the hyperuricemic group was 8.7 mg/dL (8.3 mg/dL for women and 8.9 mg/dL for men). There were no significant differences in change in eGFR between allopurinol and placebo in normouricemic (mean difference [MD] 0.35, 95%CI -2.72 to 3.42 mL/min/1.73 m²/year) and hyperuricemic (MD -0.06, 95%CI 1.20 to 1.08 mL/min/1.73 m²/year) groups. The mean serum urate levels in the lowest, middle, and highest tertiles were 6.3 mg/L, 8.0 mg/L, and 10.0 mg/L, respectively. The result for the primary outcome was consistent across all tertiles of baseline serum urate level (interaction P value for subgroup analysis = 0.49).

Conclusions: In CKD patients at risk of progression, the effect of allopurinol on eGFR decline was not modified by baseline serum urate level.

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PO0569

CKD Progression End Points as Potential Surrogates for Kidney Failure: Findings from the CKDopps

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Background: Many potential surrogate endpoints for kidney failure (KF) have been used in clinical trials and observational studies of chronic kidney disease (CKD). Individual and composite surrogate endpoints must be compared to ensure accurate research that maximizes power and facilitates harmonization across studies, particularly among an international sample of advanced CKD patients. Methods: Using data from CKD stage 3-5 patients from Brazil, France, Germany, and the US enrolled in the CKD Outcomes and Practice Patterns Study (CKDopps), we defined potential individual and composite KF endpoints based on reaching (1) eGFR<15 mL/min/1.73 m² and (2) eGFR decline of 3.0 mL/min/1.73 m²/year. Potential surrogate endpoints that combine (1) and (2) with and without kidney replacement therapy (KRT, dialysis or transplant). We used each individual and composite endpoint as a time-varying indicator that combine (1) and (2) with and without kidney replacement therapy (KRT, dialysis or transplant). We used each individual and composite endpoint as a time-varying indicator that combine (1) and (2) with and without kidney replacement therapy (KRT, dialysis or transplant).

Results: N=5242 patients had missing IQR (baseline eGFR of 26.8 (20.7-35.5) and 144 (20.7-35.5) follow-up time of a median 2.7 (1.2-3.0) years. Potential surrogate endpoints that included eGFR<15 had higher prediction discrimination compared with those that only included eGFR decline (Figure, AUCs of 0.83-0.84 vs 0.73-0.75). Composite endpoints had higher event counts than non-composite endpoints (Ns of 1622-1878 vs 1144-1556, see Figure x-axis).

Conclusions: A composite KF endpoint defined by the earliest occurrence of either KRT, eGFR<15, or eGFR decline of 40% had the highest prediction discrimination for KRT and the highest number of events among a cohort enrolled at low eGFR. This endpoint should be further evaluated and considered for clinical research studies to optimize power while sufficiently capturing KF.

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PO0570

Treatment for CKD: A Systematic Literature Review and Population Comparison

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Background: DAPA-CKD is the first renal outcomes trial assessing the efficacy and safety of a sodium–glucose cotransporter-2 inhibitor, dapagliflozin, vs placebo, added to standard of care in patients with chronic kidney disease (CKD) with/without type 2 diabetes (T2D). Several other agents have been or are currently under investigation for their effect on renal and cardiovascular outcomes in CKD; however, comparisons of efficacy are challenging, due to differences in study design, duration, patients and endpoint definitions. We conducted a systematic literature review of randomized controlled trials (RCTs) in CKD, with the aim of assessing inter-study comparability.

Methods: Searches of MEDLINE, Embase, the Cochrane Central Register of Controlled Trials and grey literature sources were conducted to identify phase 3–4 RCTs of adults (≥18 years) with albuminuric CKD with/without T2D, published in English between 1990 and March 25, 2020. Studies of a ≥12 weeks duration that reported clinical outcomes, adverse events, quality of life or patient-reported outcomes for pharmacologic CKD treatments were eligible for inclusion.

Results: Preliminarily, 13,451 unique citations were identified, and 204 full-text manuscripts were included after abstract screening (Figure). Data from 81 RCTs were included: 24, 39 and 18 in patients with CKD with/without T2D, CKD with T2D and CKD without T2D, respectively.

Conclusions: As anticipated, differences in the inclusion of patients with/without T2D between studies make comparisons difficult. Future work will compare additional relevant study characteristics, with further insights available in October 2020.

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A New Vision for Nephrology Trials in Canada

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Background: The Canadian Nephrology Trials Network (CNTN) was established in 2014 to improve the quantity and quality of clinical trials in nephrology in Canada. With inception of the Canadians Seeking Solutions and Innovations to Overcome Chronic Kidney Disease (Can-SOLVE CKD) Network in 2016, CNTN received additional funding to expand its mandate. We surveyed and assembled a broad cross-section of Canadian kidney patients, nephrology researchers, and other relevant stakeholders in order to establish an expanded new vision for CNTN.

Methods: In July-August 2018, we administered two separate surveys – one to patient members of Can-SOLVE CKD and the second to members of CNTN and other Canadian nephrology investigators. We then conducted a two-day visioning workshop in September 2018 to discuss how best to support nephrology research in Canada. Over 40 stakeholders participated, including 10 patients, 22 researchers, and members of the Can-SOLVE CKD Operations Team.

Results: Through the survey, we identified two issues that were at least moderately challenging: inability to facilitate multi-site trials (81%) and lack of engagement with community sites (74%). Three key themes emerged from the visioning exercise: peer review, training, and engagement. A summary report captured workshop discussions and was used to inform revisions to CNTN’s structure and governance. Three new working committees were created: Capacity Building, Communication and Engagement, and Scientific Operations; as well as a governing Executive Committee. Each committee is co-chaired by a nephrologist and patient, who take turns leading the Executive Committee.

Conclusions: With its new vision and committee structure, CNTN aims to promote a culture of collaboration within the Canadian kidney community and integrate patients into research. The network offers resources to enhance nephrology researchers’ ability to conduct clinical trials, directly involve patients in designing studies, and motivate change in patient care based on patient priorities through increased peer review, engagement, and training.

Funding: Government Support - Non-U.S.

Implementation of Surprise Question Assessments Using the Electronic Health Record in Older Adults with Advanced CKD

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Background: The Surprise Question (SQ; “Would you be surprised if this patient died in the next 12 months?”) is a validated prognostic tool for mortality and hospitalization among patients with advanced CKD. Yet, barriers in clinical workflow have slowed SQ implementation into practice. We sought (1) To evaluate implementation outcomes following use of electronic health record (EHR) decision support to automate collection of the SQ, and (2) To assess the prognostic utility of the SQ for mortality and hospitalization/emergency room (ER) visit.

Methods: We developed and implemented a synchronous decision support [best practice alert (BPA)] algorithm in the electronic health record (EHR) to identify patients attending an outpatient nephrology follow-up visit who were ≥ 60 years of age with an eGFR<30. At the time of the visit, a ‘pop-up’ BPA was triggered, prompting the physician to answer the SQ (dichotomized). To evaluate implementation, we assessed provider response rate, and efficiency of responses. We assessed the SQ’s prognostic utility in survival and time-to-hospital encounter (hospitalization/ER visit) analyses. We abstracted EHR data on patient sociodemographics and clinical characteristics. Physicians provided their demographic and clinical practice characteristics.

Results: Among 510 unique patients for whom the BPA triggered, 95 had the SQ completed (18.6%) by 16 unique providers. Among those patients with completed SQ, nearly all providers (97.9%) completed the SQ on the clinic appointment day, and 61 (64.2%) the first time the BPA fired. Providers answered “No” for 27 (28.4%) and “Yes” for 68 (71.6%) patients. By 12 months, 6 (6.3%) “No” patients died; 3 (3.2%) “Yes” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “No” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “No” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “Yes” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “No” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “Yes” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]). About 40% of “Yes” patients died (age-adjusted hazards ratio [HR] 0.35, CI[0.13, 0.94]).

Conclusions: We successfully integrated the SQ into the EHR for routine collection to aid in clinical practice. Our response rate indicates additional implementation efforts are needed to encourage further integration of the SQ in clinical practice. Consistent with prior research, the SQ has reasonable prognostic utility for mortality and future hospital encounters.

Funding: Private Foundation Support

Telehealth for Adults with CKD: A Systematic Review and Meta-Analysis

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Background: Evidence has supported improved quality of CKD care when assisted with telehealth, while these results were predominantly based on cohort observation or small-scale randomized controlled trials(RCTs). Moreover, robust findings regarding its effects on endpoints were still limited. This study thus aimed to evaluate impacts of telehealth on dialysis CKD patients.

Methods: This study was conducted and reported according to PRISMA statement. We searched databases including MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedicine Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Wanfang Database and VIP Database until 2019 April. Relevant studies regarding telehealth for non-dialysis CKD population were screened, reviewed, selected and assessed of quality for systematic review and meta-analysis. The protocol was registered at PROSPERO(CRD42017073665).

Results: Eighteen trials involving 4749 patients were included for systematic review and 4 for further meta-analysis. The qualitative study summarized different study population, telehealth intervention type(consultation, education, monitoring) and variable results of outcomes measured(endpoints, surrogate values, patient-centered outcomes). The quantitative analysis comparing the telehealth and control group detected no significant difference in systolic blood pressure(SBP), diastolic blood pressure(DBP) and serum creatinine(SCr) at 12 months, but found significantly lower SCr level at 6 months, preserved estimated glomerular filtration rate(eGFR) at 6 months and at 12 months in telehealth group.

Conclusions: This study detected advantages of telehealth on delaying CKD progression but uncertain impacts on decreasing endpoint incidence.

Funding: Government Support - Non-U.S.
PO0575
Telenephrology: A Feasible Option for Inmates
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Background: Socioeconomic and racial disparities are factors that contribute to the disproportionately high burden of chronic disease amongst the incarcerated population in the United States. Access to care can be compromised because of the burden of cost to a facility, lack of staff to transport patients and physical distance from specialists. Telenephrology has been shown to be a feasible option in the correctional setting for specialties such as mental health, infectious disease, cardiology, and primary care, but has not been studied in nephrology. In this quality improvement study, we showed telenephrology is a feasible option that can be implemented for CKD and hypertension management.

Methods: Using quality improvement methodology, data was collected from the electronic medical record for all telenephrology appointments from January 2015 to June 2019. Demographic data, comorbidities, appointment completion, and clinical data including eGFR and blood pressure were tracked for analysis. Data for patients seen over a period of at least 3 years were included in the CKD progression portion and those seen at least 4 times for the blood pressure management.

Results: There were 871 appointments schedule over the 4.3 year period with 86% completed. Technology limited 3.5% of the cancelled appointments. The population was predominantly men (96%) of black race (51.9%) with hypertension (78%) and CKD (75.2%) being the most common comorbidities. There were 214 patients included in the analysis for management of CKD that showed an average annual change in eGFR of -1.57 ml/min/1.73 m² (CI -2.87 to -0.27). There were 79 included in the hypertension analysis with 19.0% achieving a goal BP of 130/80 mm Hg and 63.3% achieving a BP of ≤140/90 mm Hg.

Conclusions: Telenephrology can be successfully carried out in the correctional facility environment with a low number of cancellations due to technology. The study sample showed mild-to-moderate CKD progression consistent with previously reported population rates of eGFR decline suggesting comparable management. The smaller subset in hypertension showed control that was less than the rates achieved in a nationally representative sample of CKD patients (52% and 75%). This marks an area that requires improvement. Continued rising referrals to telenephrology suggest provider acceptance but it is important to study and adjust management to provide at least equal care as in person visits.

PO0576
Nephrology eConsultation: The “Curb Side” Consult for the 21st Century
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Background: The Nephrology Division at the University of Rochester receives on average 120 new outpatient referrals per month. While every effort is made to see new referrals promptly, this demand exceeds the capacity to evaluate these patients in a timely manner. To decrease waiting time and increase efficiency, we developed a Nephrology eConsultation program. Here we report our experience with time and value-based metrics as well as primary care provider (PCP) satisfaction.

Methods: After a year-long pilot phase, in September 2019 we expanded the eConsult program to include remote provider consultation to medical providers across the University health system for renal-related issues such as mild to moderate acute kidney injury, CKD, electrolyte disturbances, and proteinuria.

Results: Within the first 8 months of the expanded program, 110 eConsult requests were received. Of these, 62 were deemed medically appropriate and completed, with 46 (74.2%) related to acute kidney injury, CKD, or azotemia, 6 (9.7%) related to electrolyte imbalances, and 4 (6.5%) related to proteinuria. The mean time for a nephrologist to complete an eConsult was 13.8 minutes (Table 1). Of the 48 deemed inappropriate for eConsults, 36 (75%) were converted to in-person visits due to complexity (Table 2). All eConsults were completed within 67 hours (mean time 15.5 hours). Survey of PCP satisfaction showed that 68% of PCPs were very satisfied and 32% were satisfied with the nephrology eConsult program.

Conclusions: eConsultation in Nephrology has the potential to provide timely, cost effective, and remote guidance to PCPs for more straightforward questions, while prioritizing the limited resource of face-to-face nephrology consultation for patients with more complex diseases. This also offers financial advantages, as the work relative value units (wRVUs) for eConsult is 0.7, or up to 2.8 wRVUs per hour in our model. eConsultation in Nephrology could also be integrated with the rapidly evolving field of telemedicine to improve delivery of care remotely and increase provider and potentially patient satisfaction.

Funding: Clinical Revenue Support

PO0577
Development of a Global CKD Personal Impact Index (CKD-PII) Assessing the Reality of Living with CKD
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Background: CKD affects >700M people globally, but its full burden and personal impact attributes (PIA)—impact on instrumental activities of daily living—are under-recognized. Qualifying of life (QoL) measures fail to show the full patient experience. A Global CKD-PII uncovering the direct and indirect daily impact of CKD on patients may improve understanding of disease burden and secondary complications. The development of the CKD-PII using a geographically diverse cohort of CKD patient-reported aggregate data is described.

Methods: A multiphase approach was used to develop CKD-PII. In Phase 1, social media landscape audit and qualitative interviews determined PIA to understand disease burden. Patient conversations within online communities gauged the social, economic and physical impact of CKD. Each attribute was assigned as high, medium or low impact based on the lexicon, overall sentiment and self-reported impact on patient’s QoL. Qualitative, moderated phone interviews followed an engagement model, whereby key PIA and language and characterization of attributes were further explored. Findings of Phase 1 informed Phase 2, a quantitative survey. Data from both phases will culminate in the development of CKD-PII.

Results: Phase 1: Social media landscape analysis leveraged 12 months of relevant patient dialogues (n=156) and shortlisted 11 key PIA from >200M internet sources. Among the key PIA identified, dietary impacts (19%), time lost to appointments/dialysis (45%) and mental health implications (44%) were rated as high impact. Qualitative interviews (n=15) uncovered key PIA identified consistently. Phase 2: An online survey questionnaire was administered to quantify the extent of patients’ experience of PIA. The CKD-PII synthesizes data from all research phases into an insights and perspectives report evaluating global perspectives.

Conclusions: Uniquely, CKD-PII will use metrics to showcase the real-life impact of CKD, beyond QoL, providing insights into the patient experience that other studies do not typically address. The social media data facilitates understanding of critical issues and prioritized areas of concern on the online landscape. This cohort of global patient-reported data will raise awareness of the deeper impact of CKD and develop tangible and realistic solutions for both patients and doctors to solve the challenges uncovered.

Funding: Commercial Support - AstraZeneca
PO0578

Lowering Mortality in CKD Stage 3B and CKD Stage 4 with Increased Outpatient Nephrology Visits

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Background: Management of Chronic Kidney Disease (CKD) is complex requiring comprehensive evaluation of multiple organ systems. We hypothesized that more frequent outpatient nephrology visits is associated with lower mortality in advanced CKD patients.

Methods: CKD Stage 3b & CKD4 patients at Kaiser Permanente Southern California Orange County were followed from 2012 to 2018. Patients were divided into 4 groups based on initial eGFR per MDRD equation; eGFR 30-44, 25-29, 20-24, and 15-19. Each eGFR group was further divided by the number of annual nephrology visits (0, 1, 2, 3, and 4+). Patients who transitioned to dialysis, kidney transplant, or lost to follow up during the 7 years were excluded. Annual all-cause mortality was analyzed based on the number of nephrology visit in each eGFR category using ANOVA.

Results: The cohort consisted of 2943 individuals, 59% female, 41% male, mean age 77.4. 42% of patients were diabetic and 89% had hypertension. Lower starting eGFR had increased mortality over time while renal function stayed fairly stable. Increased outpatient visit was seen with lower eGFR during the follow up period, Figure 1. All CKD3B and CKD4 patients gained a statistically significant reduction in mortality when seen at least twice in nephrology clinic annually, p<0.04, in Figure 2. For eGFR ≤24, the mortality benefit was observed with 1 or more nephrology visit, p<0.005.

Conclusions: CKD stage 3B and 4 patients seen in nephrology clinic at least twice a year had improved survival. More frequent follow up was associated with lower eGFR. The relationship between the lower eGFR and the improved survival warrants further investigation.

Funding: Clinical Revenue Support

PO0579

Uptake of Evidence-Based Recommendations to Improve Care for CKD Patients in the Kidney Coordinated Health Management Partnership (Kidney CHAMP) Study

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Background: Medication therapy in patients with chronic kidney disease (CKD) is focused on slowing CKD progression, managing causes of CKD, and preventing cardiovascular morbidity and mortality. The aim of this project was to assess the uptake of evidence-based medication recommendations (recs) provided to primary care providers (PCP) of patients with high-risk CKD by an interdisciplinary nephrology team.

Methods: This project is part of Kidney CHAMP, an ongoing NIH funded, pragmatic randomized controlled trial testing an electronic health record (EHR)-based population health management (PHM) approach to improve CKD care. Eligible patients are 18-85 years with CKD who have a high risk of progression to ESRD and are not being followed by a nephrologist. Patients in the intervention arm receive a nephrologist-led electronic consult and pharmacist-led telephonic medication therapy management (MTM). Recs are provided in the EHR for the PCP to review and order at the upcoming office visit. We focused on medication recs related to the progression of CKD and prevention of cardiovascular disease, which included use of RAAS inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, and HMG-CoA reductase inhibitors (statins).

Results: From July 1, 2019 to January 31, 2020, 125 patients received an e-consult and 121 patients received MTM. A total of 83 recs were provided to PCPs. Uptake of recs for initiation or dose escalation of RAAS inhibitors was the highest, with 19 of 46 recs (41%) being implemented. Two of eight recs regarding GLP-1 receptor agonists were implemented (25%) and two of 24 recs for SGLT-2 inhibitor initiation were implemented (8%). Five recs for statin initiation were made and none were implemented; however, baseline statin use was high at ≥75%.

Conclusions: Many patients with high risk CKD receive suboptimal care, which can be effectively identified by interdisciplinary nephrology teams using an EHR-based PHM platform. Uptake of RAAS inhibitor recs was highest. However, initiation of medications with recent FDA approved indications for CKD management remained poor. Future research is needed to identify barriers and strategies to increase uptake of evidence-based CKD recs and thereby improve patient care.

Funding: NIDDK Support

PO0580

Interdisciplinary Care Improves Patient Preparedness for ESRD in a High-Risk Patient Population with CKD

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Background: The Kidney Care Choice initiative has made improving the quality of care for patients with late-stage CKD a national priority. Interdisciplinary care (ICD), including nurse practitioner (NP) driven care coordination, is an intervention that may improve health outcomes in patients with CKD. Few studies have evaluated this model of healthcare delivery in racial-ethnic minorities.

Methods: We compared incident ESRD patients who received NP care coordination as part of our ICD clinic (n=84) to a contemporaneous cohort of incident ESRD patients (n=245) who received usual nephrology care alone at Montefiore Medical Center from 10/1/2013—10/31/2017. Clinical data were extracted using Clinical Looking Glass®, and chart reviews were done for validation. Patients included in our study had established care for CKD stage 4.5 and had at least one nephrology clinic visit within 3 months preceding their progression to ESRD. All patients were eligible for ICD, but receipt of ICD was limited by resource availability.

Results: Of the 329 incident ESRD patients included in our study, the mean age was 59.6 years (SD 13.8), 47% were female, and 86% were African American or Hispanic. The baseline characteristics were similar between the groups, except the ICD group had a lower prevalence of hypertension (60% vs 77%). The mean eGFR was 8 ml/min/1.73m² at dialysis initiation. Fifty percent of patients had an arteriovenous (AV) access prior to developing ESRD. However, compared to the usual care group, patients in ICD group were more likely to have a mature AV access at HD initiation (41% vs 33%); start HD as an outpatient (30% vs 19%); receive a preemptive transplant (4% vs 2%); do peritoneal dialysis (7% vs 4%); and be listed for kidney transplant (44% vs 15%) prior to developing ESRD. Receipt of ICD was associated with a higher odds (OR 3.9 [95% CI 2.0 - 7.8]. PC=.0001) of kidney transplant listing compared to usual care alone after adjusting for sociodemographic and clinical factors. Other outcomes also favored ICD but were not statistically significant.

Conclusions: Interdisciplinary care is associated with better ESRD preparedness compared to usual nephrology care alone in racial-ethnic minorities. Larger multicenter randomized studies are needed to determine the effectiveness of ICD among patients with advanced CKD.

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Patient Outcomes Following Discharge from a CKD Clinic
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Background: In Ontario, Canada multidisciplinary care for patients with advanced chronic kidney disease (CKD) is delivered in Multi-Care-Kidney-Clinic (MCKC) operated by Regional Programs funded through a provincial network based on the number of eligible patients. These eligibility criteria were progressively revised between 2016 and 2018 from an absolute estimated glomerular filtration rate (eGFR) less than 30 ml/min/1.73m² to less than 15 ml/min/1.73m² or a two-year risk of end-stage kidney disease, calculated by the Kidney Failure Risk Equation (KFRE), greater than 10%. The objective of this study was to ascertain the outcomes of existing MCKC patients who were discharged as these criteria were implemented.

Methods: This is a retrospective cohort study of prevalent CKD patients in MCKC in 2013 in the region of South Eastern Ontario, followed to January 2020. The outcomes were discharge from MCKC, re-referral, initiation of kidney replacement therapy (KRT), and death. Data were extracted from electronic medical record. Death was ascertained through Ontario’s Office of the Registrar General. Patients’ 2 and 5-year KFRE scores were calculated using the 4-variable KFRE.

Results: Of the 643 MCKC patients in 2013 with available data, 470 (73%) continued follow-up in MCKC, while 142 (22%) and 31 (5%) were discharged to primary care and general nephrology respectively. Of those discharged to primary care, 52 (37%) died, while 15 (11%) were re-referred to nephrology, and 8 (6%) initiated KRT within median (IQR) times of 982 (560) and 850 (1411) days from discharge respectively. Five (63%) of the 8 discharged patients who required KRT did so for unforeseen acute illness rather than progressive CKD.

Conclusions: The results of this study suggest that gradually moving MCKC funding eligibility criteria from absolute eGFR level to one based on both eGFR and the KFRE prediction model resulted in the discharge of a significant number of patients. Notably, few of the discharged patients ultimately required KRT that could have been prevented. This study offers a regional perspective with low loss to follow-up as there is less stringent funding eligibility criteria from absolute eGFR level to one based on both eGFR and the KFRE prediction model.

Association of CKD with Early Heart Failure Readmissions in Adults
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Background: Heart failure is a complex chronic disease with multiple comorbidities that contribute to frequent hospitalization. We aimed to examine the impact of chronic kidney disease on the 30-day readmission rate among patients hospitalized with heart failure.

Methods: We performed a retrospective analysis of the National Readmission Database (NRD) 2016-2017. We identified adult patients with a primary hospital diagnosis of heart failure. We compared baseline demographics and calculated all-cause 30-day readmission rates. Multivariate survey logistic regression was used to identify predictors of readmission.

Results: We identified a total of 865,328 patients admitted with heart failure. 839,625 patients were discharged alive. Among which 181,130 (21.5%) had at least one readmission within 30 days. The in-hospital mortality of index admissions and readmissions was 2.9% and 6.5%, respectively. The 30-day inpatient mortality was 4.0%. The mean length of stay of index admission and readmissions was 5.3 days and 6.4 days, respectively. The most common reasons for all-cause readmissions were acute on chronic heart failure (systolic, diastolic, combined), hypertensive heart and chronic kidney disease with heart failure, sepsis, acute kidney failure. After adjusting for multiple covariates, 30-day readmission was independently associated with chronic kidney disease [adjusted odds ratio (aOR) 1.2, 95% confidence interval (CI) 1.17-1.25, p<0.001], coronary artery disease (aOR 1.01, 95% CI 1.07-1.11), chronic obstructive pulmonary disease (COPD) (aOR 1.20, 95% CI 1.18-1.22). Younger age, lower-income, discharge from larger hospitals were also predictive.

Conclusions: Further prospective studies with focus on multilevel interventions are needed to help reduce early readmission associated significant morbidity and resource utilization for this high-risk population.
A Medication Use Evaluation of Patiromer in a Clinical Practice Setting at a Veteran’s Affairs Medical Center

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Background: Patiromer is cation exchange polymer approved for treatment of hyperkalemia. There is limited data regarding the utility, adverse effects, frequency of laboratory monitoring and discontinuation rate of Patiromer in a clinical practice setting.

Methods: We performed a retrospective, observational review of prescriptions written in one or more doses of patiromer between 10/2015 and 11/2019 at the Veterans Affairs Northeast Ohio Health System (VANOHS), to evaluate changes to RAAS inhibitor therapy, adverse effects resulting in patiromer discontinuation, and monitoring of serum potassium level. Patiromer prescription characteristics, concomitant medications, laboratory characteristics and adverse effects were collected for each veteran over the study time period. Baseline characteristics are reported as means; relative frequency of outcomes are reported as percentages.

Results: 69 Veterans with hyperkalemia were included for analysis. Mean age was 70 years, African-American race 29%, diabetes 90%, chronic kidney disease 91%, 17% ESRD on dialysis, and heart failure 36%. The most common patiromer dose was 8.4 g daily (78%), prescribed for a mean 207±159 days. 21% of patients had repeat labs within 2 weeks and 54% within 4 weeks of patiromer initiation. 77% of patients achieved normokalemia (K+<5.0 mEq/L) by the first follow-up lab draw. Amongst 52 veterans with chronic, continuous patiromer use, 22 (41%) were taking RAAS inhibitors at baseline; 15 (29%) of these patients had either increased RAAS inhibitor dose over the study time period. 28 (54%) discontinued patiromer with 7 (25%) veterans doing so due to GI complaints.

Conclusions: In a clinical setting at a Veteran’s Affairs hospital, patiromer therapy preserved RAAS inhibitor use and improved serum potassium levels, but was discontinued at a high rate due to adverse effects.

The Practical Patterns of Medication and the Association Between CKD Stage and Polypharmacy: The Fukuoka Kidney Disease Registry Study

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Background: Polypharmacy has emerged as one of the important medical and socioeconomic problems in an aging society. Chronic kidney disease (CKD) is also one of the important medical problems for older people. However, the extent to which CKD is involved in polypharmacy still has not been fully explored yet.

Methods: We examined 3,968 Japanese CKD patients using baseline data from a multicenter prospective cohort study in a cross-sectional manner. We used the baseline data of prescribed medicines on medical records. We evaluated the association between CKD stage and polypharmacy (defined as ≥6 medications). The primary end point was polypharmacy (≥6 medications). We used logistic regression analyses with adjustment for potential confounding factors.

Results: At baseline, the prescribed medicines varied between 0 and 17, and the median (interquartile range) was 5 (3–7). Among 3,968 CKD patients, 1,540 (38.8 %) patients showed polypharmacy. The multivariable-adjusted odds ratios for polypharmacy were 1.42 [95% confidence interval, 0.77–2.61] for G3a, 1.44 [0.78–2.65] for G3a, 2.44 [1.34–4.49] for G3b, 4.06 [2.17–7.37] for G4 and 8.46 [4.53–16.5] for G5, respectively, compared to patients in the reference category (G1). The reference value in the higher-gglomerular filtration rate (GFR) category (≥60mL/min/1.73m2), many drugs, including angiotensin-2 receptor blockers, calcium channel blockers, uric acid synthesis inhibitors, proton pump inhibitors, aspirins, loop diuretics, and cation exchange resins were prescribed more frequently, whereas less than less than low GFR category (G5). In addition, aldosterone blockers, biguanides, fbrates, non-steroidal anti-inflammatory drugs, and sulfonylureas were continuously prescribed despite decreased GFR.

Conclusions: The higher GFR categories were independently associated with higher odds of polypharmacy. This might reflect the increasing prescription for managing to control symptoms caused by decreased GFR. We also have to pay more attention to prescribe medicines according to renal function.

A Pilot and Feasibility Randomized Clinical Trial Targeting Sedentary Behavior in CKD: Sit Less, Interact, and Move More (SLIMM) Study

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Background: Sedentary behavior (engaging in activities in the seated/lying position) is highly prevalent and associated with mortality in CKD.

Methods: In a 24-week pilot and feasibility RCT, we tested the feasibility of a ‘Sit Less, Interact, Move (SLIMM)’ intervention to replace sedentary activities with casual stepping activities in CKD. Participants wore an accelerometer for 7 days before randomization for increased RAAS inhibitor dose over the study period. Baseline Kidney Function: Prespecified Analyses of the CKD-FIX Trial

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Background: The CKD-FIX trial showed that allopurinol did not slow the decline of estimated renal function in CKD stage 3 or 4, no history of gout, who were at risk of progression (identified by urine uric acid-to-creatinine ratio ≥ 2.65 mg/g or eGFR decrease ≥ 3.0 mL/min/1.73 m2 in the preceding year) were randomized to receive allopurinol or placebo. Primary outcome was rate of change in eGFR up to 104 weeks using the CKD-EPI creatinine equation. This pre-specified subgroup analysis describes outcomes in patients with CKD stage 3 and stage 4.

Methods: Three hundred and sixty nine adults with CKD stage 3 or 4, no history of gout, who were at risk of progression (identified by urine uric acid-to-creatinine ratio ≥ 2.65 mg/g or eGFR decrease ≥ 3.0 mL/min/1.73 m2 in the preceding year) were randomized to receive allopurinol or placebo. Primary outcome was rate of change in eGFR up to 104 weeks using the CKD-EPI creatinine equation. This pre-specified subgroup analysis describes outcomes in patients with CKD stage 3 and stage 4.

Results: At baseline, 178 (51%) patients had CKD stage 3 (mean eGFR 41 mL/min/1.73 m2, mean serum urate 7.9 mg/dL) and 185 (51%) patients had CKD stage 4 (mean eGFR 23.5 mL/min/1.73 m2, mean serum urate 8.4 mg/dL). In patients with CKD stage 3, change in eGFR did not differ between the allopurinol (-3.4 mL/min/1.73 m2, 95% CI -5.97 to -2.83) and placebo (-3.34 mL/min/1.73 m2, 95% CI -5.49 to -2.09) groups (mean difference [MD], -0.33 mL/min/1.73 m2/year, 95% CI -2.13 to 1.47). In patients with CKD stage 4, there was no difference in change in eGFR between the allopurinol (-2.89 mL/min/1.73 m2/year, 95% CI -3.74 to -2.03) and placebo (-2.89 mL/min/1.73 m2/year, 95% CI -5.79 to -2.04) groups (MD, 0.06 mL/min/1.73 m2/year, 95% CI -1.18 to 1.17). The interaction P value for subgroup analysis was 0.87.
Conclusions: In CKD patients at risk of progression, the effect of allopurinol on eGFR decline was not modified by baseline kidney function.
Funding: Government Support - Non-U.S.

PO0588
Effects of the SGLT2 Inhibitor Dapagliflozin on Proteinuria in Non-Diabetic Patients with CKD (DIAMOND): A Randomized Double-Blind Cross-Over Trial
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Background: Sodium glucose co-transporter 2 (SGLT2) inhibition decreases albuminuria and reduces the risk of kidney disease progression in patients with type 2 diabetes. These benefits are unlikely mediated by improvements in glycemic control alone. We therefore examined the renal effects of the SGLT2 inhibitor dapagliflozin in patients with proteinuric kidney disease without diabetes.
Methods: A multicenter double-blind placebo controlled 6-week crossover study was performed in six hospitals in the Netherlands, Canada, and Malaysia. Patients (18-75 years old), without diagnosis of diabetes, 24-h urinary protein excretion >500 mg/24h and estimated glomerular filtration rate (eGFR) >50 ml/min/1.73 m² on stable renin angiotensin system blockade were included. Participants were randomly assigned to one of the two consecutive treatment periods of first placebo and then dapagliflozin 10 mg/day or vice versa. The main secondary outcome was change in iohexol measured GFR (mGFR). The primary outcome was percentage change from baseline in 24-h proteinuria.

Results: A total of 180 patients were screened of whom 53 patients were randomized. Median baseline proteinuria was 1110 mg/24h (IQR 730, 1560) mg/24h; mean mGFR was 58 ml/min/1.73m² (SD 23). The difference in mean proteinuria change from baseline to dapagliflozin and placebo was 0.9% (95% CI: -16.6, 22.1; p=0.93). Compared to placebo, mGFR changed with dapagliflozin treatment by -6.6 ml/min/1.73 m² (95% CI: -9.0, -4.2; p=0.0001) at week 6, which was completely reversible within 6 weeks after discontinuation of dapagliflozin. Differences between dapagliflozin and placebo in body weight, systolic blood pressure and hematocrit were -1.5 kg (95% CI: -3.0, 0.0; p=0.0455), -3.6 mmHg (95% CI: 7.6, -0.4; p=0.0775) and 0.02 L/L (95% CI: 0.01; 0.03; p=0.9001). HbA1c did not change. The number of patients with adverse events during dapagliflozin treatment (n=17; 32.1%) and during placebo treatment (n=13; 25.0%) was similar. No hypoglycemic events were reported.

Conclusions: Six week treatment with dapagliflozin does not affect proteinuria in patients with chronic kidney disease without diabetes, but did induce acute and reversible decreases in mGFR, body weight, and, to a lesser extent, haematocrit, and increased homocœrination.
Funding: Commercial Support - AstraZeneca

PO0589
The Impact of Decline in Renal Function on the Clinical and Economic Burden of CKD: An Application of the DAPA-CKD Cost-Effectiveness Model
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Background: The efficacy of dapagliflozin for the treatment of chronic kidney disease (CKD) has been assessed in DAPA-CKD, which was stopped early for overwhelming efficacy. Cost-effectiveness analysis of new treatments plays an important role in the effective allocation of healthcare resources. The objective of this study was to develop a model for evaluating the cost-effectiveness of dapagliflozin based on the pending results of DAPA-CKD, and to demonstrate its functionality by characterizing the health economic burden of CKD progression from a UK payer perspective.
Methods: A lifetime microsimulation model was developed to estimate health economic outcomes in patients with CKD. Disease progression was modelled based on a historic, prospectively determined renal function curve, with standard eGFR decline (-0.65 ml/min/1.73 m² annually) and one with rapid eGFR decline (-4.20). Published cost and utility estimates were applied and discounted at 3.5%.

Results: DK patients with rapid eGFR decline had a reduced life expectancy of 9.1 years compared with 6.4 years in those with standard rates of eGFR decline. Patients with rapid eGFR decline experienced an additional 326 CV events per 1,000 patients and spent an additional 0.4 years receiving RRT. Reduced life expectancy, increased rates of CKD progression and CV event incidence translated to 2.4 fewer quality adjusted life years annually in patients with eGFR decline (5.5 versus 7.9) and an additional £1937 of direct healthcare expenditure.

Conclusions: The DAPA-CKD cost-effectiveness model is capable of estimating health economic outcomes in patients with CKD, projecting health benefits and costs consistent with published estimates. Our model improved diagnosis flow charts from DAPA-CKD. The economic burden imposed by CKD on both patients and healthcare systems.
Funding: Commercial Support - AstraZeneca

PO0590
Development of a CKD Model in Cynomolgus Monkeys and Its Application to Test Zampilimab, a Monoclonal Antibody (mAb) Specific for Human Transglutaminase 2 (TG2)
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Background: TG2, a crosslinking enzyme involved in wound healing, is linked to the development of renal fibrosis. TG2 irreversibly crosslinks proteins via ε-glutamyl lysine dipeptide bonds, including extracellular matrix (ECM) proteins. TG2 accelerates ECM deposition and renders the matrix resistant to ECM proteases, forcing ECM homeostasis towards accumulation. TG2 also crosslinks large latent TGFβ1 into the ECM, releasing the active pro-fibrotic TGFβ1 dimer. Zampilimab (IC50 0.2mL, K, 120m) humanized mAb specific for human TG2, is under investigation for the treatment of fibrosis. Application of zampilimab in a primary human cell model of renal fibrosis had positive results; however due to human specificity, zampilimab efficacy cannot be tested in rodent in vivo models.

Methods: A unilateral ureteric obstruction model of CKD was developed in aged cynomolgus monkeys. Zampilimab was applied prophylactically immediately following model induction. TG2 activity was measured using an in-situ activity assay, and zampilimab target occupancy determined by competitive immunofluorescence. Renal fibrosis was measured by computerized image analysis and histopathological scoring of Masson’s trichrome, Picosirius red and H&E stained slides with hydroxyproline measured by amino acid analysis.

Results: Ligation of the left ureter led to development of severe tubulointerstitial fibrosis associated with elevated TG2 activity, leading to end-stage fibrosis in 6 weeks. This primate model has a greater expansion of the tubular basement membrane than similar rodent models, with histology more closely resembling obstructive disease in man. Following zampilimab intervention in a 4-week study, 7 days post final dose, TG2 activity was completely and highly significantly reduced (n=6) at a low dose. However, both zampilimab doses ameliorated the level of renal fibrosis by pathology score, computerized determination of fibrotic index and hydroxyproline.

Conclusions: Our primate model of CKD demonstrated that zampilimab can effectively block TG2 activity and prevent renal fibrosis. A Phase 1/2 study of zampilimab for the treatment of post-renal transplant fibrosis is ongoing (NCT03435578).
Funding: Commercial Support - UCB Pharma

PO0591
Conditional Deletion of Myeloid-Specific Mitofusin 2 Promotes Kidney Fibrosis
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Background: Mitochondrial dysfunction is implicated in the pathogenesis of CKD. Mitochondrial dynamics regulate macrophage mitochondrial stress responses; we hypothesize that their impairment leads to kidney fibrosis. We determined the role of myeloid-specific mitochondrial fusion proteins (Mfn1) and Mfn2 in Pkn1-mediated mitophagy in experimental and human kidney fibrosis.

Methods: Pkn1-/-, myeloid-specific Mfn1 (LysM-Cre-Mfn1f/f), Mfn2 (LysM-Cre-Mfn2f/f) null mice and corresponding controls were subjected to unilateral ureteral obstruction (UUO,7-days) or adenine diet (AD,28-days). Kidneys, renal macrophages (RMs), bone marrow-derived macrophages (BMDMs), PBMCs, and plasma were analyzed by western blot, qPCR, Mito stress test, ELISA, immunohistochemistry, flow cytomtery, confocal and electron microscopy. Patients with renal biopsy-proven interstitial fibrosis & tubular atrophy (IFTA,e=6) and severe-CKD (GFR<30 ml/min,n=15) were compared to controls (no IFTA,e=9) and mild/moderate-CKD (GFR>30 ml/min,n=8).

Results: Mfn1 and Mfn2 expression decreased in kidneys after UUO or AD, and BMDMacsfer TGF-β1 treatment AD-fed-LysM-Cre-Mfn1f/f but not LysM-Cre-Mfn2f/f mice displayed increased renal expression of CD11b+ F4/80+ macrophages than AD-fed controls. Increased in fibroconnectin, CD206, galectin-3, and TGF-β1 expression in the kidneys and RMs were higher in AD-fed LysM-Cre-Mfn2f/f mice than AD-fed controls. TGF-β1-induced inhibition of mitophagy and increases in mitochondrial mass, size, and superoxide levels were greater in LysM-Cre-Mfn2f/f RMs and BMDMs than LysM-Cre-Mfn1f/f and controls. The reduction in colocalization of Mfn2 but not Mfn1 with renal mitochondria after UUO was higher in Pkn1-/- mice. BMDMs from patients with severe-CKD showed higher superoxide levels and lower Mfn2 expression than mild/moderate-CKD. IFTA was associated with lower renal expression of Mfn1 and Mfn2 and higher circulating CCL2 levels than controls. Decreased Mfn2 and Pkn1 expression in TGF-β1-treated human RMs was associated with increased fibrotic response.

Conclusions: This study is the first to suggest that myeloid-specific Mfn2 but not Mfn1 regulates renal macrophage mitophagy biogenesis and mitophagy prevents fibrosis. Mitophagy inducers may attenuate macrophage superoxide production and progression of kidney fibrosis.
Funding: NIDDK Support, Other NIH Support - NHLBI
PO0592
EZH2 Mediates Renal Fibrosis and Links Activation of Notch Signaling and Suppression of Klotho and BMP-7 Expression
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Background: Our previous studies have shown that pharmacological blocking EZH2 (Enhancer of Zeste Homolog 2), a histone H3 lysine 27 methyltransferase, attenuates renal fibrosis in a murine model of renal fibrosis, but the underlying mechanism in this process remain undefined.

Methods: In this study, we used two highly selective EZH2 inhibitors and conditional knockout mouse to evaluate the effect of EZH2 inhibition on renal fibrosis and activation of profibrotic signaling pathways and expression of renoprotective proteins in two in vivo mouse models of chronic kidney disease (CKD) induced by UUO and 5/6 nephrectomy (SNx).

Results: Global inhibition of EZH2 by administration of gamboxic acid or GSK-126 and conditional depletion of EZH2 in pericytes suppressed renal fibroblast activation and fibrogenesis in the kidney with UUO and SNx. Treatment with these inhibitors or EZH2 siRNA also inhibited serum- and TGF-β1-induced activation of renal fibroblasts in culture. Moreover, pharmacological and genetic inhibition of EZH2 suppressed expression of Notch-1, Notch-3, Jagged-1 and HES-1 and HEY-2 in vivo and in vitro. Similarly, inhibition of EZH2 was effective in inhibiting phosphorylation of extracellular signal-regulated kinase 1/2, AKT and NF-kB as well as expression of multiple profibrogenic cytokines/chemokines and renal macropage infiltration. In contrast, EZH2 inhibitors prevented injury-induced downregulation of Klotho and BMP-7, two anti-fibrotic proteins in the kidney.

Conclusions: These results revealed that EZH2 may promote renal fibrosis and activation of renal fibroblasts by activation of Notch signaling, downregulation of Klotho and BMP-7 and induction of inflammation in the injured kidney. Targeting EZH2 may be a novel therapeutic strategy to treat CKD.

Funding: NIDDK Support, Other NIH Support – National Natural Science Foundation of China

PO0593
Kidney Targeted Renalase Agonist Peptide Rescues Severe Model of Cisplatin-Induced AKI and CKD
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Background: Cisplatin (CP) causes Chronic Kidney Disease (CKD) upon repeated doses and limits its chemotherapeutic use. Renalase (RNLS) is a protein that activates kinases linked to survival and attenuates acute ischemic and CP-induced kidney injury. We now seek to target delivery of RNLS specifically to kidney to prevent CP-induced CKD.

Methods: CKD was induced in RNLS knockout (KO) (severe) and wild type (WT) mice by 2 doses of CP 15 mg/kg 2 weeks apart. The RNLS agonist peptide RP81 was synthesized and encapsulated in mesoscale nanoparticles (MNP) that target the kidney. Its cytoprotective activity was tested in vitro using TKPTS proximal tubule cells and in vivo using RNLS-KO mice. RP81MNP or empty MNP was administered weekly for 4 weeks. RP81MNP was synthesized and encapsulated in mesoscale nanoparticles (MNP) that target the kidney. Its cytoprotective activity was tested in vitro using TKPTS proximal tubule cells and in vivo using RNLS-KO mice. RP81MNP or empty MNP was administered weekly for 4 weeks.

Results: Wild-type type mice showed increased expression of collagen I, collagen IV, vimentin and a-SMA in kidney tissues. The increase of collagen I was significantly attenuated in iRT-PKM2-KO mice, while collagen IV and vimentin induction was marginally inhibited and no inhibition for fibronectin and a-SMA in these mice. Wild-type type and iRT-PKM2-KO kidney tissues had similar levels of Sirius red staining of collagen fibrils. We further examined Lotus Tetragonolobus lectin (LTL) staining of proximal tubules, which detected obviously more intact proximal tubules in iRT-PKM2-KO mice than in wild-type litters.

Conclusions: Together, these results indicate a pathogenic role of glycolysis in maladaptive kidney repair. Importantly, PKM2 and associated metabolism contribute to the regeneration of renal tubules after acute kidney injury.

Funding: NIDDK Support, Veterans Affairs Support

PO0594
Pyruvate Kinase M2 in Renal Tubular Cells Is a Key Regulator of Kidney Repair After Ischemic Injury
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Background: Tissue injury and repair is associated with changes of metabolism. In kidneys, metabolic changes including mitochondrial dysfunction and induction of glycolysis have been reported in renal fibrosis and chronic kidney disease. It remains unclear whether and how the metabolic changes contribute to kidney injury and repair. We have examined the effects of glycolysis inhibitors and the ablation of pyruvate kinase M2 (PKM2, an enzyme in glycolysis) in kidney tubules. Glycolysis inhibitors (including PKM2 inhibitor shikonin) suppressed renal fibrosis in the mouse model of unilateral ureter obstruction (UUO). Interestingly, in vitro the inhibitors suppressed fibrotic gene expression (e.g. fibronectin and a-SMA) in fibroblasts, but not in cultured renal tubular cells.

Methods: To further understand the role of glycolysis in renal tubular cells in vivo, we established a mouse model in which PKM2 ablation in renal tubule cells can be induced by doxycycline. To this end, PKM2-floxed mice were bred with Pax8-rtTA/LC1 CRE recombinase mice to create an inducible renal tubule-specific PKM2 knockout (iRT-PKM2-KO) mouse model. Exposure to doxycycline for 5-7 days induced PKM2 ablation in all renal tubules in iRT-PKM2-KO mice, but not in wild-type littersmates. These mice were subjected to 30 minutes of unilateral renal ischemia-reperfusion one day after initial doxycycline treatment, and kidneys were collected at 2 weeks later for histology, immunoblot analysis, and fibrosis staining.

Results: Wild-type type mice showed increased expression of collagen I, collagen IV, vimentin and a-SMA in kidney tissues. The increase of collagen I was significantly attenuated in iRT-PKM2-KO mice, while collagen IV and vimentin induction was marginally inhibited and no inhibition for fibronectin and a-SMA in these mice. Wild-type type and iRT-PKM2-KO kidney tissues had similar levels of Sirius red staining of collagen fibrils. We further examined Lotus Tetragonolobus lectin (LTL) staining of proximal tubules, which detected obviously more intact proximal tubules in iRT-PKM2-KO mice than in wild-type litters.

Conclusions: Together, these results indicate a pathogenic role of glycolysis in maladaptive kidney repair. Importantly, PKM2 and associated metabolism contribute to the regeneration of renal tubules after acute kidney injury.

Funding: NIDDK Support, Commercial Support - Dialysis Clinics Inc.
in vitro studies, Sphk2 deficient perivascular cells expressed less inflammatory cytokines, such as Cxcl1, Itk, Tnf, after LPS stimulation compared with control perivascular cells. Sphk2 deficient and control perivascular cells robustly expressed Smn2, but not Md2h2, and S1pr1-3 among the five S1P receptor subtypes. Among S1pr1-3, only knockdown of S1pr1 resulted in suppressed expression of inflammatory cytokines after LPS stimulation.

Conclusions: Sphk2 deletion in renal perivascular cells was protective against kidney fibrosis. In vitro studies suggested that S1P produced by Sphk2 is exported through Smn2 and reacts with S1PR1 to enhance the inflammatory signal in these cells, leading to immune cell infiltration and subsequent fibrosis in the kidneys.

Funding: NIDDK Support

PO0598

Histone Demethylase JMJD3 Protects Against Renal Fibrosis by Suppressing TGF-β and Notch Signaling

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Background: The Jumonji domain containing-3 (JMJD3), a specific histone demethylase for trimethylation on histone H3 lysine 27 (H3K27me3), is associated with the pathogenesis of many diseases, but its role in renal fibrosis remains unexplored. Here, we examined the role of JMJD3 and mechanisms involved in the activation of renal fibroblasts and development of renal fibrosis.

Methods: Murine models of 5/6 nephrectomy (SNx) and ureteral unilateral obstruction (UUO) were used to assess the effect of a specific JMJD3 inhibitor, GSKJ4, and genetic deletion of JMJD3 from FOXD1 stroma-derived renal interstitial cells on the development of renal fibrosis and activation of renal interstitial fibroblasts. Cultured rat renal interstitial fibroblasts (NRK-49F) and mouse renal epithelial (mTECs) cells were also used to examine JMJD3-mediated activation of profibrotic signaling.

Results: JMJD3 and H3K27me3 expression levels were upregulated in the kidney of mice subjected to SNx, 5/6 and UUO. Pharmacological inhibition of JMJD3 with GSKJ4 completely prevented the activation of JMJD3 led to worsening of renal dysfunction as well as increased deposition of extracellular matrix proteins and activation of renal interstitial fibroblasts in the injured kidney. This was coincident with decreased expression of Smad7 and enhanced expression of H3K27me3, transforming growth factor β1 (TGFβ1), Smad3, Notch1, Notch3 and Jagged1. Inhibition of JMJD3 by GSKJ4 or its specific siRNA also resulted in the similar responses in cultured NRK-49F and mTECs exposed to serum or TGFβ1. Moreover, JMJD3 inhibition augmented phosphorylation of AKT and ERK1/2 in vivo and in vitro.

Conclusions: These results indicate that JMJD3 confers anti-fibrotic effects by limiting activation of multiple profibrotic signaling pathways and suggest that JMJD3 modulation may have therapeutic effects for chronic kidney disease.

Funding: NIDDK Support

PO0599

Induction of CKD by Gene Deletion of Canonical Transient Receptor Potential 1 (TRPC1) Channels Independent of Hypertension and Nephromegaly Despite Diabetes and Metabolic Syndrome

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Background: TRPC1 gene on chromosome 3q22-24 is in the linkage region for diabetic nephropathy. Despite reduced expression in diabetes, no causal relationship has been established. Since null mice are obese, hyperterglycemic and diabetic with fatty liver, we evaluated potential renal phenotypes, testing the hypothesis of impaired Ca signaling, as we found reduced cell free Ca in bone, renal, and parathyroid cells.

Methods: From 3rd to 22nd mon, metabolic, cardiac & abdominal ultrasound (US) & clearance (CL) studies were done in age- & sex-matched littermates of TRPC1 +/-, +/-, & -/- mice. Creatinine (Cr) was analyzed by creatininase or HPLC; glomerular filtration rate (GFR) by inulin Cl. Systolic (S) & diastolic (D) BP was measured by arterial (A) cannulation.

Results: Null mice were hyperglycemic from the 3rd mon & developed diabetes to 6 to 22 mon by standard IP glucose tolerance test. Nephromegaly was absent in null mice since kidney volume by US (0.38 vs 0.46 at 7 mon & 0.4 vs 0.5 cc at 11-20 mon) was 16% smaller & kidney (K) to body (B) weight (Wt) (1.2 vs 1.55 at 7 mon & 1.1 vs 1.5% at 11-20 mon) was lighter by 17-28%. Chronic injury & scarring were suggested by 37% increase in ecchogenicity at 20 mon, though normal at 7 or 11 mon. Urine albumin/cre ratio in null mice rose barely (64-71%). But at 17 mon, CrCl fell by 30% (p<0.01) in null ♀ & by 46% (p<0.01) in null ∆. GFR at 22 mon corroborated stage III CKD as inulin Cl fell by 44%. Whether expressed per mouse, per g Wt, or per 100 g BW, haploid TRPC1 deletion reduced CrCl by 40% (p<0.05) at 16 mon vs 44% by diplodip deletion (p<0.02).

TRPC1 deletion significantly reduced, not raised, mean SBP (113 vs 131 tort), DBP (77 vs 86 tort), & MABP (89 vs 98 tort). Since TRPC1 was implicated in cardiac hypertrophic signaling, smooth muscle proliferation & mesangial cell contraction, we did cardiac US & found 33% reduced cardiac output in -/- mice (14 vs 21 ml/min) & 14% smaller heart mass, corroborated by 20% lower weights measured at 22 mon.

Conclusions: 1. TRPC1 deficiency impairs Ca signaling, retards renal & heart development, compromises hemodynamics and modulates hypothalamic nephropathy. 2. Null mice provide an excellent model to study progressive CKD independent of hypertension and heavy proteinuria.

Funding: NIDDK Support, Veterans Affairs Support, Clinical Revenue Support

PO0597

Sphingosine Kinase 2 in Kidney Perivascular Cells Promotes Inflammation and Fibrosis Through S1PR1 Signaling

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Background: Sphingosine-1-phosphate (SIP) is a sphingolipid, which is produced by two different kinases, sphingosine kinase (Sphk)1 and 2. SIP is exported through Spn2 or Mfd2h, and then reacts with S1P receptors (SIPR1-5) to affect myriad cell functions. We investigated whether the administration of PAR-1 antagonist vorapaxar, an FDA-approved drug for reducing thrombotic cardiovascular events, has any renoprotective effect in a robust kidney fibrosis murine CKD model following unilateral ischemia reperfusion injury (UIRI), as well as in hypoxia-induced cultured rat proximal tubular epithelial cells (NRK-52E).

Results: Vorapaxar reduced morphological abnormalities and the expression of tubular injury marker Kim-1 in URIIR mice. Mice treated with vorapaxor showed less intrarenal accumulation of ECM proteins including fibronectin, α-smooth muscle actin and collagen 1 via TGF-β-Smaling signaling after URIIR. IR-induced endothelial dysfunction and macrophage infiltration were also decreased by vorapaxar treatment. In NRK-52E cells, PAR-1 expression was activated under a hypoxic milieu associated with upregulation of TGF-β-induced ECM protein accumulation.

Conclusions: Vorapaxor diminishes renal fibrosis through TGF-β-Smaling signaling in URIIR model, and protects against tubular injury during AKI to CKD transition. A PAR-1 targeted strategy by vorapaxor as a therapeutic approach in human CKD warrants further. Funding: Health and Medical Research Fund (HMRF) of Hong Kong (grant no. 05163596), Research Grants Council of Hong Kong (Collaborative Research Fund, grant no. C7081-16A), and Hong Kong Society of Nephrology/ HK Foundation Kidney Research Grant 2018.

PO0596

The PAR-1 Antagonist Vorapaxor Protects Against AKI to CKD Transition

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Background: Protease-activated receptor-1 (PAR-1) has been reported as a coagulation regulator in the pathophysiology of AKI. Beyond its normal function in haemostasis, aberrant PAR-1 signaling may lead to the development of tubulointerstitial fibrosis, and subsequently CKD.

Methods: We investigated whether the administration of PAR-1 antagonist vorapaxor, an FDA-approved drug for reducing thrombotic cardiovascular events, has any renoprotective effect in a robust kidney fibrosis murine CKD model following unilateral ischemia reperfusion injury (UIRI), as well as in hypoxia-induced cultured rat proximal tubular epithelial cells (NRK-52E).

Results: Vorapaxor reduced morphological abnormalities and the expression of tubular injury marker Kim-1 in URIIR mice. Mice treated with vorapaxor showed less intrarenal accumulation of ECM proteins including fibronectin, α-smooth muscle actin and collagen 1 via TGF-β-Smaling signaling after URIIR. IR-induced endothelial dysfunction and macrophage infiltration were also decreased by vorapaxar treatment. In NRK-52E cells, PAR-1 expression was activated under a hypoxic milieu associated with upregulation of TGF-β-induced ECM protein accumulation.

Conclusions: Vorapaxor diminishes renal fibrosis through TGF-β-Smaling signaling in URIIR model, and protects against tubular injury during AKI to CKD transition. A PAR-1 targeted strategy by vorapaxor as a therapeutic approach in human CKD warrants further. Funding: Health and Medical Research Fund (HMRF) of Hong Kong (grant no. 05163596), Research Grants Council of Hong Kong (Collaborative Research Fund, grant no. C7081-16A), and Hong Kong Society of Nephrology/ HK Foundation Kidney Research Grant 2018.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Histone Deacetylase 6 Inhibition Mitigates Renal Fibrosis by Suppressing TGF-β/SMAD3 and eGFR Signaling Pathways

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Background: We have recently shown that histone deacetylase 6 (HDAC6) is critically involved in the pathogenesis of acute kidney injury, however, its role in renal fibrosis remains unclear.

Methods: In this study, we examined the effect of ricolinostat (ACY-1215), a selective inhibitor of HDAC6, on the development of renal fibrosis in a murine model induced by unilateral ureteral obstruction (UUO).

Results: We found that HDAC6 was highly expressed in the kidney following UUO injury, which was coincident with deposition of collagen fibrils and expression of α-smooth muscle actin, fibronectin, and collagen III. Administration of ACY-1215 reduced these fibrotic changes and inhibited UUO-induced expression of transforming growth factor β1 and profibrotic marker Smad3, and Smad7. ACY-1215 treatment also suppressed phosphorylation of epidermal growth factor receptor and several signaling molecules associated with renal fibrogenesis, including AKT, signal transducer and activator of transcription 3 and NF-kB in the injured kidney. Furthermore, ACY-1215 was effective in inhibiting de novo formation of renal fibroblasts to myofibroblasts in cultured renal interstitial fibroblasts.

Conclusions: Collectively, these results indicate that HDAC6 inhibition can attenuate renal fibrosis development by suppression of TGFβ1 and EGFR signaling.

Funding: NIDDK Support, Other NIH Support • National Natural Science Foundation of China.

Inhibition of KIM-1-Mediated Fatty Acid Uptake by a Novel Inhibitor Attenuates Pro-Fibrotic Responses in Multiple Models of Human Primary Kidney Epithelial Cells Including Kidney Tubuloids

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Background: Tubulointerstitial damage is strongly associated with many forms of kidney injury including diabetic kidney disease. Kidney Injury Molecule-1 (KIM-1), a scavenger receptor, is the most upregulated proximal tubule protein with kidney injury. We hypothesized that KIM-1-mediated uptake of fatty acids (FAs) contributes to tubulointerstitial damage.

Methods: Human DKD renal biopsy samples were analyzed. Human primary epithelial cell cultures were established from the non-tumor kidney tissue removed from patients with a renal mass. To grow human renal tubuloids, primary cells were cultured on ultra-low attachment plates for several days. Cells were transferred into media containing multiple growth factors and 5% fetal bovine serum. Cells and tubuloids were treated with palmitate acid with certain groups having siRNA knockdown of KIM-1. Conditioned media from FA-treated human primary cells and tubuloids were applied to mouse primary kidney fibroblasts. An inhibitor for KIM-1-mediated FA-uptake was identified from cell depleted of KIM-1. We confirmed that KIM-1-mediated fatty acid uptake at least in part by inhibiting the direct binding of FA to KIM-1.

Results: KIM-1 expression in DKD patients was positively correlated with tubulointerstitial inflammation and fibrosis. FA-BSA uptake was markedly reduced in cells depleted of KIM-1 indicating the relative importance of KIM-1 to proximal tubule FA uptake. High-dose FA treatment increased cell death. FA treatment increased H2AX expression, a marker for DNA damage response. FA also increased the number of cells in the G2/M phase without an increase of those in S phase by cell cycle analysis, indicating that cells are likely arrested in G2/M phase. Our newly identified inhibitor for KIM-1, JB1, prevented FA uptake at least in part by inhibiting the direct binding of FA to KIM-1.

Conclusions: KIM-1 enhances the proximal tubular uptake of FA, leading to proximal tubule damage, pro-fibrotic responses and increase in cell death. Our findings support JB1 as a novel therapeutic target for chronic kidney disease including DDK and our work introduces a new candidate therapeutic agent.

Funding: NIDDK Support, Commercial Support • Boehringer Ingelheim
Results: WT mice fed a HPI diet showed a significant 70% reduction in kidney HNF4α mRNA and protein expression, suggesting that hyperphosphatemia, a hallmark of progressive CKD, contributes to HNF4α downregulation in the kidney. Kidney molecular profiling by RNAseq of Col4a3<sup>−/−</sup> mice showed increased acquired mitochondrial dysfunction and reduced oxidative phosphorylation, suggesting that impaired mitochondrial function strongly contributes to CKD progression. Downstream pathway analyzes showed that the vast majority of these genes (~80%) are regulated by HNF4α. Pharmacological inhibition or HNF4α in Col4a3<sup>−/−</sup> mice led to an accelerated decline in kidney function (200% increase in BUN), demonstrating the crucial role of HNF4α in CKD progression.

Conclusions: These results suggest that HNF4α is a master regulator of mitochondrial function in kidney and might represent a novel therapeutic target to improve outcomes in CKD.

Funding: NIDDK Support

**PO0605**

An In Vitro Model to Elucidate the Synthesis of Extracellular Matrix Proteins Involved in Renal Interstitial Fibrosis

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**Background:** Accumulation of extracellular matrix (ECM) proteins is a hallmark of renal fibrosis, which can lead to altered tissue homeostasis, kidney failure, and ultimately death. Many different cell types are involved in this process, but fibroblasts are the main source of ECM proteins such as fibronectin, collagen type I (COL I), III (COL III), and VI (COL VI). Recently it was suggested that a fragment of COL VI released during collagen maturation is, in fact, a bioactive molecule (endotrophin; ETP) with signaling potential, indicating that collagens are not just passive structural proteins. In this study, we investigated the effect of transforming growth factor (TGF)-β and ETP on the synthesis of different ECM proteins by human renal fibroblasts in the scar-in-a-jar (SiaJ) cell model.

**Methods:** Cells were seeded in 48-well plates at 30,000 cells/well and incubated for 24h in DMEM + 10% FBS for adherence. Cells were starved by incubating them for further 24h in DMEM + 0.4% FBS. Fresh medium was added at day 0 with 250/150 mg/mL Ficol 70/400 and 1% ascorbic acid, containing 0.02 nM TGF-β or either 12 or 30 nM ETP. Medium was changed and collected on days 3, 6, 10, and 13. Biomarkers of ECM formation, could be used to elucidate the mechanisms behind acute and sustained matrix production profiles.

**Results:** Stimulating renal fibroblasts with 0.02 nM TGF-β significantly increased the formation of COL I (P<0.0001), III (P<0.0001), and fibronectin (P<0.0001) compared to unstimulated cells. Interestingly, TGF-β treatment suppressed the formation of COL VI (P<0.0001) and E-cadherin (P<0.0001) in unstimulated cells. Stimulation with 30 nM ETP significantly increased the formation of COL I (P<0.0001) and III (P<0.0001) compared to unstimulated cells. 12 nM ETP significantly increased the synthesis of fibronectin compared to unstimulated cells (P<0.0001).

**Conclusions:** Different growth factors induce different protein expression profiles in fibroblasts. Interestingly, ETP, which originates from the ECM, drives renal fibrosis through increasing COL I and III as well as fibronectin. This SiaJ model, combined with the investigated biomarkers of ECM formation, could be used to elucidate the mechanisms behind acute and sustained matrix production profiles.

**PO0606**

FoxM1 Inhibition Ameliorates Renal Interstitial Fibrosis (RIF) by Decreasing Extracellular Matrix and Epithelial-to-Mesenchymal Transition

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**Background:** FoxM1 is a transcriptional regulator involved in tumor development, pulmonary fibrosis, and cardiac fibrosis. However, its role in RIF has yet to be elucidated.

**Methods:** We established a TGF-β1-stimulated human proximal tubular epithelial cell (HKT-2) model in vitro and a unilateral ureteral obstruction (UUO)-induced rat RIF model in vivo. FoxM1 inhibition was achieved by siRNA interference in vitro and by injecting thiostrepton into UUO-induced RIF rats in vivo. The degree of renal damage and fibrosis were determined by histological assessment via hematoxylin and eosin staining.

**Results:** Different growth factors induce different protein expression profiles in fibroblasts. Interestingly, ETP, which originates from the ECM, drives renal fibrosis through increasing COL I and III as well as fibronectin. This SiaJ model, combined with the investigated biomarkers of ECM formation, could be used to elucidate the mechanisms behind acute and sustained matrix production profiles.

**Conclusions:** Different growth factors induce different protein expression profiles in fibroblasts. Interestingly, ETP, which originates from the ECM, drives renal fibrosis through increasing COL I and III as well as fibronectin. This SiaJ model, combined with the investigated biomarkers of ECM formation, could be used to elucidate the mechanisms behind acute and sustained matrix production profiles.

**PO0607**

The Macrophage Recruitment in the Unilateral Ureteral Obstruction Is Associated with the Raise of MCP-1 and Is Dependent of Lipoclin 2 Expression

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**Background:** The persistent renal inflammation has been proposed as a crucial mechanism at the early stages of renal disease. The macrophages recruitment, as part of the pathogenic events, depends of the monocyte chemoattractant protein-1 (MCP-1) raise. In addition, studies in patients have demonstrated that neutrophil gelatinase-associated lipocalin (NGAL, also called Lipocalin-2), is overexpressed during early stages of renal lesion. However, whether NGAL is relevant for macrophages recruitment at renal level, and if this is related to the increase of MCP-1, remains unknown. Our objective was to determine whether NGAL promotes the pro-inflammatory status during the unilateral ureteral obstruction (UUO), characterized by the macrophage recruitment and the increase of MCP-1.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Methods: Male C57BL/6 Wild type (WT) y Ngal-KO mice (8-12 weeks) were underwent to UUO surgery (control group) or Sham (2, 4, 5, 7 and 10 weeks), in order to determine the associated damage at kidney level and the raise of MCP-1 in peripheral blood mononuclear cells (PBMC).

Results: In WT mice, the UUO induced luminal tubular dilation starting at 3 days (P<0.001 vs Sham), and an induction of plasma area (76.36 ± 3.57 mL/D, P<0.001 vs Sham). In addition, UUO increased NGAL levels in PBMC, plasma and urine (24.1 ± μg/L in Sham vs. 103.8 ± μg/L and 134.5 ± μg/L in UUO, at 3 and 7 days, respectively). This was in accordance with the renal induction of NGAL (mRNA and protein, P<0.001 vs Sham), and increased expression of pro-inflammatory mediators: TGF-β1, CCL5 (RANTES) and MCP-1, with a peak at 7-days. The genetic ablation of NGAL prevented tubular dilation (34.24 ± 6.55 μm) (P<0.01 vs UUO WT) and the rise of MCP-1 induced by UUO in kidney and PBMC (P<0.01 vs WT). This was accompanied with a low grade of macrophagia in kidney of NGAL-KO mice underwent to UUO (15.2% in WT vs 7.3% in NGAL-KO).

Conclusions: The renal overexpression of MCP-1 and the macrophage recruitment induced by UUO is dependent of NGAL presence. Our results suggest that NGAL, by a regulation on MCP-1, may be crucial for macrophage chemotraction during the early stages of renal disease. Acknowledgments. Fondedey #1201251 and Fondedey #3201016

P00608
Enabled Icos + Rte-Tresp Proliferation Is Involved in the Pathogenesis of Active Systemic Lupus Erythematosus (SLE)

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Background: Dysfunction of CD4+ regulatory T-cells (Tregs) and CD4+ responder T-cells (T-resps) is an important trigger in the development of active systemic lupus erythematosus. By now, underlying mechanisms are not fully understood.

Methods: To determine differences in the differentiation of inducible costimulatory molecule (ICOS)- and ICOS- Tresps/Tregs, their percentages of CD45RA CD31- recent thymic emigrant (RTE)-Tresp differentiation compared to healthy control patients. Hence, the ratio of ICOS -RTE-Tresp differentiation compared to healthy control patients. In contrast, proliferation of ICOS- RTE-Tressps into ICOS CD31-memory-Tregs is inhibited. Similarly, active SLE patients show an impaired proliferation of ICOS -CD31-memory Treg/Tresps within CD4+ Treg/Tresps were calculated. Additionally, subsets were stained for the proliferation marker Ki67. 124 healthy control patients and 117 with a preexist lupus erythematosus (102 patients in remission, 15 patients with a flare) were measured.

Results: SLE patients in remission showed an increased differentiation of ICOS+ RTE-Tregs and ICOS-RTE-Tresps via resting MN-Tregs into CD31-memory-Tregs compared to healthy control patients. In contrast, proliferation of ICOS- RTE-Tressps into ICOS CD31-memory-Tregs is inhibited. Similarly, active SLE patients show an increased differentiation of ICOS- RTE-Tresps and ICOS-RTE-Tresps via resting MN-Tregs. Moreover, proliferation ability of ICOS- RTE-Tresps is not inhibited but enhanced in these patients. Both SLE patients in remission and active SLE patients show an impaired ICOS- RTE-Tresp differentiation compared to healthy control patients. Hence, the ratio of ICOS-Tregs/ICOS-Tresps within CD4+T-cells is significantly increased in both SLE remission and active SLE patients compared to healthy control patients. In contrast, the ratio of ICOS-Tregs/ICOS-Tresps is significantly increased in SLE remission patients, but decreased in active SLE patients compared to healthy control patients.

Conclusions: Proliferation of ICOS- RTE-Tressps is medically inhibited in SLE remission patients. In active SLE patients, proliferation is enabled decreasing the ICOS- Treg/ICOS-Tresp ratio.

P00609
Involvement of Calcium-Sensing Receptor in the Development of Interstitial Fibrosis

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Background: Physiological and pathophysiological role of renal Ca sensing receptor (CaSR) have not been well understood. We have reported the down regulation of CaSR in obstructive chronic renal fibrosis along with the down regulation of Mg transporting molecules, suggesting that CaSR plays an important role in the development of renal damage associated with Mg deficiency. We have reported the down regulation of CaSR expression of claudin-14, 16 and 19, Mg transpirting molecules, seemed to be increased by parathyroid surgery (t), however, it was not statistically significant. However, Cinacalcet partially, but significantly increased the mRNA expression of TRPM6 compared to UUO group (sham: 1.01±0.07, UUO: 0.35±0.01, Cinacalcet: 0.41±0.02).

Conclusions: The expression of claudin-16 and TRPM6 was significantly decreased with development of fibrosis in UUO. The effect of CaSR activation and upregulation by Cinacalcet was limited, however, it restored the progression of fibrosis and impairment of Mg reabsorption. CaSR may play a key role for the Mg loss-related renal fibrosis.

P00610
Fibroblast-Specific LRP-1 Promotes Renal Fibrosis

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Background: LRP-1, a scavenger receptor up-regulated during obstructive nephropathy, has been shown to mediate the actions of multiple profibrotic factors including TGF-β1, TGF-β1, and CTGF. However, the in vivo role of LRP-1 in kidney fibrosis remains largely unknown.

Methods: We generated a novel fibroblast-specific LRP-1 knockout mouse (Lrp-1−/−) and induced the unilateral ureteral obstruction (UUO), a classic model of chronic kidney disease (CKD), in these mice to investigate the in vivo role of LRP-1 in kidney fibrosis.

Results: It was found that LRP-1−/− mice had similar phenotype as their littermate controls (Lrp-1+/−). However, after UUO injury, Lrp-1−/− mice displayed significantly decreased fibrosis, as demonstrated by reduced renal collagen content and FSP-1 abundance, in comparison with their littermates. We further found that obstruction-induced epithelial damage was alleviated in Lrp-1−/− mice. After UUO, LRP-1+/− mice displayed decreased E-cadherin and increased vimentin expression, suggesting that epithelio-mesenchymal transition (EMT) was induced in the obstructed kidneys. Intriguingly, Lrp-1−/− mice showed significantly reduced EMT as demonstrated by restoration of E-cadherin and elimination of vimentin induction.

Conclusions: Thus, it is clear that fibroblast LRP-1 promotes kidney fibrosis through EMT.

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P00611
Essential Renal Tubular Proteins Are Lost by Excretion Within Novel Large Extracellular Vesicles During Chronic Renal Insufficiency

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Background: Within weeks of surgery, the 5/6 nephrectomy (5/6Nx) rat spontaneously develops renal disease including tubular damage, brush border loss, and the production of very large extracellular vesicles present in the tubule lumen. These large renal tubule extracellular vesicles (LRT-EVs) are too large to be microsomes or exosomes, and lack markers of apoptotic bodies, and thus may represent an undescribed vesicle. We hypothesized that formation and excretion of these vesicles represents a pathological mechanism by which important tubule proteins are lost in chronic renal insufficiency.

Methods: We performed a longitudinal, histologic examination for the presence of LRT-EVs isolated from 5/6Nx rat urine 10 weeks following surgery.

Results: Histologic examination revealed virtually no LRT-EVs in sham-operated rat tubules at any time point. LRT-EVs were present in 5/6Nx rat tubules at all measured time points including 2, 4, 5, 7, and 10 weeks post-surgery, and exhibited a marked increase in percentage of tubule presence between week 5 (7.0 ± 2.7%) and week 7 (51.1 ± 6.5%). This increase temporally corresponds to a time of rapid progression of renal disease. Median LRT-EV diameter upon microscopic image analysis was 2.5 μm. Protemic analysis of isolated LRT-EVs revealed them to contain a wide array of functionally essential tubule proteins including but not limited to basolateral Na+/K+ ATPase subunits, sodium-glucose co-transporters, aquaporin 1, megalin, cubulin, and mitochondrial VDAC.

Conclusions: Loss of important tubule proteins through production and urinary excretion of previously unidentified LRT-EVs may represent a hitherto unappreciated aspect of chronic renal insufficiency.

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P00612
Indoleamine-2, 3-Dioxygenase Activates Wnt/β-Catenin to Induce Kidney Fibrosis

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Background: Dysorder of tryptophan metabolism catalyzed by indoleamine-2, 3-dioxygenase (IDO) is common in chronic kidney disease which manifests as increased kidney fibrosis. IDO is also reported to be involved in fibrosis of other organs while little is known about correlations of IDO and fibrosis in kidney disease.

Methods: Wild type (WT) mice and IDO− mice were employed. Mice in Sham group underwent exposure of renal artery while mice in AKI group received unique renal artery ischemia-reperfusion injury (IRI) and the contralateral kidney was removed at day 13 after surgery. The IDO markers were analyzed. Prostaglandin E2 (PGE2) was administrated to WT AKI mice. Clinically, a total of 115 CKD patients and 30 non-CKD patients were recruited. IDO was

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Underline represents presenting author.
calculated by the ratio of kynurenine and tryptophan. Correlations between indicators were analyzed. The ROC curve was also performed. 

**Results:** WT AKI mice revealed elevated expression of IDO and worse kidney function. PAS staining exhibited less loss of tubular epithelial cells and atrophy tubules in IDO−/− AKI mice. Additionally, fibrosis markers, including α-SMA, fibronectin and vimentin, were more severer in WT AKI mice. GSK-3β and β-catenin were significantly decline in IDO−/− AKI mice. On top of that, PGE2 administration revealed reduced IDO expression and decreased levels of GSK-3β and β-catenin resulting in lower expressions of α-SMA, fibronectin and vimentin in WT AKI mice. In patients, IDO had negative correlations with eGFR (r = -0.742, p = 0.001). Further, the linear regression showed IDO was an independent influence factor of eGFR. ROC curve showed the area under the ROC curve was 0.825 for IDO.

**Conclusions:** IDO could activate Wnt/β-catenin pathway to induce kidney fibrosis. PGE2 could ameliorate kidney fibrosis via inhibiting IDO expression.

**Figure:** Scatter plot of IDO associated with eGFR

**PO0613**

**Human Induced Pluripotent Stem Cell-Derived Kidney Micro-Organoids for High Throughput Disease Modeling in Drug Discovery**

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**Background:** Human kidney contains around 1 million nephrons, more than 2 dozen different cell types. Reproducing physiological kidney cell types in vitro is limited. Recent advancements in human iPSCs differentiation provide an opportunity to culture and utilize multicellular kidney structures “kidney-organoids”. We have employed a kidney micro-organoid in suspension culture this method eventually accelerates kidney organoids to the industrial scale and differentiates from traditional low throughput transplant organoids. This method involves differentiation of iPSCs to intermediate mesoderm using CHIR and FGF9 and spontaneous aggregation in the swirler culture leads to mature to kidney organoids, this can be used to study kidney disease in a high-throughput manner.

**Methods:** We aimed to model human kidney inflammatory and genetic disease in vitro using kidney micro-organoids, treatment with different insults to reproduce CKD microenvironment eg. IL-1β, TGFβ, Angiotensin-II and prostate sulphate.

**Results:** After 24h of stimulation, we noted significant upregulation of kidney injury biomarkers including KIM1 and inflammatory cytokines. Reproducing genetic diseases like PKD is very challenging in vitro, we show treatment of cultured micro-organoids with forskolin (to elevate intracellular cAMP) altered the transportation of ciliary proteins and promoted cyst formation, resembling human PKD. These observations clearly demonstrate the use of micro-kidney organoids to study renal diseases in vitro for drug discovery applications with human translatable functional biomarkers.

**Conclusions:** Impact statement: Kidney micro-organoids provide a platform for high throughput modeling of human kidney diseases related fibrosis, inflammation and genetic disease like polycystic kidney disease with human translatable biomarkers in drug discovery.

**PO0614**

**CKD of Unknown Origin (CKDuo): Is the Problem Dehydration, Water Contamination, or Both?**

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**Background:** An increasing number of people of Central America develop CKDuo. The disease is characterized by chronic tubulo-interstitial nephritis. Occasionally, it presents as an acute kidney injury (AKIuo). The cause(s) remain unknown. Some sustain that dehydration is responsible. Others believe the disease is caused by water contaminated with heavy minerals or agrochemicals. To prevent dehydration, workers in these regions ingest 8-12L of water/day. Hence, even if concentrations of toxins are in “acceptable range”, the cumulative intake may reach toxic levels. If this hypothesis is correct, purified water should reduce the incidence of the disease. In 2017 a Nicaraguan sugarcane factory (SER) adhered to the Adelante initiative, consisting of reducing working hours, exposure to heat and dehydration. In 2017-18, these measures had no impact on the incidence of AKIuo.

**Methods:** During the 2019 season, SER adopted the policy of providing highly purified drinking water to > 6000 workers (1L/hour during working hours). The effects on AKIuo were monitored. Comparisons were made of the monthly incidence of AKIuo during years 2017, 2018 and 2019, by One-way ANOVA.

**Results:** With the introduction of purified water, the incidence of AKIuo decreased from 4.0±1.3 cases in 2017 and 3.4±2.1 in 2018 to 2.0±1.5 cases/1000 workers/month in 2019 (P< 0.02). (Fig.1)

**Conclusions:** Although preliminary, these data support the hypothesis that contaminated water may play a major role in AKIuo. This raises enormous public health issues. If dehydration is responsible, the remedies are hydration and less heat exposure. If toxins and agrochemical are responsible, the remedy is providing highly purified water to those at risk. The potential impact of these measures on CKDuo remains to be determined.
Results: Under normoxia, the serum phosphorus (P*) tend to be lower in umod− group compared with WT group (1.9±0.2 vs 2.1±0.2 mmol/L, P=0.064). Under normoxia environment, the α-diversity of gut microbiota decreased in umod− group compared with WT group (Chao1 index, 301.8±55.3 vs 374.3±80.7, P=0.005), and the composition of microbiota was clearly separated between two groups (PCoA, P<0.001). The abundance of g-Lactobacillus (P<0.002) and g-Phascolarctobacterium (P=0.026) increased and g-Ruminococcus (P=0.023) decreased in umod+ group compared with WT group. g-Ruminococcus showed positive relationship with serum phosphorus (R=0.511, P<0.001). Results: Under normoxia, the serum phosphorus (P*) tend to be lower in umod− group compared with WT group (1.9±0.2 vs 2.1±0.2 mmol/L, P=0.064). Under normoxia environment, the α-diversity of gut microbiota decreased in umod− group compared with WT group (Chao1 index, 301.8±55.3 vs 374.3±80.7, P=0.005), and the composition of microbiota was clearly separated between two groups (PCoA, P<0.001). The abundance of g-Lactobacillus (P<0.002) and g-Phascolarctobacterium (P=0.026) increased and g-Ruminococcus (P=0.023) decreased in umod− group compared with WT group. g-Ruminococcus showed positive relationship with serum phosphorus (R=0.511, P<0.001). When CIH was added as an environment condition, the serum phosphorus (P*) increased in umod− group obviously (2.3±0.3 vs 1.8±0.2 mmol/L, P=0.002). Gut composition in umod− were still clearly separated from WT (PCoA, P<0.001). The abundance of g-Lactobacillus, g-Phascolarctobacterium and g-Ruminococcus showed no difference. The abundance of g-Blautia (P=0.008), g-Sutterella (P=0.008), g-Anaerostipes (P=0.008) increased and g-Flavonifractor (P=0.008) and g-Anaerotruncus (P=0.008) decreased in umod− CIH group compared with wild type CIH group. G-Sutterella showed positive relationship with Phosphorus (R=0.831, P<0.001).

Conclusions: Chronic intermittent hypoxia can interact with uromodulin to affect serum phosphorus in umod− rats. These changes were strongly linked to the alterations in gut microbiota.

PO0616
Influence of Colonic Dialysis on the Distribution of Gut Microbiome in CKD Stage 3-5 Patients
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Background: Chronic kidney disease (CKD) becomes a major public health challenge given high incidence rates in the world. colonic dialysis (CD) has been used in pre-dialysis CKD patients (CKD3-5) in many hospitals of China because of its advantages of simple operation, low price and few complications. The gut microbiome is a potential cause of CKD progression and serve as a promising therapeutic target. We raise the question that whether CIH improve renal function by affecting intestinal microbiome in CD patients. Improving the imbalance of intestinal microbiome is considered a potential therapeutic target to decline chronic kidney disease (CKD) progression. We aimed to investigate the influence of colonic dialysis (CD) on the distribution of gut microbiome in CKD3-5 patients.

Methods: We studied gut microbiota in 50 patients with CKD, 25 CD patients, 25 outpatients (OP), and compared to 34 healthy subjects (HS). The gut microbiome composition was analyzed by a 16S ribosomal RNA (16S rRNA) gene-based sequencing protocol.

Results: We found that there was no significant difference in the richness of intestinal microbiota between CD and HS, but the richness of bacterial in OP decreased significantly (HS VS. OP p = 0.062). CD can increase the abundance of some short chain fatty acid (SCFA) producing bacteria and decrease the abundance of some uremic toxin producing bacteria. CD also can increase the abundance of some anaerobic bacteria in intestine. Compared with OP, the profile of intestinal microbiota in CD group and HS group was more similarity.

Conclusions: Our study reveals CD treatment alters microbiome profile and increases microbiome richness in CKD3-5.

PO0617
Asymptomatic Hyperuricemia, a Regulator of Innate Immunity in CKD
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Background: Asymptomatic hyperuricemia (HU) is common in patients with chronic kidney disease (CKD) but the causative role of HU on CKD progression remains controversial. Two large multi-center randomized controlled trials, CKD-FIX and PERL study, have now disproven a causal relation. On the other hand, a causative role of HU exists with gout but a rapid correction of HU with urate lowering therapy can also elicit acute gout attacks. This suggests a more complex role of HU in this context. Hence, we hypothesized that soluble uric acid (sUA) has immunomodulatory effects on neutrophil function during the immune response to monosodium urate (MSU) crystals.

Methods: Alb-creERT2;Glut9lox/lox and Glut9lox/lox control mice were injected with tamoxifen and placed either on a chow or acidogenic diet with inosine to induce HU with or without CKD. After 3 weeks, MSU crystals or vehicle were injected into air pouches or postcapillary venules in the cremaster muscle of transgenic mice. Leukocyte infiltration and the extent of inflammation were assessed by flow cytometry, intravital microscopy, and ELISA. Blood neutrophils were isolated from CKD stage G2-4 and G5D patients or healthy individuals and neutrophil transwell migration assays performed.

Results: We found that HU impaired leukocyte recruitment into MSU crystal-injected air pouches of mice with or without CKD. Intravital microscopy revealed that HU specifically reduced leukocyte adhesion, extravasation, and tissue inflammation. The CKD-mediated attenuation of MSU crystal-induced inflammation was fully reversible by treating HU with urate lowering therapy. In neutrophils isolated from healthy individuals, sUA diminished β2 integrin activation and expression, and hence impaired neutrophil migration ex vivo. This process was dependent on the intracellular uptake of sUA via the urate transporter SLC2A9/GLUT9. An impaired migratory capability was also observed in neutrophils from CKD patients.

Conclusions: We identify sUA as an endogenous modulator of innate immunity. HU modulates neutrophil migration by altering efficient β2 integrin activation via SLC2A9 in gouty arthritis related or unrelated to CKD. This process provides a molecular explanation for several previously unexplained clinical phenomena in the context of gout and renal failure.

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Serum Lysyl Oxidase Is a Potential Diagnostic Biomarker for Kidney Fibrosis
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Background: Kidney fibrosis is the ultimate consequence of advanced stages of chronic kidney disease (CKD); however, there are currently no reliable biomarkers or noninvasive diagnostic tests available for the detection of kidney fibrosis. Lysyl oxidase (LOX) promotes collagen crosslinking, and serum LOX levels have been shown to be elevated in patients with fibrosis of the heart, lungs and liver. However, serum LOX levels have not been reported in patients with kidney fibrosis. We explored whether serum LOX levels are associated with kidney fibrosis.

Methods: Overall, 202 patients with kidney disease underwent renal biopsy, scoring of kidney fibrosis and determination of the area of kidney fibrosis. LOX levels were measured in serum and in kidney tissues. We analyzed the association of circulating LOX and tissue LOX levels with the scores and areas of kidney fibrosis. LOX expression was also investigated in vitro and in vivo kidney fibrosis models.

Results: Serum LOX levels were higher in patients with kidney fibrosis than in those without kidney fibrosis (p<0.001) and higher in patients with moderate-severe kidney fibrosis than in patients with mild kidney fibrosis (p=0.001). Both serum LOX and renal tissue LOX levels correlated with the area of kidney fibrosis (r=0.74, p<0.001; r=0.899, p<0.001, respectively). ROC curve analysis of serum LOX levels showed an AUC of 0.80 (95% CI: 0.74 to 0.86). The optimal serum LOX level cutoff point was 235.34 μg/ml for the prediction of kidney fibrosis and 306.56 μg/ml for the prediction of moderate-severe renal fibrosis. LOX expression levels were significantly upregulated (2.3-, 2.6- and 6-fold, respectively) in vitro and in vivo interstitial fibrosis models.

Conclusions: Both serum LOX and tissue LOX levels correlated with the presence and degree of kidney fibrosis in patients with CKD. These results suggest that serum LOX level can be a novel potential diagnostic biomarker for kidney fibrosis and may further potentially serve as a stratified biomarker for the identification of mild and moderate-severe kidney fibrosis.

Funding: Government Support - Non-U.S.

Proximal Tubule Albumin Uptake: Potential Role for Endothelin System in Sickle Cell Disease Mice
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Background: Elevated plasma endothelin-1 (ET-1) reported in sickle cell disease (SCD) patients correlate with microalbuminuria, a major mortality risk factor in SCD. ET-1 contributes to glomerular and tubular injury in SCD, as evidenced by increased glomerular permeability to albumin and urinary excretion of tubular injury markers. Although selective ET receptor antagonism reduces albuminuria in humanized sickle cell (HbSS) mice, the mechanism of this action remains unclear. The aim of the study was to determine whether selective ET receptor antagonism prevents albuminuria by preserving the expression of tubular albumin-associated transporters in proximal tubule (PT) cells.

Methods: Male C57BL/6 or HbSS and genetic control (HbAA) mice were used to determine the effect of ET-1 on the expression of proximal tubule albumin trafficking mediators, such as megalin and NHE-3.

Results: Exposure of primary mouse PT cells to ET-1 (50μM) for 8h decreased megalin (53% reduction) and doubled NHE-3 expression. Pre-treatment with the ETα antagonist, BQ123 (1 μM), preserved megalin expression and had no effect on NHE-3. Moreover, selective ETα receptor blockade (BQ788, 1 μM) prevented ET-1 mediated increase in NHE-3 expression. Primary PT cells isolated from HbSS mice showed decreased megalin mRNA expression as well as protein abundance relative to HbAA PT controls. Ten-week treatment with selective ETα receptor antagonist (10mg/kg/day) preserved expression of megalin at control levels. There were no differences in NHE-3 mRNA expression in HbSS PT cells regardless the treatment. Interestingly, PT cells from HbSS cultured with HbSS plasma and ET-1 (10μM) had decreased NHE-3 protein abundance compared to non-treated cells.

Conclusions: These results potentially uncover a novel role for ET-1 in PT albumin handling. Our data suggest that PT ET-1 receptor signaling contributes to albuminuria in SCD.

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Phosphate and Fibroblast Growth Factor 23 Are Mediators of Lung Injury in CKD
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Background: Although well-documented in chronic kidney disease (CKD), the role of phosphate diet in pulmonary pathology is not widely known. Phosphorus, or phosphate in its oxidized circulating form, is normally removed from the body by healthy kidneys. CKD disrupts this process, leading to hyperphosphatemia in later stages. We have shown that fibroblast growth factor 23 (FGF23), a key regulator of phosphate metabolism, is elevated in inflammatory lung diseases; that increase in FGF23 contributes to unfavorable clinical outcomes. To improve outcomes for patients with concomitant CKD and pulmonary disease, we wanted to examine direct actions of phosphate and FGF23 and their potential underlying mechanisms.

Methods: For in vitro experiments, human lung fibroblasts were treated with 0 to 5 mM sodium phosphate. Expression levels of interleukin (IL)-8 and collagen (COL1)A1 were analyzed by qPCR. Cell counts and viability were quantified with trypan blue staining. In vivo, we placed C57BL/6 mice on a high phosphate (3%) diet to elevate serum phosphate levels in absence of kidney injury and administered bleomycin via oropharyngeal aspiration to generate an acute pulmonary inflammatory response. Serum FGF23 levels were measured by ELISA and serum analysis for phosphate and renal function were obtained. Expression of FGF23 pathway and inflammatory markers were analyzed in murine lung and kidney tissue using qPCR and western blotting.

Results: Augmented phosphate concentrations increased IL-8 and COL1A1 expression from human lung fibroblasts with a concomitant reduction in overall cell number. Serum FGF23 levels were significantly upregulated in mice on a high phosphate diet and further increased in these mice when exposed to bleomycin. Serum phosphate and creatinine levels were significantly elevated. High phosphate and bleomycin increased local FGF23 expression in murine lung tissue.

Conclusions: Upregulation of FGF23 in response to bleomycin during a high phosphate diet suggests that inflammation induced by primary lung injury is worsened by systemic elevation of serum phosphate levels. Our data suggest that in CKD, high serum phosphate levels may increase susceptibility and progression of lung injury. Our results indicate that the existence of a pulmo-renal crosstalk is exaggerating pulmonary injury.

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PO0622
APOL1 Risk Variants Mediate Increased Oxidative Phosphorylation Complexes Biogenesis and Mitochondrial Dysfunction
Mengyuan Ge,1 Gloria Michelle Ducasa,1 Shamroop Kumar Mallela,1 Shaoyi Liu,2 Hazel H. Szeto,2 Jeffrey B. Kopp,1 Flavia Fontanesi,1 Sandra M. Merscher,1 Alesia Fornoni,1 Katz Family Division of Nephrology and Hypertension/ Drug Discovery Center, University of Miami, Miami, FL; 2Social Profit Network Research Lab, Alexandria LaunchLabs, New York, NY; 1Kidney Disease Section, NIDDK, NIH, Bethesda, MD; 2Department of Biochemistry and Molecular Biology, University of Miami, Miami, FL.

Background: Susceptibility to focal segmental glomerulosclerosis (FSGS) in African Americans is associated with genetic variants of the Apolipoprotein L1 gene (APOL1) named G1 and G2. APOL1 risk variants (RV) are a major driver of mitochondrial dysfunction. The mitochondrial specific lipid cardiolipin (CL) interacts with oxidative phosphorylation (OXPHOS) complexes and plays an important role in the biogenesis of OXPHOS complexes. While APOL1 function was assessed in tagged and overexpressed systems, studies evaluating the functions of endogenous APOL1 protein are missing.

Methods: We studied mitochondrial function using human urinary podocyte-like epithelial cells (HUPECs) established from patients with FSGS carrying different APOL1 alleles. Protein and mRNA levels were measured by WB and quantitative PCR respectively. TEM was performed to study mitochondrial morphology. OXPHOS complexes were studied by BN-PAGE analysis followed by WB. To study how APOL1 RV contributes to mitochondrial dysfunction, we purified APOL1-G0/R4 protein using HeLa cells infected with lentivirus carrying the APOL1 G0/G1 under the CMV promoter, followed by protein-lipid overlay assay.

Results: The expression of endogenous APOL1 was decreased in HUPECs carrying RVs (G1/G2 HUPECs) when compared to G0/G0 carrying HUPECs. We observed reduced mitochondrial function in the presence of increased OXPHOS complexes in G1/G2 HUPECs. Using TEM, reduced mitochondrial matrix density and increased mitochondrial area were detected in G1/G2 HUPECs. Hyperbranched mitochondria in G1/G2 HUPECs were validated by the mRNA levels of mitochondrial fission and fusion proteins FIS1 and MFN1. The affinity of APOL1 G1 to CL was significantly higher than the affinity of APOL1 G0 to CL, when normalized to 6His tagged APOL1 expression. We found the mRNA levels of cardiolipin synthase (CRSL1) was significantly increased in G1/G2 HUPECs, which is consistent with the overexpression of OXPHOS complexes in G1/G2 HUPECs.

Conclusions: Our findings indicate that endogenous APOL1 RV expression in human podocytes is associated with mitochondrial dysfunction in the presence of increased OXPHOS complexes, and that APOL1 RVs interact with CL thus interfering with CL function in mitochondria.

Funding: NIDDK Support, Private Foundation Support

PO0623
Uncovering Genomic Alterations in DOCA-Salt Nephropathy Rats Treated with Finerenone
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Background: The aldosterone antagonist spironolactone has antibiotic effects but its clinical use is limited due hyperkalaemia, especially in patients with kidney disease. The mitochondrial specific lipid cardiolipin (CL) interacts with oxidative phosphorylation (OXPHOS) complexes and plays an important role in the biogenesis of OXPHOS complexes. While APOL1 function was assessed in tagged and overexpressed systems, studies evaluating the functions of endogenous APOL1 protein are missing. Our previous work has shown that mitochondrial dysfunction is increased in the presence of endogenous APOL1 RV expression in human podocytes. We have recently developed with pronounced antibiotic activity at doses which have only limited effect on the potassium homeostasis. The exact mitochondrial transcriptional targets of spironolactone and finerenone, however, remain unknown. Since there are more than 20 different members in the ATP synthase, single cell RNA and single cell epigenome (ATAC) profiling can help to define transcriptional targets.

Methods: We treated uninephrectomized, Sprague-Dawley rats injected with DOCA and salt with a high dose of finerenone (10mg/kg/d), spironolactone (50mg/kg/d), or vehicle. Blood pressure parameters included blood pressure, serum and urine electrolytes, albuminuria, renal and cardiac histology. Single nuclei suspensions was prepared from kidneys and hearts for single nuclear RNA and single nuclear open chromatin (ATAC) profiling using the 10X Genomics Chromium platform as well as bulk RNA sequencing.

Results: Fierenone and spironolactone resulted the same degree of blood pressure reduction. DOCA treated rats developed severe myocardial hypertrophy and focal vascuopathy, glomerulosclerosis and tubulointerstitial fibrosis. Fierenone significantly attenuated cardiac and renal histological damage. DOCA-salt rats developed marked albuminuria which was significantly attenuated by spironolactone and finerenone. Serum potassium was elevated in the spironolactone group at weeks 6, but it was unchanged compared to controls in the finerenone group. Bulk RNA-seq results revealed the reduced enrichment of immune response related transcripts in finerenone group compared with DOCA and spironolactone group. Single-cell RNA-seq and single cell epigenome profiling uncovered genomic alterations in different cell types in finerenone-treated kidneys.

Conclusions: Taken together, these findings demonstrated that treatment with finerenone protected from DOCA salt induced cardiac hypertrophy, glomerulosclerosis and tubulointerstitial fibrosis without a significant increase in serum potassium. Single cell epigenome analysis highlighted transcriptional targets of aldosterone, spironolactone and finerenone.

Funding: NIDDK Support, Commercial Support - Bayer AG

PO0624
Cell Type-Specific Chromatin Architecture Reveals Target Genes for Kidney Disease Risk Variants
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Background: Although GWAS studies have identified hundreds of genetic variants associated with kidney diseases, the identification of causal variants and their target genes are rather limited. Most of disease-associated variants locate in non-coding elements. The roles of these elements are cell type-specific. Additionally, due to the non-linear regulation of the elements, the identification of causal variants as well as their target genes is even more challenging.

Methods: In order to understand the genetic risk of kidney diseases, we generated a cell type-specific set of epigenetic landscape including transcription-centered 3D chromatin organization, histone modifications distribution and transcriptome with HiChIP, ChIP-seq and RNA-seq respectively, in kidney tubule cells. We further pinpointed the target genes for the variants and validated two target genes by CRISP techniques in zebrafish, demonstrating that SLC24A1 and MTX1 were indispensable genes to maintain kidney function.

Conclusions: Our results produce valuable multi-omic resource and establish a bioinformatic pipeline in dissecting functions of kidney diseases-associated variants based on cell type-specific epigenetic landscape.

PO0625
A Comprehensive Transcriptome Profiling of Adipocyte Na-K-ATPase Signaling in Uremic Cardiomyopathy by RNA Sequencing Analysis
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Background: Oxidant stress plays a key role in the development and progression of uremic cardiomyopathy. We have recently demonstrated that adipocyte dysfunction and uremic cardiomyopathy developed in partial nephrectomy mice model, were significantly ameliorated by adipocyte-specific expression of NaKide, an antagonist of Na-K-ATPase signaling. Hence, to better characterize the cellular transcriptome that are involved in various biological pathways associated with adipocyte function, we aim to explore the genomic approach in the present study, through RNAseq analysis.

Methods: For invitro studies, mouse adipocytes were subjected to oxidized LDL (oxLDL) or indexyl sulfate (IS) with or without pNaKide treatments. Partial nephrectomy was performed in C57Bl6 mice in order to produce experimental uremic cardiomyopathy. Specific expression of NaKide in adipocytes was achieved using a lentivirus construct driven by an adiponectin promoter. A complete RNAseq analysis was performed using DESeq2 R package in combination with packages to perform over-representation analysis (ORA) and gene set enrichment analysis (GSEA).

Results: Several gene subsets corresponding to various biological processes and molecular phenotype were differentially expressed in adipocytes in vitro oxLDL/IS treatments and in vivo PNx model. These genes, compared using GSEA analysis, showed that more than 75% of the Kegg pathways were similar among the in vitro treatments and in vivo model. The pathways that were common between in vitro and in vivo treatments, including adipogenesis, ROS signaling, inflammatory response and oxidative phosphorylation pathways, have profound impact on the pathogenesis of uremic cardiomyopathy. The overall analysis showed a widespread normalization of gene expression by pNaKide/adipose specific NaKide treatments that were altered in uremic cardiomyopathy.

Conclusions: The study provides a detailed genome-wide molecular information about adipocyte function in relation to uremic cardiomyopathy pathogenesis. These data provide deeper insight into the activation of pathways associated with adipocyte Na-K-ATPase signaling, which may be a viable clinical target for the prevention and treatment of uremic cardiomyopathy.

Funding: Private Foundation Support

PO0626
Transcriptomic Profiling Identifies Potential Mediators of Tubular Injury Sensitization of Glomeruli to Subsequent Secondary Hits
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Background: Previous studies have shown that even isolated mild tubular injury leads to more severe glomerular damage in response to subsequent injury. The responsible mediators for this sensitization are unknown.

Methods: Double transgenic male mice, Nep25/DTR (- expressing human CD25 receptor on podocytes and Diphtheria toxin receptor on proximal tubular cells) and Nep25/DTR (-5=5 group) were used. Tubular injury was induced by injecting diphtheria toxin, followed by uninurephrectomy (Nx) 4 weeks later and induction of glomerular injury
by LMB2 toxin (CD25 ligand) one week after Nx. Mice were sacrificed 4 weeks after LMB2. Glomeruli and tubules from Nx were separated by sieving technique, RNA was isolated from tubules and next generation RNA sequencing was performed.

**Results:** Histopathological analysis and urinary Kim-1 at Nx and sacrifice confirmed mild tubulointerstitial fibrosis at Nx in Nep25/DTR+ but not Nep25/DTR- mice, and more severe glomerulosclerosis and albuminuria at sacrifice after LMB2 in Nep25/DTR+ vs Nep25/DTR- mice. RNA sequencing revealed 283 differentially expressed genes between the groups, with 93 over-represented and 190 under-represented in Nep25/DTR- mice. STRING analysis of protein-protein interactions (PPI) based on cellular processes detected interactions between the Serpin family members: plasminogen activator inhibitor PAI-1 (Serpinel1), alpha-1-antitrypsin 1-2 (Serpinel1b), protein Z-dependent protease inhibitor (Serpinel1f) and complement C4b (C4b). In addition, members of the non-canonical Wnt signalling pathway Wnt-9a (Wnt9a) and VANG planar cell polarity protein 2 (Vang2) were over-represented and PPI of these genes was found. Quantitative real-time PCR confirmed numerically higher expression of all above-mentioned genes in Nep25/DTR- mice.

**Conclusions:** High-throughput RNA sequencing of isolated tubules with mild injury revealed potential novel mediators of glomerular sensitization to a subsequent injury. Further experimental validation of the effects of the identified molecules on glomerular injury are warranted.

**Funding:** NIDDK Support

**PO0627**

**A Novel Short ACE2 Variant Causes ACE Suppression and Fosters Ang 1-7 Formation in a Murine Model of CKD**

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**Background:** ACE2 is a monocarboxypeptidase that cleaves Ang II to form Ang-(1-7). It is a large molecule the administration of which leads to increased enzyme activity in plasma, but not in the urine or kidney tissue. We have developed a truncated form of ACE2 that has a longer half-life by fusing it with an Albumin-binding domain (ABD) and is still short enough to be filtered by the kidney. In this study we examined the impact of this novel variant of ACE2 on kidney RAS in a model of CKD.

**Methods:** We used a 5/6 Nephrectomy model in CD-1 mice. The ACE2-ABD was given 3 days post-ablation surgery and thereafter every 3-4 days (3 ug/g BW) for 5 weeks. Afterwards, mice were euthanized and kidneys collected for analyses of RAS components.

**Results:** Administration of ACE2-ABD resulted in increased plasma ACE2 activity (768 vs. 12 RFU/ug/hr, p=0.0001). In kidney lysates there was also an increase in ACE2 activity (32 vs. 22 RFU/ug protein/hr, p=0.03) and a decrease in ACE activity (7187 vs. 4006 RFU/ug protein/hr, p=0.0001). These changes in enzymatic activities were correlated with the highest amount of genes involved in cellular processes, biological regulation and metabolic processes. STRING analysis of protein-protein interactions (PPI) based on cellular processes detected interactions between the Serpin family members: plasminogen activator inhibitor PAI-1 (Serpinel1), alpha-1-antitrypsin 1-2 (Serpinel1b), protein Z-dependent protease inhibitor (Serpinel1f) and complement C4b (C4b). In addition, members of the non-canonical Wnt signalling pathway Wnt-9a (Wnt9a) and VANG planar cell polarity protein 2 (Vang2) were over-represented and PPI of these genes was found. Quantitative real-time PCR confirmed numerically higher expression of all above-mentioned genes in Nep25/DTR- mice.

**Conclusions:** A long-acting form of a short ACE2 variant fused with ABD given every 3-4 days resulted in sustained plasma ACE2 activity and an increase in kidney ACE2 activity associated with suppressed kidney ACE activity. These enzymatic changes provide a favorable kidney RAS profile with increased Ang-(1-7), which overall should be renoprotective.

**Funding:** NIDDK Support

**PO0628**

**Disruption of the H3K4 Methyltransferase MLL-1/Menin Complex Attenuates Renal Fibrosis Development by Inhibiting Epithelial-Mesenchymal Transition and Fibroblast Activation**

**Jianan Zou, Shougang Zhuang. Rhode Island Hospital, Brown University Rhode Island Hospital, Brown University Providence, China.**

**Background:** The MLL-1/menin was disrupted by MI-503 and/or siRNA in a murine model of renal fibrosis induced by unilateral ureteral obstruction (UUO), cultured mouse proximal tubular cells and fibroblasts exposed to serum and transforming growth factor β1 (TGFβ1). Protein expression or activation was determined by immunofluorescent microscopy and immunoblot analysis.

**Methods:** The MLL-1/menin was disrupted by MI-503 and/or siRNA in a murine model of renal fibrosis induced by unilateral ureteral obstruction (UUO), cultured mouse proximal tubular cells and fibroblasts exposed to serum and transforming growth factor β1 (TGFβ1). Protein expression or activation was determined by immunofluorescent microscopy and immunoblot analysis.

**Funding:** NIDDK Support, Other NIH Support - National Natural Science Foundation of China
Transcriptomic Profiling of Thick Ascending Limb Cells In Vivo Reveals the Complex Network of Genes Regulated by Uromodulin
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Background: Tamm-Horsfall Protein (THP or Uromodulin, gene: Umod) is a protein uniquely made in the kidney by cells of the thick ascending limbs (TAL) of the loop of Henle. We previously established that THP has protective biological functions. Furthermore, THP production is decreased with chronic kidney disease (CKD). It was suggested that the promoter region of the Umod can regulate other genes. THP deficiency itself could alter the expression of other genes. Here, we used an unbiased approach to study the effect of a deletion in the Umod promoter/gene and the resultant THP deficiency on the transcriptomic profile of TAL cells in vivo.

Methods: THP-/- mice resultant from deletion of exons 1-4 and part of the Umod promoter were used, along with THP+/- controls. Immuno-fluorescence guided laser microdissection was performed to isolate TAL cells from the medulla of kidneys of THP+/- and THP-/- mice. After RNA extraction, next generation RNA sequencing and transcriptomic analysis was performed.

Results: The transcriptomic profile of medullary TAL cells was comprehensively defined in vivo. 85% of the top 250 expressed genes were common between THP+/- and THP-/- TAL cells. Overall, 33 protein-coding genes, including Umod, were differentially expressed (FDR<0.05). These encompassed genes with a variety of functions such as immunomodulation (Erk1, Gp2), cytoskeletal/extracellular matrix fibers (Lama1, Ctnnb1) and signal transduction (Camk2b, Pirrn2). One down-regulated gene was a direct neighbor to the Umod locus (Gp2) on chromosome 7. However, many other affected genes were on different chromosomes. Bioinformatic analysis revealed that THP deficiency is associated with significant clustering of genes involved in connective tissue formation and activation or dysfunction of molecular mechanisms that could lead to fibrosis.

Conclusions: We delineated a comprehensive transcriptomic profile of TAL cells in vivo from mouse kidneys. Although highly expressed genes in TAL may not be altered by THP deficiency, many close and distant genes are regulated by the Umod locus or altered by the absence of THP. The absence of THP may also prime the TAL cells towards a fibrosis program. These findings may contribute to understanding the pathogenesis of CKD progression.

Funding: NIDDK Support, Veterans Affairs Support

Lipid Metabolic Profiling of Ex Vivo Isolated Glomeruli as a Screening Platform for Modelling Glomerular Metabolic Dysfunction During Renal Disease
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Background: Dysregulated renal metabolism is a hallmark of loss of function in CKD. It is established that changes in tubular metabolism impact tubular functionality during progression of CKD. However, lipid metabolism in the glomerulus during CKD remain poorly described. Here, we use Isolated Glomeruli (IRG) to study lipid metabolism for metabolic drug discovery in kidney diseases.

Methods: Sprague Dawley rat glomeruli were isolated by differential sieving. We used two disease inducers: Adriamycin 1mM (ADR) and AngiotensinII 100nM (AngII) for 24h. To probe metabolic activity, we used an LC-MS approach to quantify uptake and excretion rates of relevant metabolites in culture media, and to measure intracellular metabolites and lipids.

Results: We developed a new cultivation protocol for IRG, using organoids media and shaking platform to maximize the biological activity. Metabolic and lipidomic profiles of IRG were monitored up to 150h. We saw significant metabolic activity for a wide range of metabolites: Uptake and excretion rates rapidly changed during the first 24h of culture, after which they declined. Metabolic rates for glucose, glutamate and alanine were comparatively stable. Following treatment with AngII or ADR glomeruli exhibited metabolic changes after 24h: AngII reduced asparagine uptake, and induced trends towards lower substrate uptake consistent with reduced metabolic activity. Both ADR and AngII perturbated intracellular metabolic levels: glucose nadir (-17%); glucose (17%), increase in NAD+ (209%), which suggest alterations in pentose phosphate pathway. Multivariate analysis revealed differentially responding lipid clusters: specifically, significant abundance and saturation ratio increases of intracellular FFA, including stearate (+34%), oleate (+102%) and arachidonic (+197%), as well as the depletion of several phosphatidylcholine and phosphoethanolamine species following AngII, which have been implicated as renal injury markers and/or relevant to renal injury protection.

Conclusions: Our results show alterations in lipid metabolism after IRG stimulation with AngII and ADR after 24h. We propose IRG/lipid metabolome as a novel platform tool for understanding lipid signalling and improving CKD drug discovery.

Funding: Commercial Support - AstraZeneca

Study on the Mechanism of Microinflammation in Uremia Caused by Lactobacillus Activation of Intestinal Macrophages by Mingle Lingshuang Sun, Hongli Jiang. First Affiliated Hospital of Medicine School, Xi’an Jiaotong University, Xi’an, China.

Background: My previous studies have found that Intestinal macrophages in the uremic rats are polarized towards a proinflammatory phenotype and assist bacterial translocation resulting in microinflammation. However, it is still unclear what kind of mechanism activates intestinal macrophages in uremia.

Methods: Male Sprague-Dawley rats were randomly divided into two groups: sham, uremia. Immunohistochemistry was used to analyze the expression of macrophage-inducible C-type lectin (Mincle). RT-PCR and western blot were employed to assess the mRNA and protein expression of toll-like receptor 4 (TLR4).

Results: Our RCT study found that the number of Lactobacilli in the intestines of patients with end-stage diabetic nephropathy was significantly higher than that in non-diabetic patients. The plasma levels of endotoxin, CRP, IL-6, and TNF-a in the uremia group were greater than those in the sham group (p<0.05; Table 1). Compared with the sham group, the uremia group exhibited macrophages with higher staining intensities for Mincle and higher mRNA and protein expression of TLR4(Figure1-2).

Conclusions: The solution to this scientific problem will not only clarify the molecular mechanism of intestinal bacteria in controlling the activation of intestinal macrophages, but also to clarify the micro-inflammation state of uremia.

Funding: Government Support - Non-U.S.

Table 1. Body weight, hematocrit, and blood chemistry results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>n</th>
<th>Body weight (g)</th>
<th>Hematocrit (%)</th>
<th>Urea (mmol/L)</th>
<th>Creatinine (µmol/L)</th>
<th>Lipiduria (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Shaker</td>
<td>10</td>
<td>55.0 ± 5.6</td>
<td>43.7 ± 2.3</td>
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<td></td>
<td>ADR</td>
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<td>53.0 ± 5.8</td>
<td>43.0 ± 2.5</td>
<td>15.0 ± 2.5</td>
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</tr>
<tr>
<td></td>
<td>AngII</td>
<td>10</td>
<td>56.0 ± 5.5</td>
<td>43.5 ± 2.4</td>
<td>16.0 ± 2.0</td>
<td>1.10 ± 0.05</td>
<td>7.0 ± 1.9</td>
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</tbody>
</table>

Data are presented as the mean ± SD.

*p < 0.05 vs. the sham group
PO0632
Angiotensin II Type 1a Receptor Loss Ameliorates Chronic Tubulointerstitial Damage After Renal Ischemia Reperfusion
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Background: Although angiotensin II (Ang II) type 1 receptor blocker was reported to attenuate chronic tubulointerstitial damage (TID) after renal ischemia reperfusion (IR), its effect is limited. The aim of this study is to reveal whether suppressed activation of angiotensin II type 1a receptor (AT1a) ameliorates severe chronic tubulointerstitial damage (TID) after renal ischemia reperfusion (IR).

Methods: To induce severe chronic TID after IR, unilateral renal ischemia for 45 min was performed via clamping of right renal pedicle using cerebral aneurysm clip in AT1a knockout homo (AT1a−/−) male mice and wild type (AT1a+/+) male mice. Right and left kidneys were removed at 3, 28 and 70 days postischemia. Left kidneys were used as control. Furthermore, another AT1a−/− mice were administered hyalurazeline to maintain the same levels of systolic blood pressure (SBP) as the AT1a+ mice because the SBP levels of the AT1a+ mice were significantly lower compared to the AT1a−/− mice.

Results: Acute tubular necrosis in IR-kidneys of both AT1a+ mice and AT1a−/− mice was observed at 3 days postischemia, and the degree was significantly more severe in the IR-kidneys of AT1a−/− mice than in the IR-kidneys of AT1a+/+ mice. Conversely, the degrees of both interstitial fibrosis at 28 and 70 days postischemia and proximal tubular loss at 70 days postischemia were significantly attenuated in the IR-kidneys of AT1a−/− mice compared to the AT1a+/+ mice. While marked renal atrophy at 70 days postischemia was induced in the AT1a+ mice, such a development was not provoked in the AT1a−/− mice. Although the administration of hyalurazeline in the AT1a−/− mice mildly attenuated the degree of TID at 70 days postischemia, the degree of the AT1a−/− mice was significantly greater compared to the AT1a+ mice. Because renal expression levels of angiotensin (A1/3) protein at 28 days postischemia was significantly higher in the AT1a+ mice compared to the AT1a−/− mice, renat angiotensin-(1-7) may contribute to amelioration of chronic TID after IR in the AT1a+ mice.

Conclusions: Early administration of Ang II type 1 receptor blocker in recovery phase after AKI may be useful for prevention of AKI-to-CKD transition.

Funding: Private Foundation Support

PO0633
Anti-Interleukin 22 Antibody Relieves Angiotensin II-Induced Renal Injury in Mice Through Inhibiting NLRP3 Inflammasome Activation
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Background: Interleukin-22 (IL-22) is considered as a proinflammatory cytokine and participates in the pathogenesis of autoimmune and inflammatory diseases. Previously, we found that serum IL-22 increased significantly in hypertensive renal damage patients, and IL-22 was positively correlated with renal damage. The aim of this study was to investigate whether anti-IL-22 antibody exerts renoprotective effect by inhibiting NLRP3 inflammasome activation in angiotensin II (Ang II) induced hypertensive renal damage mice.

Methods: Ang II was infused subcutaneously at a rate of 1.5 mg/kg/d to C57BL/6 mice for 28 days to establish the hypertensive model. One day after modeling, mice were randomly divided into five groups: control, Ang II, Ang II+rIL-22, Ang II+anti-IL-22 mAb. After 28 days of treatment, mice were sacrificed, serum, kidney, liver and lung were collected for further analysis. Proteinuria, Serum creatinine (Scr) and renal histopathology were evaluated by western blot. Protein expressions of pro-inflammatory and pro-fibrotic mediators [CXCL9, CXCL10, MCP-1, IL-6, TGF-β] were detected by western blot in kidney and liver. The renal pathological changes were evaluated by H&E staining, Masson's trichrome and elastic van Gieson staining.

Results: Treatment with anti-IL-22 mAb significantly decreased proteinuria excretion, Scr and renal pathological changes. In addition, anti-IL-22 mAb decreased protein expressions of pro-inflammatory and pro-fibrotic mediators in kidney and liver.

Conclusions: Anti-IL-22 mAb therapy ameliorated proteinuria excretion, Scr and renal pathological damage in mice with established hypertensive renal injury. The possible renoprotective mechanism involves anti-IL-22 mAb inhibits IL-22/NLRP3 inflammasome activation and ameliorates renal fibrosis.

Funding: Government Support - Non-U.S.

PO0634
PD-1 Regulates Group 3 Innate Lymphoid Cells in Renal Fibrosis
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Background: Group 3 Innate Lymphoid Cells (ILC3) belong to a new family of innate cells, participating in lots of inflammatory and fibrotic diseases. However, limited information exists on the molecular mechanisms regulating these cells. Here, we investigated the expression and function of the immune checkpoint programmed cell death-1 (PD-1) in ILC3 during renal fibrosis.

Methods: Unilateral ureteral obstruction (UIO)-induced renal injury tested subsets of ILC3 activities in immune responses and tissue fibrosis. Kidney and intestine were collected to define the frequency, localization and characterization of PD-1+ ILC3. Loss/gain-of-ILC3 in U/O mice were designed to investigate their roles in renal fibrosis progression. And the fibrogenic effects of ILC3 and the regulatory activity of PD-1 were determined by in vitro co-culture experiments.

Results: ILC3 were accumulated rapidly in fibrotic kidneys, with surrounding by increasing number of active myofibroblasts, and more interestingly, coincided with a robust depletion from the intestines of mouse models, suggesting a functional recruitment of ILC3 after kidney injury. Moreover, fibrosis was associated with an increase of PD-1 expression in ILC3s, and up-expression of PD-1 ligand, PD-L1 was also detected in fibrotic kidney, suggesting a possible involvement of PD-1/PD-L1 pathway. Adoptive transfer of purified intestinal ILC3 into U/O mice significantly enhanced renal fibrosis than those with PBS, whereas PD-1-deficient ILC3 protects kidney from fibrosis. Notably, mice that lacked ILC3 exhibited reduced inflammatory infiltration and decreased fibroblast activation. In vivo studies, direct co-culture of WT-ILC3 with primary renal fibroblasts exacerbates inflammatory response and extracellular matrix production (ECM), which could be blocked by the treatment with neutralizing anti-IL-17A and anti-IL-22 antibodies. Yet co-cultured with PD-1-deficient ILC3 displayed reduced fibrotic activity.

Conclusions: Our findings provided the first evidence that during renal fibrosis, PD-1/PD-L1 axis might play a regulatory role in ILC3 migration and fibrogenesis via producing pro-fibrotic cytokines IL-17A and IL-22.

Funding: None

PO0635
Interaction Between the Na-K-ATPase and CD40 Signaling in Proximal Tubule Epithelial Cells (PTECs) Contributes to Renal Inflammation and Fibrosis
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Background: We have demonstrated that signaling through the Na-K-ATPase-c1 subunit/c-Src kinase (NKA-c1/c-Src) complex and activation of the pro-inflammatory receptor, CD40 induce renal inflammation and fibrosis in both clinical and experimental models of ischemic and chronic kidney disease (CKD). Circulating cardiotonic steroids (specific ligands of Na-K-ATPase) are significantly elevated in CKD that not only stimulate NKA-c1/c-Src signaling, but also regulate CD40 signaling by upregulation of CD40 expression in PTECs. Furthermore, soluble CD40 ligand (sCD40L)-stimulated CD40 signaling in PTECs is dependent on NKA-c1/c-Src signaling. However, the interplay between Na-K-ATPase and CD40 signaling-induced renal inflammation and fibrosis has not been thoroughly investigated.

Methods: RNA sequencing was performed on pig PTECs with and without a functional NKA-c1/c-Src signaling complex (Ly-22 cells and Ly-22r cells, respectively) following treatment with sCD40L (100ng/ml) for 24hrs. In pig PTECs LCC-PK1 cells treated with the cardiotonic steroid telocinobufagin (TCB), immunoprecipitation was performed to detect protein-protein interaction.

Results: Treatment with sCD40L in Ly-22r cells demonstrated a significant increase in gene expression of pro-inflammatory and pro-fibroictic mediators (CXXCL9, CXXCL10, IL1R1, complement C3, and COL1A2 [all > 5-fold increase]) compared to Ly-22r cells. In LCC-PK1 cells, short-term TCB treatments (up to 1 hr) stimulates interaction between NKA-c1 and CD40 that presents under resting conditions. Long-term TCB treatment (24 hr) still shows the NKA-c1 and CD40 interaction, but reduced NKA-c1 and CD40 interaction was also observed in comparison to control, suggesting a possible endocytosis of NKA-c1 (by the cardiotonic steroid) and CD40.

Conclusions: In renal proximal tubular cells, CD40-induced pro-inflammatory and pro-fibrotic signaling is dependent on the NKA-c1/c-Src complex, and there is an
interaction between NKA-α1 and CD40 that was enhanced by activation of the NKA-α1 (c-Src signaling) A regulation through expression level and/or endocytosis of NKA-α1 and CD40 might be involved to control signaling strength.**

**Funding:** NIDDK Support

PO0636

**Soluble Uric Acid, a Negative Regulator of Monocyte Activation in Innate Immunity**

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**Background:** While monosodium urate (MSU) crystals are known to trigger acute inflammatory responses in gouty arthritis, soluble uric acid (sUA) in this context is discrepancy. We hypothesized that diverse sUA preparation methods account for this discrepancy and that a novel animal model with clinically relevant levels of asymptomatic hyperuricemia (HU) and gouty arthritis can ultimately clarify this issue.

**Methods:** Soluble UA was prepared either by pre-warming or solubilized with NaOH. THP-1 cells or CD14+ monocytes from patients with HU and healthy individuals were pre-incubated with sUA prior to stimulation with MSU crystals or LPS. Intracellular sUA uptake via urate transporters was quantified using siRNA technology. In vivo, Alc-aE2/CreERT2/ Glut9 b/c mice were injected with tamoxifen and placed on a chow diet with inosine to induce HU. After 3 weeks, MSU crystals or vehicle were injected into air pouches, and leukocyte infiltration and the extent of inflammation were assessed by flow cytometry, RT-PCR, ELISA.

**Results:** We found that pre-warmed UA created erroneous results because of microcrystal contaminants triggering IL-1β release. Solubilizing UA with NaOH avoided such artifact. This microcrystal-free preparation suppressed LPS- or MSU crystal-induced monocyte activation, a process dependent on the intracellular uptake of sUA via the urate transporter SLC2A9/GLUT9. CD14+ monocytes isolated from HU patients were less responsive to inflammatory stimuli compared to monocytes from healthy individuals. Treatment with plasma from HU patients impaired the inflammatory function of CD14+ monocytes, an effect fully reversible by removing sUA from HU plasma with rasburicase. Moreover, Alc-aE2/CreERT2/ Glut9 b/c mice with HU (serum UA of 9-11mg/dL) showed a suppressed inflammatory response to MSU crystals compared to Glut9 b/c controls without HU.

**Conclusions:** We unraveled a technical explanation for discrepancies in the published literature on the role of sUA and identify HU as an intrinsic suppressor of innate immunity, where sUA modulates the capacity of monocytes to respond to danger signals. Thus, sUA is not only a substrate for the formation of MSU crystals but also an inhibitor of sterile inflammation and may explain several clinical observations in the context of gout and CKD.

**Funding:** Government Support - Non-U.S.

PO0637

**PP2Ac Promotes Macrophage Accumulation and Activation to Accelerate Tubular Cell Death and Kidney Fibrosis Through Regulating Rap1 and TNFα Production**

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**Background:** Macrophage accumulation and activation play an essential role for kidney fibrosis, the underlying mechanisms remain to be explored.

**Methods:** Analyzing the kidneys of patients and animal models with kidney fibrosis. Generating the mice with macrophage PP2Ac ablation.

**Results:** We observed a significantly increased induction of PP2Ac in macrophages. We then generated mice with macrophage-specific deletion of PP2Ac. These mice developed less renal fibrosis as indicated by less macrophage accumulation, tubular atrophy or extracellular matrix deposition. In cultured cells, the deficiency of PP2Ac in macrophages resulted in decreased cell motility by inhibiting the activity of Rap1. Furthermore, TNFα production was downregulated in macrophages with PP2Ac deficiency and co-culture of PP2Ac-deficient macrophages and renal tubular cells resulted in less tubular cell death, which was due to decreased TNFα production via phosphorylation of STAT3 in macrophages.

**Conclusions:** This study shows that PP2A promotes macrophage accumulation and activation, hence accelerating tubular cell death and kidney fibrosis through regulating Rap1 and TNFα production.

**Funding:** Government Support - Non-U.S.

PO0638

**Investigating LOX and Its Role in AT1R-β-Arrestin Biased Signaling Pathway-Induced Renal Interstitial Fibrosis**

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**Background:** We studied the downstream and mechanism of β-arrestin signaling in renal fibrosis process and the role of lysyl oxidase (LOX) in the AT1R-β-arrestin signaling. A regulation through expression level and/or endocytosis of β-arrestin signaling was studied in normal rat kidney tubule epithelial cells (NRK-52E) treated with SII in vitro. BAPN or placebo was administered during ischemia reperfusion (IR)-induced fibrosis progression. Collagen crosslinking and fibrosis progression were assessed histologically and biochemically.

**Results:** The mRNA and protein levels of β-arrestin-1 and β-arrestin-2 were significantly upregulated in renal fibrosis model both in vitro and in vivo. SII activated the ERK-STAT3 PY705 but not STAT3-TR727 in nucleus of NRK-52E cells, which effects were abolished when transfection of siRNA targeting β-arrestin-1 and β-arrestin-2 or pretreated with PD98059 (MEK inhibitor). LOX was strongly induced in fibrotic kidney and NRK-52E cells treated with SII. Active LOX significantly increased collagen crosslinking. In established IR-28d renal fibrosis, LOX inhibition promoted fibrosis progression with a 25% decrease insoluble collagen. Gene silencing of β-arrestin-1 or -2 or STAT3 significantly inhibited SII-induced LOX expression in vitro. Besides, chronatin immunoprecipitation (ChIP) assay clearly demonstrating the interaction between STAT3 and the LOX promoter, which indicated LOX is a direct target gene of β-arrestins-STAT3 signaling.

**Conclusions:** The ERK-STAT3 was downstream of AT1R-β-arrestins, ERK entered the nucleus and activated STAT3-PY705. LOX mediates collagen crosslinking and fibrotic matrix stabilization during renal fibrosis via the AT1R-β-arrestins-ERK-STAT3-PY705 signaling. By blocking this profibrotic pathway, therapeutic LOX inhibition attenuates the fibrosis and suggesting target the LOX has significant potency for the treatment of patients with fibrotic kidney disorders.

**Funding:** NIDDK Support

PO0639

**Downregulated Endothelial JMJD3 Accelerates Neointimal Hyperplasia of Arteriovenous Fistula in CKD**

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**Background:** Epigenetic changes are involved in vascular remodeling. The histone demethylase, JMJD3, is a transcriptional co-activator that promotes endothelial regeneration. Despite the importance of JMJD3 in maintaining endothelial function, its role in neointima formation in AVFs remains unknown.

**Methods:** Mice with JMJD3 specific knockout (KO) in ECs was generated. CKD and AVF models were created in Wild type and JMJD3 EC-specific KO mice. Evans blue, immunostaining assays were used to characterize JMJD3 expression and vascular pathology. Mouse primary ECs and VSMCs were isolated to study the signaling pathways that regulate JMJD3 expression and endothelial mesenchymal transition (EndMT). The changes found in mouse AVFs were assessed in AVFs from ESRD patients.

**Results:** JMJD3 expression was downregulated in endothelium of CKD mice. Specific KO of JMJD3 in EC stimulated endothelial barrier dysfunction, EndMT, and inflammatory cells infiltration in AVFs. There were more VSMC proliferation and collagen deposition in AVFs created in JMJD3 KO mice vs. that of in WT mice. Specific KO of JMJD3 in EC accelerated AVF remodeling. EC proliferation was associated with endothelial dysfunction, EndMT, and ECM deposition plus neointimal hyperplasia. Remarkably, endothelial expression of Hes1 in AVFs from ESRD patients was correlated with the decreased JMJD3 level.

**Conclusions:** These findings demonstrate that TGFβ1-Hes1-JMJD3 signaling exist in ECs which epigenetically regulates EC differentiation and barrier function leading to neointimal hyperplasia of AVF in CKD.

**Funding:** Government Support - Non-U.S.
Renal Macrophage Infiltration Precedes Macrophage to Myofibroblast Transition and C-T Cell Recruitment Following Repeated Low-Dose Cisplatin Treatment

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Background: Cisplatin is a commonly used chemotherapeutic agent with dose-limiting nephrotoxicity. 30% of patients who receive cisplatin develop acute kidney injury (AKI), which significantly increases the risk of developing renal fibrosis and chronic kidney disease (CKD). There are currently no therapies approved to prevent or treat cisplatin-induced kidney injury (CDDP-KI) and fibrosis. Other models of renal fibrosis have demonstrated that macrophages can play a pro-fibrogenic role by differentiating into myofibroblasts, the main effector of fibrotic development. Macrophage to myofibroblast transition (MMT) is proposed to occur when bone marrow derived M2 macrophages undergo chronic TGFβ stimulation. We hypothesize that cisplatin promotes fibrosis and CKD development through stimulating chronic macrophage activity and MMT in the kidney.

Methods: We used a clinically relevant, repeated low dose model of CDDP-KI to characterize the immune response and MMT in the kidney following cisplatin treatment.

Results: Flow cytometric analysis revealed significantly increased numbers of renal infiltrating macrophages and F4/80+ cells from rats treated with repeated low doses of cisplatin after four doses of cisplatin. These populations remained elevated above vehicle treated controls after a 6-month age-out. At the four dose timepoint, we observed an increase in CD206+ F4/80+ cells and Arg-1 mRNA, indicating M2 polarization. We also identified a population of F4/80+ CD206+ eSMA+ cells present in the kidney, suggesting MMT is occurring. Interestingly, at the 6-month timepoint renal CD4+ and CD8+ T cell populations remained significantly elevated in cisplatin-treated mice compared to vehicle treated controls.

Conclusions: These studies provide insight on how the immune response to CDDP-KI can promote CKD via infiltration of bone marrow derived macrophages and subsequent M2 polarization and MMT. These early events orchestrate an immune response that continues up to 6-months after cisplatin treatment. Therefore, targeting macrophages could be a potential strategy for preventing the AKI to CKD transition triggered by cisplatin.

Funding: NIDDK Support

Microvascular Loss and Remodeling in Human Kidneys Distal to Severe Atherosclerotic Renovascular Disease

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Background: Renovascular disease (RVD) may induce hypertension and kidney injury, but its effect on the microcirculation of the post-stenotic human kidney remains unclear.

Methods: Kidneys were collected from patients with RVD undergoing unilateral nephrectomy due to refractory hypertension (n=5) and deceased donor kidneys (DK) (n=5). Injury to the microcirculation was assessed by counting tubules containing small arterioles (PTC), medium-sized arterioles (MSA), and capillaries at 243× magnification. Angiopoietin-1 (Ang-1) expression was analyzed by qRT-PCR and Western Blot. Vascular density of small (0.02-0.2 mm) and large (0.3-0.5 mm) microvessels (MV) was determined by immunofluorescence and optical densities were measured. Vascular tortuosity was measured by the ratio of the arc length to the straight line distance between endpoints of the vessels.

Results: Angiopoietin-1 expression were unchanged. Ang-1 expression was inhibited by atherosclerotic RVD, compared to DK. Ang-1 expression was significantly reduced (p<0.05), whereas VEGF (p=0.9) and FLK-1 (p=0.2) protein or gene expression were unchanged. Angiopoietin-1 expression, whereas VEGF (p=0.9) and FLK-1 (p=0.2) protein or gene expression were unchanged.

Conclusions: Human RVD kidneys develop marked MV remodeling and loss, particularly of PTC and medium-size MV. Angiopoietin-1 upregulation may promote new PTC formation, but fails to offset overwhelming MV loss distal to severe RVD. These findings underscore the major component of microvascular injury in the development of ischemic kidney disease.

Funding: NIDDK Support

Combined Efficacy of the Novel Nonsteroidal and Selective Mineralocorticoid Receptor Antagonist Finerenone and the SGLT2 Inhibitor Empagliflozin in a Non-Diabetic Cardiorenal Rat Model

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Background: Finerenone and SGLT2 inhibitors have demonstrated clinical benefits in CKD patients with T2D. Efficacy of finerenone and SGLT2i, especially in combination, is unknown in non-diabetic kidney disease.

Methods: Cardiorenal morbidity and mortality was studied in hypertensive and proteinuric L-NAME (20 mg/L) treated renin-angiotensin (mRen2)27 rats. Rats (10-11 weeks old female, n=13-17/group) were treated once daily orally for up to 7 weeks with placebo, finerenone (1 and 3 mg/kg), empagliflozin (3 and 10 mg/kg), or a combination of the respective low doses. Key outcome parameters included mortality, blood pressure, proteinuria, kidney histology and gene expression.

Results: Placebo-treated rats demonstrated a 50% mortality rate over the course of 7 weeks (figure). Drug treatment resulted in variable degrees of survival benefit, most prominent and statistically significant in the low dose combination group (figure). Low dose combination revealed an early, sustained and efficacious proteinuria reduction (~86%, p<0.05) and was highly efficient on renal histology parameters. Monotherapies of finerenone (~27% @ 1 mg/kg, p = n.s.; ~87% @ 3 mg/kg, p<0.05) and empagliflozin (~38% @ 3 mg/kg, p = n.s.; ~64% @ 10 mg/kg, p = n.s.) dose-dependently reduced proteinuria with a comparable protection from renal lesions at higher dosages. Treatment with finerenone and the combination significantly decreased systolic blood pressure while empagliflozin alone and in combination acted strongly glucosoric.

Conclusions: Both, MRA by finerenone and SGLT2i by empagliflozin confer renal protection in preclinical non-diabetic, hypertensive kidney disease. Combination of these two modes of action at low dosages revealed efficacious reduction in proteinuria and mortality indicating a strong potential for combined clinical use in respective cardiorenal patient populations.

Funding: Commercial Support - BAYER AG
**PO0643**

**Novel Small Molecule Inducers of ABCA1-Dependent Cholesterol Efflux**

**Preserve Renal Function in Mouse Models of FSGS and Alport Syndrome**

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**Background:** Pathological accumulation of cholesterol in podocytes is associated with the progression of kidney disease. Depletion of podocyte cholesterol by non-specific means, with agents such as cycloextrim, or by specific upregulation of ABCA1-mediated cholesterol efflux, have shown promise in renal disease models, but have not progressed in clinical development.

**Results:** The effects of novel compounds (Cpd A and G) that induce ABCA1-mediated cholesterol efflux were evaluated in comparison to LXR agonists in differentiated human podocytes in vitro. In vivo efficacy studies of Cpd A & G were conducted in mouse models of proteinuric kidney disease (Adriamycin-induced nephropathy and Alport Syndrome).

**Results:** ABCA1-mediated cholesterol efflux was significantly increased in podocytes by all agents. While an LXR agonist resulted in accumulation of ABCA1 at the plasma membrane, it also induced significant accumulation in microsomal fractions. In contrast, Cpd A & G induced the redistribution of ABCA1 from intracellular sites to the plasma membrane. In A PRO and podocytes challenged for 6 weeks with Cpd A and G, reduced ACR by 8 and 30-fold, respectively, compared to controls. In CoA3A knockout mice, Cpd G significantly reduced ACR, serum creatinine and blood urea nitrogen, as well as prevented weight loss and mortality vs. control mice. We found that increased accumulation of cholesterol esters in kidney (30% at 4 months) and mRNA for ATG5, an autophagy protein, strongly correlated with albuminuria. In both the FSGS and Alport mouse models, Cpd G significantly reduced lipodropplet formation and cholesterol ester content in kidney cortex.

**Conclusions:** In summary, we describe the effects of novel small molecule drugs in renal disease models that induce ABCA1-mediated cholesterol efflux independently of LXR. This may represent a promising new therapeutic strategy for the treatment of kidney diseases and disorders of cellular cholesterol homeostasis.

**Funding:** NIDDK Support, Commercial Support - Hoffman-La Roche, Boehringer Ingelheim, Private Foundation Support

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**PO0644**

**Metformin Therapy Is Able to Halt the Progression of Established CKD in Rats**

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**Background:** Metformin, first-line drug for type-2 diabetes, exerts benign pleiotropic actions beyond its prescribed use and emerging data show protective effects against the development/progression of renal impairment. Current treatment strategies for chronic kidney disease (CKD) mainly focus on controlling important risk factors, while effective treatment directly targeting the kidney is lacking. However, in 2019, the FDA approved the use of the sodium-glucose co-transporter-2 (SGLT2) inhibitor, canagliflozin, to treat diabetic nephropathy. Here, the ability of metformin to attenuate the progression of established, non-diabetic CKD was investigated and compared to canagliflozin.

**Methods:** Adipone-mediated CKD rats (n=86) were assigned to different treatment groups to receive 200 mg/kg metformin, 4 or 5 weeks after the start of the adenine diet (0.25%), i.e. after CKD had developed, or 25 mg/kg canagliflozin 4 weeks after the start of the diet, by daily oral gavage, for 4 weeks. Each treatment group was compared to a vehicle (1% carboxymethylcellulose) group.

**Results:** Serum creatinine levels dramatically rose in vehicle-treated CKD rats: from 0.7 ± 0.1 mg/dL (week 0) to 1.5 ± 0.1 mg/dL (week 4), 2.6 ± 1.2 mg/dL (week 5) and further to 6.2 ± 0.3 mg/dL (week 8) and 4.8 ± 1.1 mg/dL (week 9). Canagliflozin treatment did not alter the increase in serum creatinine as indicated by serum creatinine levels at week 5 (5.8 ± 0.4 mg/dL). In contrast, metformin treatment almost completely prevented the increase from week 4 or 5 on, as indicated by the serum creatinine levels after 8 (2.0 ± 0.5 mg/dL) and 9 (2.9 ± 0.5 mg/dL) weeks (p<0.05 vs. vehicle). Canagliflozin treatment did not alter the tubulointerstitial area percentage, while this parameter was 33% lower at week 8 and 23% lower at week 9 in metformin-treated CKD rats compared to vehicle-treated (p=0.05 vs. vehicle). Further histological examination revealed more tubular proliferation (PCNA positive cells) and less interstitial inflammation (CD45 positive cells) in metformin-treated rats compared to vehicle-treated animals.

**Conclusions:** In conclusion, metformin is able to attenuate the progression of pre-existing, non-diabetic CKD. Our data do not present new evidence for a beneficial effect of canagliflozin on progression of non-diabetic CKD.

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**PO0645**

**The Novel Soluble Guanylyl Cyclase (sGC) Activator Runcaciguat Attenuates Hypertensive Cardiorenal Rat Diseases**

Aynes M. Benardau, Johannes-Peter Stasch, Michael G. Hahn, Jutta Meyer, Jan R. Kraehling, Frank Eitner, Peter Sandner, Bayer AG, Leverkusen, Germany.

**Background:** Chronic kidney disease (CKD) is often associated with arterial hypertension, leading to the development of hypertensive nephropathy and ultimately kidney failure that is poorly prevented by current treatment options. Hypertension and nephropathy are associated with impaired NO/sGC/cGMP signaling, low cGMP production and increased oxidative stress. Runcaciguat is a novel potent and selective, NO- and cGMP-dependent sGC activator. Here we investigated the therapeutic potential of Runcaciguat in rat models of hypertension associated chronic kidney disease.

**Methods:** Hypertensive rats (Sprague Dawley, 12–13 weeks old, n=15/group, angiotensin II (ANG) minipumps, 450mg/kg/min) were treated orally twice daily for 2 weeks with Runcaciguat (0.3, 1 or 3 mg/kg), losartan (30 mg/kg) or placebo. In a second study, male Renin-transgenic rats (mRen2/27, 8 weeks old, L-NAME 30-50 mg/L, n=18-24/group) were treated twice daily orally for up to 8 weeks with Runcaciguat (1, 3 or 10 mg/kg) or placebo. Key outcome parameters included mortality, blood pressure (BP), proteinuria, kidney histology, kidney and heart biomarkers and kidney gene expression.

**Results:** In the 2-week-treated ANG-rats, Runcaciguat dose-dependently and significantly reduced proteinuria without changing BP. Losartan significantly decreased proteinuria. Runcaciguat reduced kidney LCN2 (NGAL) expression. In the 8-week-treated Renin-transgenic rats, Runcaciguat significantly and dose-dependently improved mortality from 58% (placebo) to 56%, 39% and 28% (@ 1, 3, 10 mg/kg). At all tested doses, Runcaciguat significantly reduced kidney and heart hypertrophy and increased creatinine clearance. At the highest dose, Runcaciguat also significantly reduced BP and proteinuria.

**Conclusions:** The novel oral sGC activator Runcaciguat exhibits cardio-renal protection and improved survival in hypertensive rat models. Our data strongly suggest that Runcaciguat represents a promising treatment option for hypertensive kidney disease patients.

**Funding:** Private Foundation Support

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**PO0646**

**The Novel Nonsteroidal and Selective Mineralocorticoid Receptor Antagonist Finerenone Differentiates from SGLT2 Inhibitor Empagliflozin by Anti-Fibrotic Effects in a Progressive Mouse Kidney Fibrosis Model**

Karoline Droebner, Mira Pavkovic, Manuel Grundmann, Elke Hartmann, Laura Goen, Johannes Nordlohne, Frank Eitner, Peter Kolkhof, Bayer AG, Wuppertal, Germany.

**Background:** Finerenone and SGLT2 inhibitors have demonstrated clinical benefits in CKD patients with T2D. Cellular and molecular mechanisms responsible for these benefits are incompletely understood. MR-signaling has been linked to fibrosis in vitro via plasminogen activator inhibitor-1 (PAI-1) modulation. Here we investigated potential drug effects and mechanisms in a relevant preclinical mouse kidney fibrosis model.

**Methods:** Kidney fibrosis was induced in mice via unilateral ureteral obstruction. In a series of experiments, mice (C57/B6J, 8 weeks old male, n=10-12/group) were treated orally for 10 days with the MR antagonist finerenone (3 and 10 mg/kg), the SGLT2 inhibitor strongly increased creatinine clearance. In the 2-week-treated ANG-rats, Runcaciguat dose-dependently and significantly reduced proteinuria without changing BP. Losartan significantly decreased proteinuria. Runcaciguat reduced kidney LCN2 (NGAL) expression. In the 8-week-treated Renin-transgenic rats, Runcaciguat significantly and dose-dependently improved mortality from 58% (placebo) to 56%, 39% and 28% (@ 1, 3, 10 mg/kg). At all tested doses, Runcaciguat significantly reduced kidney and heart hypertrophy and increased creatinine clearance. At the highest dose, Runcaciguat also significantly reduced BP and proteinuria.

**Conclusions:** From the novel oral sGC activator Runcaciguat exhibits cardio-renal protection and improved survival in hypertensive rat models. Our data strongly suggest that Runcaciguat represents a promising treatment option for hypertensive kidney disease patients.

**Funding:** Private Foundation Support

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**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline represents presenting author.**

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PO0647
The Novel Potent and Selective Vasopressin V1a Antagonist BAY2372949 Blocks Arginine Vasopressin-Mediated Decline of Renal Blood Flow and Tissue Oxygenation
Hana Cernecka, Karoline Droebner, Hanna Tinel, Elisabeth Pook, Chantal Fuerstner, Marie-Pierre L. Collin, Peter Hein, Frank Eiter, Peter Kolkhof, Bayer AG, Research & Development, Pharmaceuticals, Wuppertal, Germany.

Background: Hypoxia is a major contributor to kidney disease progression. Arginine vasopressin (AVP) potently induces renal medullary vasoconstriction via vascular V1a receptors resulting in reduced renal blood flow (RBF). Here we characterized the kidney-protection properties of a recently identified, potent and selective V1a receptor antagonist.

Methods: BAY 2372949 was characterized in Chinese hamster ovary cells expressing recombinant human and rat V1a and V2 receptors. Vasodilatory effects were investigated on isolated A. renalis rings from male Wistar rats (n=10). RBF and intrarenal tissue oxygenation were studied in isolated perfused rat kidneys and in anesthetized rats (n=5-8 per group) via Laser Doppler Flowmetry.

Results: In vitro receptor profiling showed high potency and selectivity of BAY 2372949 for human V1a receptor (IC50=1.2 nM). BAY 2372949 reduced perfusate-mediated dose-dependent relaxation (IC50=3.1 nM) of isolated rat A. renalis vessel rings precontracted by AVP. BAY 2372949 improved the AVP-mediated reduction of perfusate and venous flow (figure) without affecting urinary volume. In vivo, infusion of AVP significantly increased mean arterial pressure (CON: 97±1, AVP: 135±2, means±SD) which was normalized by BAY 2372949 in a dose-dependent manner (90±5; p<0.0001). Infusion of AVP reduced both renal perfusion (CON: 1060±107; AVP: 17±4) and tissue oxygenation (CON: 27±1; AVP: 17±4). BAY 2372949 dose-dependently restored RBF (960±30; p<0.0001) and increased pO2 (25±1, AVP: 17±4; p<0.0001).

Conclusions: BAY 2372949 is a novel potent and selective vasopressin V1a receptor antagonist blocking the detrimental effects of elevated vasopressin levels on renal perfusion and oxygenation in rats, suggesting potential benefit for patients with cardiorenal diseases.

Funding: Commercial Support - Bayer AG

PO0648
Apabetalone, an Inhibitor of BET Proteins, Downregulates Alkaline Phosphatase and Improves Cardiovascular Risk
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Background: Elevated serum alkaline phosphatase (ALP) predicts major adverse cardiac events (MACE). ALP is associated with vascular calcification (VC) & inflammation. We studied apabetalone’s modulating gene expression in pathological VC & inflammation. We studied apabetalone's protective properties of a recently identified, potent and selective V1a receptor antagonist.

Methods: Expression of TNALP (gene symbol ALPL) was measured in primary vascular smooth muscle cells (VSMC) & vascular endothelial cells by q-PCR. TNALP was assessed by immunoblot in four vascular cell types: human aortic smooth muscle cells, human umbilical vein endothelial cells, human microvascular endothelial cells (VMSC) and human umbilical vein endothelial cells by q-PCR. TNALP was assessed by immunoblot & flow cytometry, ALP activity by enzymatic assays. Serum ALP was measured in CVD patients in phase 2 trials (ASSERT, SUSTAIN & ASSURE). Subpopulations had CKD (eGFR<60).

Results: Apabetalone downregulated ALPL expression in liver cells by 60-80%, HepG2s had lower TNALP protein -55%, enzyme activity ~40% & TNALP positive cells 15-30%; renal MCs had >90% decreases in ALPL expression & TNALP enzyme activity (p<0.001). ALPL was suppressed 50-70% in 3 vascular endothelial cell types with apabetalone. In VMSCs, apabetalone lowered ALPL expression, TNALP protein, enzyme activity & extracellular calcium deposition. In ASSERT, apabetalone dose dependently reduced serum ALP (p<0.001). In combined phase 2 analysis, apabetalone lowered ALP (p<0.001). Overall, the apabetalone-mediated decreases in serum ALP in phase 2 correlated with reduced MACE at 12-14 weeks (HR 0.64 per 1-SD in ALP, 95% CI 0.46-0.90; p=0.00 1-SD=13U/L); similar associations were observed at 24-26 weeks (HR 0.66 per 1-SD in ALP 95% CI 0.43-0.99; p=0.045, 1-SD=14U/L).

Conclusions: Apabetalone lowers serum ALP, consistent with reduced hepatic, renal & vascular TNALP production. Modulation of ALP by apabetalone may affect pathogenic processes to lower cardiovascular risk. This study provides insight to MACE reductions in phase 2 clinical trials.

Funding: Commercial Support - Resverlogix

PO0649
Renal Expression of L-Type Fatty Acid Binding Protein in Addition to Angiotensin II Type 1a Receptor Loss Ameliorates Chronic Tubulointerstitial Damage After Renal Ischemia Reperfusion
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Background: Although angiotensin II (Ang II) type 1 receptor blocker was reported to attenuate chronic tubulointerstitial damage (TID) after renal ischemia reperfusion (IR), its effect is limited. We had revealed the importance of renal L-type fatty acid binding protein (L-FABP) with antioxidative effect in various renal disease models. Therefore, the aim of this study is to elucidate the renoprotective effect of renal L-FABP and Ang II type 1a receptor (AT1a) loss against chronic TID after IR.

Methods: To induce severe chronic TID after renal IR, unilateral renal ischemia for 60 min was performed via clamping of right renal pedicle using 4 types of male mice; wild type mice (h-L-FABP+/+), human L-FABP homosomal transgenic mice (h-L-FABP AT1a-), AT1a knockdown homo mice (hL-FABP AT1a-), and generated h-L-FABP AT1a mice. Right and left kidneys were removed at 10 weeks after IR.

Results: While marked renal atrophy and progressive TID were found in each IR-kidney of h-L-FABP AT1a- and h-L-FABP AT1a- mice, the degrees of both atrophy and TID were significantly ameliorated in the IR-kidneys of the h-L-FABP AT1a- mice. These results suggested that antioxidative effect of L-FABP in addition to AT1a loss may be related to suppression of chronic TID after IR.

Conclusions: Increased expression of renal L-FABP in addition to suppressed activity of AT1a may be a useful strategy for prevention of AKI-to-CKD transition.

Funding: Private Foundation Support

PO0650
Development of a Synthetic Biotic, SYNB8802, for the Treatment of Enteric Hyperoxaluria
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Background: Enteric hyperoxaluria (EH) is a metabolic disease that results from excessive absorption of oxalate from dietary sources. Increased oxalate levels can lead to the formation of kidney stones and, ultimately, to kidney failure. EH occurs most frequently in patients with underlying gastrointestinal disorders, including inflammatory bowel disease, short bowel syndrome, or individuals who have undergone bariatric surgery. There is a high unmet need for new EH therapies, as a low oxalate diet is the only option currently available to patients. Synlogic is developing a novel Synthetic Biotic™ medicine for the treatment of EH, designated as SYNB8802.

Methods: SYNB8802 is an engineered bacterium derived from Escherichia coli Nissle 1917 (EcN) that has been engineered to metabolize oxalate to formate and CO2 in the gastrointestinal tract.

Results: Inoculation of SYNB8802 into minimal media showed significant consumption of oxalate and production of formate as compared to un-engineered (EcN) bacterial strain. When administered concomitantly with “C-oxalate to healthy mice, SYNB8802 decreased the urinary recovery of “C-oxalate, indicative of its ability to consume oxalate in vivo. In healthy non-human primates (NHP) administered approximately 400 mg of dietary oxalate, SYNB8802 lowered the urinary recovery of oxalate and “C-oxalate in a dose dependent manner by up to 75% as compared to vehicle. In addition, Synlogic has developed a mathematical model that predicts clinically meaningful reductions in urinary oxalate in EH patients.

Conclusions: Overall, SYNB8802 represents a promising new approach for the treatment of enteric hyperoxaluria.
PO0651
A Novel Small Molecule Modulating the Mitochondrial NEET Proteins Improves Inflammation and Fibrosis in Kidneys of Nonalcoholic Steatohepatitis Mice
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Background: Non-alcoholic steatohepatitis (NASH) is a disease characterized by excessive fat accumulation, inflammation, and ballooning degeneration of hepatocytes, with or without fibrosis in the liver. It is now reported that NASH not only affects the liver but is also associated with chronic kidney disease (CKD). However, the morphological appearance of NASH kidneys has been poorly characterized. These observations highlight the need for a treatment that targets both conditions. Here, we assessed the effect of a novel chemistry that regulates the function of 3 mitochondrial proteins called the NEET proteins, previously reported to be important in metabolic diseases, on a diet-induced NASH model in mice.

Methods: Mice were fed with a high fat diet for 30 weeks prior treatment with ENYO’s molecule for 8 weeks. The kidneys and livers were collected at sacrifice and sections were stained with H&E, PAS and picrosirius red staining to analyze their morphology. Specific immunostainings and qRT-PCR were performed to quantify the extent of inflammation (CD3, MAC1 and F4/80) and fibrosis (Col1a1, Col3a1, fibronectin).

Results: NASH mice displayed severe renal lesions such as glomerulosclerosis, tubular casts, tubular lipid accumulation and interstitial fibrosis. Mononuclear cell infiltration was also massively increased, in particular in the perivascular areas. Quantitative RT-PCR revealed a significant increase of the expression of several fibrosis and inflammation markers. Therapeutic administration of ENYO’s molecule was shown to resolve these lesions with a return back to normal regarding fibrosis, and a 50% and 35% decrease in lymphocyte and macrophage accumulation, respectively. In the liver, inflammation and fibrosis were also attenuated, specifically in the periporal zone that has been shown to be correlated with the severity of the disease. Interestingly, the most significant responders in the liver were also the best responders in the kidneys.

Conclusions: We have shown that NASH mice developed CKD, recapitulating the phenotypes observed in humans. Moreover, we have identified a new treatment, that by targeting NEET proteins, protects mice from the development of both liver and renal lesions.

PO0652
SIRT3 Deacetylates PDHE1α to Regulated Mitochondria Metabolism in Tubular Epithelial Cells During Renal Fibrosis
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Background: Abnormal energy metabolism is considered to be related to renal interstitial fibrosis. Pyruvate dehydrogenase α (PDHE1α) is the main catalytic enzyme of pyruvate dehydrogenase complex (PDHC) linking glycolysis to the TCA cycle. N-lysine acetylation is an important post-translational modification involves in energy metabolism. SIRT3 is a mitochondrial deacetylase that mediates the activity many metabolic enzymes.

Methods: Unilateral ureteral obstruction (UUO) or ischemia-reperfusion (I/R) were used to induce renal fibrosis in C57BL/6j mice or SIRT3 knockout mice. Primary tubular epithelial cells (PTCs) were stimulated by TGF-β1. Protein array and the acetylation array by LC-MS/MS were performed on tubules separated from sham or UUO-operated mice. K149R, K267R, K385R mutations in PDHE1α were transfected into PTCs.

Results: Acetylation showed that the majority of proteins were hyper-acetylation after UUO. GO enrichment analysis revealed that PDH was the mostly enriched GO term. Immunoprecipitation analysis confirmed that PDHE1α acetylation was enhanced after UUO or I/R operation. Activation of SIRT3 by HKL could block the hyper-acetylation of PDHE1α, restored PDH enzyme activity, and inhibited the phosphorylation of PDH in mice with UUO or I/R. On the contrary, Sirt3 KO mice had more acetylated PDHE1α, more phosphorylated PDHE1α and defective PDH enzyme activity. In vitro, increased PDH1 acetylation was accompanied by reduced PDH enzyme activity and increased PDHE1α phosphorylation in PTCs after TGF-β1 stimulation. Activation of SIRT3 by HKL reduced the effect of TGF-β1. Inhibition SIRT3 activity by 3-TYP or SIRT3 siRNA transection have the same effect as TGF-β1. K149, K267, K385 were identified as the main poteintially acetylated sites in PDHE1α. Acetylation of PDHE1α, the activity of PDH and PDHE1α phosphorylation remained unchanged in PTCs with the K385R mutation stimulated with TGF-β1 or SIRT3 siRNA transection.

Conclusions: In summary, we showed that mitochondrial proteins involved in regulating energy metabolism were acetylated and targeted by SIRT3 in PTCs. The deacetylation of PDHE1α at lysine 385 by SIRT3 plays a key role in metabolic reprogramming in renal fibrosis.

Funding: Government Support - Non-U.S.

PO0654
Empagliflozin Restores CKD-Induced Impairment of Endothelial Regulation of Cardiomyocyte Relaxation and Contraction
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Background: Chronic kidney disease (CKD) promotes development of cardiac abnormalities and is highly prevalent in patients with heart failure (HF), particularly HF with preserved ejection fraction (HFpEF). CKD and HF are associated with endothelial dysfunction and have been shown to benefit from a sodium-glucose co-transporter 2 inhibitor, empagliflozin. We hypothesized that uricemic serum from CKD patients impairs cardiomyocyte (CM) relaxation and contraction by inducing endothelial cell dysfunction and empagliflozin protects against this effect.

Methods: Co-culture system of human cardiac microvascular endothelial cells (CMECs) with adult rat ventricular cardiomyocytes (CMs).

Results: We showed that CMECs promote CM relaxation (return velocity, Fig. A) and contraction (sarcomere shortening, Fig. B). Serum from CKD patients impaired endothelial enhancement of CM function which was rescued by empagliflozin (Fig. A-B). Exposure to uricemic serum reduced nitric oxide (NO) bioavailability in CMECs and increased mitochondrial reactive oxygen species (ROS) and 3-nitrotyrosine level, indicating NO scavenging by ROS. Empagliflozin restored endothelial enhancement of NO level in CMs by restoring endothelial NO bioavailability and reducing endothelial mitochondrial ROS, an effect that was largely independent of sodium-hydrogen exchange.

Conclusions: Serum from CKD patients impairs CM relaxation and contraction through induction of endothelial dysfunction driven by an increase in mitochondrial ROS production. Empagliflozin restores the enhancement effect of CMECs on CM function by reducing mitochondrial oxidative damage, leading to reduced ROS accumulation and increased endothelial NO bioavailability.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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differences in whole kidney analysis of inflammatory cytokine qPCR between them, renal macrophages isolated from CD148KO mice showed a highly expressed inflammatory cytokine expression (TNF-α, IL-1β, IL-6). Peritoneal macrophages derived from CD148KO mice showed higher inflammatory cytokine expression (TNF-α, IL-1β, IL-6) to LPS, accompanied by higher phosphorylation of Erk. In addition, Erk inhibitor, U0126 diminished the difference between WT and CD148KO macrophages.

Conclusions: Our data suggests that CD148 negatively regulates macrophage M1 polarization through Erk and its deficiency accelerates macrophage inflammation in uUo kidneys, leading to advanced tubular injury and renal fibrosis.

Funding: Commercial Support - Bayer AG

PO0655

LRG1 Promotes Renal Fibrosis by Enhancing TGF-β-Induced Smad3 Pathway
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Background: Renal fibrosis is a final convergent pathway for CKD progression, but effective fibrosis therapy is lacking. We recently showed that leucine-rich alpha-2 glycoprotein-1 (LRG1), a secreted glycoprotein, is highly upregulated in diabetic kidneys and potentiates the endothelial TGF-β signaling, mediated by ALK1 receptor and Smad1/5 activation, to increase angiogenesis and worsen DKD progression. However, increased LRG1 expression was not limited to the endothelial cells in the diabetic kidneys, but also found in the renal tubular epithelial cells (RTECs). Therefore, we examined whether LRG1 is upregulated in RTECs leading to renal fibrosis progression.

Methods: We examined the expression of LRG1 in the tubulointerstitium RNAseq datasets of human CKD. We explored the potential mechanism in LRG1 upregulation in cultured RTECs and examined the specific TGF-β/Smad signaling pathway mediated by LRG1 using shRNA-knockdown. We examined the effects of LRG1 ablation in unilateral ureteral obstruction (UUO) and aristolochic acid nephropathy (AAN) models of renal fibrosis. We also examined the effects of RTEC-specific overexpression of LRG1 in renal fibrosis in vivo. We further compared the activation of Smad proteins in the RTECs of control, Lrg1-/- and Ren2 LE mice with UUO.

Results: We found that the LRG1 mRNA transcript was markedly increased in the microdissected tubulointerstitial of human CKD. In cultured RTECs, LRG1 expression was upregulated by a pro-inflammatory cytokine TNF-α, and chromatin IP assay confirmed the binding of p65 subunit NF-kB to the LRG1 promoter region. Importantly, LRG1 enhanced the TGF-β-induced Smad3 activation, but not of Smad1/5, and the expression of pro-fibrotic genes in RTECs. The global knockout of Lrsg attenuated renal fibrosis in mice with UUO or AAN. In AAN mice, Lrg1 ablation also improved renal function. In contrast, the RTEC-specific overexpression of LRG1 markedly heightened the renal fibrosis in vivo. The level of Smad3 phosphorylation in RTECs in the obstructed kidneys was directly associated with the loss or gain of LRG1 expression.

Conclusions: Our current study attributes a previously undescribed role of LRG1 as a key modulator of the canonical TGF-β/Smad3 signal transduction in RTECs and suggests that the targeting of LRG1 may be an effective approach against renal fibrosis.

Funding: NIDDK Support

PO0656

Single-Nucleus RNA Sequencing Identifies New Classes of Renal Proximal Tubular Epithelial Cell in Kidney Fibrosis
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Background: Proximal tubular cells (PTC) play a central role in nephron recovery versus fibrosis following renal injury. PTC heterogeneity is well-documented but poorly-characterized in extant single-cell sequencing data. Here we have determined PTC phenotype in renal fibrosis by single-nucleus RNA sequencing (snRNA-seq).

Methods: Kidneys were harvested from naïve mice and mice with renal fibrosis induced by chronic aristolochic acid administration. Nuclei were isolated using Nuclei EZ Lysis buffer. Libraries were prepared on the 10X platform and snRNA-seq completed using Illumina NextSeq 550. Downstream bioinformatics analyses used Seurat.

Results: A total of 23,885 nuclei were analyzed. PTCs were found in five abundant clusters, mapping to S1, S1-2, S2-cortical S3, and medullary S3 segments. Additional cell clusters were present (“new PTC clusters”) at low abundance in normal kidney and in increased number in kidneys undergoing regeneration/fibrosis following injury. These clusters exhibited clear molecular phenotypes, permitting labeling as, proliferating, differentiated-intermediate, differentiated-regenerating, and (present only following injury) differentiated-senescent. Each of these clusters exhibited a unique gene expression signature, including multiple genes associated with renal injury response and fibrosis progression. Comprehensive pathway analyses revealed metabolic reprogramming, enrichment of cellular communication and cell motility, and various immune signatures in new PTC clusters. In ligand-receptor analysis, new PTC clusters promoted fibrotic signaling to fibroblasts and inflammatory activation to macrophages.

Conclusions: SnRNA-seq permits the dissection of cell-type and cell-subtype-specific responses. We identified previously unknown, injury-associated PTC clusters. These exhibit highly specific and restricted gene signatures, including canonical PTC injury response and fibrosis progression. Comprehensive pathway analyses with compelling novel biology within our renal portfolio.

Funding: Government Support - Non-U.S.

PO0657

Artificial Intelligence-Driven Target Identification in CKD
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Background: Involvement of multiple pathways and complex pathophysiology are few of the hallmarks of Chronic Kidney Disease (CKD). These reasons contribute to the challenge for drug discovery in CKD, which is a major contributor to global disease burden. Availability of a wealth of CKD omics data has opened avenues for novel insight generation through unbiased integrative analysis. In a pioneering effort AstraZeneca and BenevolentAI initiated a collaboration to leverage the potential of artificial intelligence (AI) to generate novel hypotheses for drug targets in CKD.

Methods: We have created a CKD knowledge graph (CKD-KG) - a knowledge base of biological and chemical entities (genes, small molecules, etc) and their relationships (gene-disease associations, therapeutic drugs, biological processes, etc) and augmented with CKD specific information derived from both public and AstraZeneca proprietary data sets. The CKD-KG was constructed by aggregating information from structured biomedical databases, machine learning (ML)-based extraction from unstructured sources, and patient-centric omics datasets (unstructured: 140M documents, 1B relationships, (ii)-structured: 56M relationships, 3B omics data points, (iii) 35 licensed data sources, and (iv) 53 CKD omics datasets. The CKD-KG was used as input to BenevolentAI’s relational inference and causal reasoning ML models to produce target hypotheses for CKD.

Results: The fleet of models identified 295 potential targets that were triaged down to 69 targets. These 69 targets have been further prioritized based on an in-house human target validation pipeline, and additional criteria such as safety and druggability, in line with AstraZeneca’s 5R framework.

Conclusions: CKD-KG enables a transformative approach to generating novel target hypotheses with the potential of improving health outcomes for CKD patients.

Funding: Commercial Support - AstraZeneca AB
Twist1 in T Lymphocytes Exaggerates Kidney Fibrosis After Ureteral Obstruction
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**Background:** T cells play a critical role in directing kidney fibrogenesis. The transcription factor Twist1 limits pro-inflammatory cytokine production in T cells, but the role of T cell-derived cytokine mediators regulated by Twist1 in kidney damage has not been fully elucidated. To explore the role of T cell Twist1 in kidney scar formation, we subjected mice with Twist1 lymphocyte-specific deletion (“TKO”) of Twist1 and controls to the UUO.

**Methods:** 129/SvEv mice with a floxed allele for the gene encoding Twist1 or TNFα were bred with CD4-Cre mice to yield Twist1 TKO or TNFα TKO mice while robust selective deletion of Twist1 mRNA >90% vs. WTs in CD4+ T cells, and >85% vs. WT in CD8+ T cells (p<0.0001) or TNFα mRNA in T cells (published), respectively. Twist1 TKO, TNFα TKO, and WT controls underwent UUO with assessment of kidney fibrosis and T cell phenotype at 14 days.

**Results:** 2 weeks after UUO, Twist1 TKO mice developed less kidney fibrosis compared to WT as quantified by western blot for Colla1 (0.75±0.06 vs 1.0±0.05; p<0.02) and edema (0.56±0.01 vs 1.0±0.08; p<0.001) and by RT-PCR for Colla1 (0.69±0.08 vs 1.0±0.10; p<0.048), fibronectin (0.76±0.07 vs 1.0±0.06; p<0.003), TGFβ1 (0.73±0.08 vs 1.0±0.04; p<0.004) and Pai-1 (0.47±0.05 vs 1.0±0.09; p<0.001). Twist1 TKO mice also showed attenuated kidney injury as indicated by NGAL mRNA expression (0.50±0.06 vs 1.0±0.16; p<0.04). Twist1 can suppress promyelocytic leukemia mediators such as TNFα and IL17A in T cells. In 14d, flow cytometry revealed similar T cell and macrophage numbers in the obstructed WT and Twist1 TKO kidneys. We then used fluorescent cell sorting to isolate CD4+ and CD8+ T cells from obstructed WT and Twist1 TKO kidneys. Sorted CD4+ T cells from Twist1 TKO kidneys expressed similar mRNA levels for TNFα and IL17A compared to WT (p>0.08). CD8+ T cells from obstructed Twist1 TKO kidneys expressed higher mRNA levels for TNFα (1.8±0.39 vs 1.0±0.19; p=0.03), but not IL17A vs WT controls. To further explore the role of TNFα in T cells during fibrogenesis, we subjected TNFα TKO and WT mice to UUO. We found that TNFα deletion in T cells exaggerated kidney fibrosis and injury as quantified by real time PCR for fibronectin (1.4±0.09 vs 1.0±0.13; p=0.03) and NGAL (1.3±0.10 vs 1.0±0.05; p<0.01) mRNA expression, respectively.

**Conclusions:** Twist1 in T cells drives fibrosis in the injured kidney, possibly by limiting TNFα production.

**Funding:** NIDDK Support, Veterans Affairs Support

PO0659
Evaluation of the Effects of a Resistant Starch Diet and Metaproteomics Study of Microbiome-Host Interactions in a 5/6 Nephrectomy Murine Model of CKD
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**Background:** Chronic kidney disease (CKD), a progressive decline in kidney function, is a growing health problem: 13% of all US have CKD. In 40% of cases, CKD leads to irreversible loss of kidney function, end-stage renal disease. Prebiotic resistant starch (RS) changes gut flora and alleviates CKD. However, mechanisms of RS action remain unclear.

**Methods:** Male mice (n=8) were used to reduce renal mass and to induce CKD. 8 mice served as healthy controls. Each of the two groups was further split in two subgroups (n=4, each), either supplemented with RS or regular diet. PEAKS was used to identify peptides via de novo sequencing in cecal content. To better understand the differences between CKD, CKDRS, HRS and H phenotypes we combined all bacteria that were differentially abundant in six comparisons to infer bacterial co-abundance (BCoA) network. Histopathological evaluation was used for kidney damage comparison.

**Results:** Histopathological evaluation showed that CKDRS mice had less kidney damage compared to CKD group. Using metaproteomics we found that the most abundant bacterium in HRS phenotype is indole-producing Oscillibacter sp. 1-3, confirming the result of BlasZEGO that indole metabolism is upregulated in HRS phenotype as compared to CKDRS and CKD. The most connected network hub Firmicutes bacterium ASF500 is significantly overrepresented in CKDRS as compared to CKD and is not significantly different between HRS and H. Firmicutes bacterium ASF500 belongs to 20 bacterial strains from human intestine that can induce Th17 cells in the mouse and rat intestine and have immunostimulatory effects. Experiments to validate effect of butyrate on host immunity in 5/6 nephrectomy model. For the first time we demonstrate decrease in kidney fibrosis and bacteria species responsible for beneficial effects of RS. MST2 analysis allows for understanding fission/fusion cycles, and respiratory performance in mitochondria can affect the onset to many pathologies. Premenopausal females are typically less prone to cardiorenal associated with mortality. The odds of mortality among AKI patients varied significantly among gender.

**Funding:** Other NIH Support - NHLBI, Commercial Support - Dialysis Clinics Inc

PO0660
Sex Differences in Renal Mitochondrial Function of Young Healthy Rats
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**Background:** Sex differences in mitochondrial function have been linked to many pathologies. Premenopausal females are typically less prone to cardiovascular damage than males. Differences in the ability to manage oxidative stress, calcium uptake, fission/fusion cycles, and respiratory performance in mitochondria can affect the onset and progression of the diseases. While characteristic sex-related dissimilarities have been reported in renal function, nothing is known with regards to how sex may affect the performance of renal mitochondria. The goal of this study was to compare renal mitochondrial function in young healthy male vs female rats.

**Methods:** Mitochondria were isolated from the kidneys of Sprague Dawley (SD) rats (10-11 weeks). Mitochondrial membrane potential, superoxide and H2O2 levels were measured with luminescent (MCLA) or fluorescent (TMRM, Amplex Red) dyes, and Seahorse analysis was performed. Antioxidant capacity was measured with a Trolox-based assay. Lipid peroxide radicals were detected using with spin resonance spectroscopy (ESR) with in vivo spin trapping.

**Results:** Kidneys from SD male (SDm) and female rats (SDf) were divided into cortex (SDc; 13) and medulla (SDm; 14). First, we report significantly higher membrane potential in SDm compared to SDf (p<0.001). H2O2 levels were elevated in both the cortex and medulla (SDm compared to SDf; p<0.01). Interestingly, mitochondrial superoxide production was increased in the medulla compared to the cortex for both SDm and SDf, while SOD2 expression was lower (p<0.001). Antioxidant capacity was lower in SDm tissues compared to all other groups, which is consistent with higher H2O2 levels (p<0.001). H2O2 levels were higher in the mitochondria of SDf than in SDm, as well as reserve and maximal capacity compared to males. In addition, we report that these parameters were lower in medulla than corticomedulla, independent of sex. ESR analysis showed similar lipid peroxide radical levels in males and females, but detected different reactive adducts – an amine or amino acid-centered radical – in the medulla.

**Conclusions:** We report sex-related differences in mitochondrial function in the kidneys of young healthy rats. Further studies are needed to establish the mechanisms that they may affect the predisposition to kidney disease development later in life.

**Funding:** Other NIH Support - NHLBI, Commercial Support - Dialysis Clinics Inc

PO0661
Renal Involvement in Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis
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**Background:** COVID-19 caused substantial casualty worldwide. As the reported renal involvement varied across regions, we sought to review the global prevalence of renal manifestations among COVID-19 patients and determine the risk factors associated with AKI.

**Methods:** We systematically searched 6 databases for peer-reviewed reports and 7 data portals for grey literature for all trials, cohorts, case-control studies and case-series that reported the prevalence of renal manifestations including AKI, RRT, proteinuria and hematuria, and their associated risk factors. All papers were screened, assessed and extracted by at least 2 researchers independently. Quality was assessed according to NIH assessment tools. To avoid duplicate of patient data, we matched the location, institution and time period, and only included the largest data source if studies overlapped. Prevalence of renal manifestations was pooled from studies that consecutively recruited patients from the general population, and with clear definition of outcome. This review was prospectively registered at PROSPERO (CRD42020184621).

**Results:** 36 studies from 8 countries and over 50 cities with a total of 14,712 patients were identified. 34 and 2 were cohorts and case-control studies respectively. 24, 7 and 5 studies reported COVID-19 patients from the general population, severe / critical patients and patients with history of RRT. AKI occurred in 14.3% of all COVID-19 cases and was highest in New York City. 4.7% of hospitalized COVID-19 patients underwent RRT. Proteinuria and hematuria were present in 42.5% and 26.7% of all COVID-19 cases. The odds of mortality among COVID-19 patients who developed AKI was 15 times higher than non-AKI COVID-19 patients (pooled OR=16.85, 95% CI: 10.06 to 28.23, 2 cities, 6 studies, 9,297 patients) and was higher in Hubei. Such effect was not observed among kidney transplant patients (pooled OR=0.95, 95% CI: 0.12 to 7.22, 2 studies, 30 patients). Higher C-reactive protein, leukocyte count, serum lactate dehydrogenase and creatinine levels on admission were associated with AKI.

**Conclusions:** AKI was prevalent among COVID-19 patients and significantly associated with mortality. The odds of mortality among AKI patients varied significantly between cities, which could be associated with differences in healthcare infrastructure and delayed hospitalization and treatment initiation.
PO0660
Forecasting Continuous Renal Replacement Therapy Shortages During the COVID-19 Pandemic in the United States
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Background: The coronavirus disease 2019 (COVID-19) pandemic has increased continuous renal replacement therapy (CRRT) demand in the US, however total CRRT demand and capacity remain unclear. Our objective was to project national and statewide CRRT demand and capacity during the COVID-19 pandemic.

Methods: We projected CRRT demand using a model in which 4% of patients admitted with COVID-19 develop acute kidney injury (AKI) requiring CRRT for 12 days. To estimate non-COVID-19 CRRT demand, we applied the prevalence of AKI requiring CRRT among other ICU patients of 8.8%. We assumed capacity would be double this demand and that this demand would decrease to 25% during the pandemic. We compared CRRT demand and capacity to estimate shortage. In sensitivity analysis, we varied parameters influencing CRRT demand and capacity.

Results: We estimated a national CRRT shortage of 1529 (95% uncertainty interval: 1264-3837) machines with a capacity of 9375 machines, and shortages in 8 states during the COVID-19 pandemic (Table 1 and Figure 1).

Conclusions: Several US states are projected to have CRRT shortages during the COVID-19 pandemic. A national strategy, such as the creation of a federal stockpile, is needed to mitigate CRRT shortages during this pandemic and future healthcare crises.

Funding: NIDDK Support

Model-generated results for 8 states with CRRT shortages

PO0663
Acute Tubular Injury in Patients with Severe COVID-19 Infection
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Background: Novel coronavirus, severe acute syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread all over the world. SARS-CoV-2 enters host target via angiotensin-converting enzyme-2 which are ubiquitously expressed in many organs including proximal tubules in kidney. Indeed, autopsy cases with coronavirus disease-2019 (COVID-19) revealed the existence of coronavirus particles in the renal tubular cells. Here, we evaluated tubular injury in patients with severe and non-severe COVID19.

Methods: We investigated the relationship between urinary levels of tubule markers (NAG, β2-MG, L-FABP, and D-dimer) and laboratory markers in 17 COVID-19 patients without chronic kidney disease on admission. We also analyzed the relationship between the laboratory markers and respiratory status in severe (n=7) or non-severe (n=10) COVID-19 patients which were defined by requirements of supplemental oxygen.

Results: Although only 2 patients developed AKI in severe cases, serum Interleukin-6 (IL-6) level significantly increased in all of severe patients and correlated with levels of proteinuria (R2=0.37, p<0.01), NAG (R2=0.41, p<0.006), β2-MG (R2=0.47, p<0.007), L-FABP (R2=0.57, p<0.001) on admission. In addition, severe patients had significantly higher levels of proteinuria (severe: 0.14g/gCr vs non-severe: 0.15g/gCr), NAG (33.3 vs 11.0IU/L), β2MG (17134.4 vs 1168.5g/l), β2-MG (63.6 vs 12.4mg/l), L-FABP (57.9 vs 7.5g/gCr) as compared to non-severe cases. Proteinuria and elevated tubular markers were observed only in 2 and 6 cases respectively in non-severe patients, despite those were found in all severe cases.

Conclusions: We found that acute tubular injury was associated with the severity of COVID-19 infection. Since the pathophysiological hallmark of COVID-19 is severe systemic inflammation, it remains obscure whether progressive damage of tubules in SARS-CoV-2 is the result of direct viral infection, ischemic injury, or exposure of any humoral factors. Further large scaled studies focusing on tubular damage should be needed to elucidate underlying mechanisms of renal complication in COVID-19 infection.

Heat maps demonstrating states with CRRT shortages during the COVID-19 pandemic under scenarios: A) base case, B) highest CRRT capacity estimate and C) lowest CRRT capacity estimate

PO0665
Prolonged Intermittent Renal Replacement Therapy for AKI in COVID-19 Patients with Acute Respiratory Distress Syndrome
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Background: Patients with COVID-19 associated acute respiratory distress syndrome (ARDS) frequently develop severe AKI. Although continuous renal replacement therapy (CRRT) is standard of care for critically ill patients, prolonged intermittent renal replacement therapy (PIRRT) is a feasible option.


Results: Of 142 severe COVID-19 patients, 91 (64%) developed AKI, 42 (29%) Stage 3, and 14 (7%) initiated PIRRT; median age 51 y [IQR 51-59, range 40-73], male 11 [78%], diabetes 5 [36%], median BMI 31 kg/m² [27-51], SOFA score 10 [IQR 9-11], ferritin 790 [158-1374 ng/mL] and D-dimer 3076 [929-8558 ng/mL]. In 81/101 (81%) PIRRT sessions, ultrafiltration (UF) goal was achieved. Duration of PIRRT was 6-8 h in 65/101 (64%) yet in 16/101, procedure was extended 2-4 additional h, to reach UF goal. In subjects with vasoressors, there was a mean norepinephrine dose increase of
COVID-19: AKI and Outcomes

PO0667

COVID-19 AKI: Risk Factors and Markers of Disease from a Large U.K. Cohort

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Background: Acute kidney injury (AKI) is a significant complication of COVID-19 infection. UK NICE guidelines have been developed. Aim: to examine our local patient-level COVID-19 Hospitalisation in England Surveillance System (CHESS) database to elucidate potential risk factors for AKI vs. guidelines.

Methods: 564 COVID positive admissions between 7 March-24 May 2020 at University Hospital Southampton were examined using Python (Anaconda distribution) and SPSS®. AKI was staged by RIFLE and AKIN criteria consistent with NICE guidance. X2-test, Mann-Whitney U-test and logistic regression were used to analyse the data.

Results: AKI was present in 177 patients (31%). At peak, 108 (61%) stage 1; 42 (24%) stage 2; 27 (15%) stage 3. There were no significant differences in cohorts with respect to white vs non-white ethnicity, gender, obesity or anti-COVID-19 treatment. 44% of patients with AKI died vs 19% in the non-AKI group (p<0.001). AKI was associated with ICU admission (27% vs 10% p=0.001), requirement of non-invasive (13% vs 4%) and invasive ventilation (14% vs 4%) (both p<0.001). Prior diabetes (18% vs 8%), hypertension (47% vs 34%), chronic respiratory and cardiac disease (both 25% vs 15%) were more common in the AKI group (p<0.001). Increased age was associated with AKI (p=0.02) and length of stay (LOS) positively correlated to AKI stage (p<0.001). Peak levels of biomarkers: ferritin, D-dimer, C-reactive protein, high sensitivity troponin-I, neutrophil count and total white cell count, were all significantly raised (p<0.001) in the AKI group. Increasing with stage of AKI (p<0.001). However, in multivariable analysis, first clinical observations, neutrophil count, haemoglobin, D-Dimer and albumin came out as the most significant predictors of AKI: Specificity 88.7%, Sensitivity 43.6%.

Conclusions: AKI is a frequent complication of COVID-19 and we identified similar risk factors to those in the NICE guidelines. In addition, we found hypotension and chronic respiratory disease to increase risk of AKI whilst ethnicity, gender, obesity and COVID-19 treatments did not. Furthermore, AKI was associated with increased mortality, ICU admissions and LOS, concordant with previous studies. This data also points to several biomarkers as possible predictors of AKI development and severity. Further analysis of this data is ongoing.

PO0668

Hematuria and Elevated Lactate Dehydrogenase Are Associated with AKI in Hospitalized COVID-19 Patients

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Background: Acute kidney injury (AKI) can be a severe complication of COVID-19, particularly in those who require intensive care. Its relationship to the incidence of proteinuria, hematuria, and elevated inflammatory markers has not been well characterized. Our objective is to describe the incidence of AKI in COVID-19, and its association with inflammatory markers.

Methods: Retrospective cohort study of adult patients hospitalized at the Cleveland Clinic with COVID-19. SARS-CoV-2 infection was confirmed by virus detection in respiratory specimens using RT-PCR. AKI was diagnosed per KDIGO serum creatinine-based classification. We selected stage 2 and higher as our primary endpoint for the study. Baseline creatinine was defined as the most recent pre-admission level available within 3 months of presentation. Acute lung injury was defined by the need for mechanical ventilation.

Results: The incidence of AKI was 14% in 621 hospitalized COVID-19 patients, with half requiring kidney replacement therapy (KRT). The incidence of proteinuria and microscopic hematuria were high in these patients (83% and 77% respectively). Seventy-five percent of patients with AKI needed mechanical ventilation, and timing of KRT overlapped with time of mechanical ventilation. Inflammatory markers and acute phase reactants, including LDH, ferritin, and C reactive protein were significantly higher in patients with AKI compared to those without AKI. On adjusted analysis, hematuria and elevated LDH levels were significantly associated with AKI (Figure).

Conclusions: Elevated lactate dehydrogenase levels and microscopic hematuria on presentation are independently associated with 50% probability of moderate to severe AKI. Our findings suggest a possible pathogenetic mechanism of endothelial cell injury and thrombotic microangiopathy as a cause of AKI in COVID-19 patients. Additional studies are needed to explore this potential mechanism of AKI in COVID-19.

PO0669

High C-Reactive Protein and D-Dimer on Admission Predict the Development of AKI in Patients Hospitalized with COVID-19

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Background: COVID-19 infection is characterized by an acute respiratory syndrome that causes severe symptoms in some patients including a high incidence of acute kidney injury (AKI), which is associated with poor prognosis. COVID-19 infection results in a complex host response including a cytokine storm and severe inflammation. We aimed to identify whether high inflammatory markers on admission predict the development of AKI.

Methods: We performed a cohort study utilizing data from 430 patients admitted to the COVID-19 to the University of Colorado Hospital. We excluded patients with a known history of end stage kidney disease or chronic kidney disease or with missing data. A total of 203 patients were included in this analysis. The primary predictors were initial serum C-reactive protein (hsCRP) >100 mg/L and D-dimer >1000 ng/mL, FEU admission to the hospital. The primary outcome was AKI, defined by KDIGO definition of AKI based on serum creatinine levels. AKI diagnosis was confirmed by chart review. Multivariable logistic regression analysis was used to examine the association between CRP and D-dimer on admission and development of AKI.

Results: The mean age and body mass index of patients was 53.7 (16.9) years and 31.5 (8.4) kg/m2 respectively. Fifty-nine percent of patients were male, 40% were Hispanic and 22.7% were Black. 44.3% had hypertension, 35.0% had diabetes and 23% had underlying respiratory disease. Twenty-seven (13.3%) patients developed AKI. After adjustment for age, gender, race/ethnicity, diabetes, hypertension, respiratory disease, cardiovascular disease and ACEi/ARB use, admission CRP level >100 mg/L was associated with nearly a 4-fold increased odds of developing AKI (OR 3.8, 95% CI 1.4-9.8). After full adjustment, admission D-dimer level greater than 1000 ng/mL was associated with a 5-fold increased odds of AKI (OR 5.0, 95% CI 1.8 to 13.5).

Conclusions: High CRP and D-dimer on admission were associated with a significantly higher risk of developing AKI, independent of underlying comorbidities. Thus, high CRP and D-dimer on admission should trigger due deliberation and avoidance of nephroticcy medicines and close monitoring for the development of AKI.

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Acute Peritoneal Dialysis in Patients with COVID-19 and AKI: A Single-Center Experience in a Time of Crisis in the United States
Maryanne Sourial,1,2 Mina Sourial,1,2 Rochelle Dalsan,1,2 Jay A. Graham,1,2 Michael J. Ross,1,2 Wei Chen,1,2 Ladan Golestaneh,1,2 Montefiore Medical Center, Bronx, NY; 1Yeshiva University Albert Einstein College of Medicine, Bronx, NY.

Introduction: In developed countries such as the United States, intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT) are the primary mode of renal replacement therapy (RRT) for the management of AKI. However, during the COVID-19 pandemic, the ability to provide HD in our hospital system was overwhelmed due to the surge in the number of patients with AKI requiring RRT combined with limited inpatient beds. We present this single-center experience with fluid management on CRRT in relation to respiratory parameters.

Case Description: At Montefiore Medical Center (MMC), in Bronx, NY, the first case of COVID-19 was admitted on March 11, 2020. As the number of patients with COVID-19 rose, we initiated an acute PD program starting on March 25th. As of April 13th, there were 2,015 patients with COVID-19 admitted to the ICU at the University of Michigan between 3/23 and 4/26, with follow-up through 5/12/2020. All patients received post-filter continuous venovenous hemodiafiltration with regional citrate anticoagulation per institutional protocol. Daily cumulative fluid balance and respiratory parameters (P/F and PEEP) were recorded for the first 7 days of CRRT. We assess the relationship between cumulative fluid balance on CRRT and respiratory parameters (P/F and PEEP) with repeated measures modeling adjusted for fluid accumulation at CRRT start, height, weight, and age.

Results: Mean age 54.8, majority black (75%), and comorbidities included hypertension (90.6%), diabetes (56.2%), CKD (53.1%), and organ transplantation (18.8%). Median length of mechanical ventilation was 15.0 (12-25) days. Median cumulative fluid balance from admission to CRRT start was -3.3 (2.0-5.6) liters. There was a trend toward increasingly negative fluid balance on CRRT (figure). When adjusting for age, weight, height and cumulative fluid balance at CRRT start, there was no association between cumulative fluid balance on CRRT and P/F (p=0.21) or PEEP (p=0.47). At end of data collection, 9 (28.1%) patients remained in the hospital, 10 (31.3%) survived to hospital discharge and 13 (40.6%) had died.

Conclusions: Cumulative fluid balance on CRRT did not correlate with change in P/F or PEEP, even after accounting for baseline fluid balance. Nevertheless, it is possible that more aggressive fluid removal is required to demonstrated an effect.

Funding: NIDDK Support

Mean Daily Fluid Balance

Acute Peritoneal Dialysis in Patients with COVID-19 and AKI: A Single-Center Experience in a Time of Crisis in the United States
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Funding: NIDDK Support

Mean Daily Fluid Balance
Results: The 20 patients initiated early RRT after 6.4±3.6 days from ICU admission. The median hospital length of stay was 42.2 days, the net ultrafiltration rate was 65.5±65.2 ml/h. One patient in control group also received RRT after ICU admission due to AKI. No statistical difference was found in the two subgroups in baseline. 61.3% patients died during hospitalization. The median survival time was 12 days and the average observation time was 19 days. Kaplan-Meier analysis showed that the incidence of AKI, dialysis (HD) and death in ICU patients diagnosed with COVID pneumonia in a Brazilian center. Methods: Analysis from medical records of ICU patients with diagnosis of COVID pneumonia in a brazilian single-center. AKI was defined according to KDIGO criteria. Results: During the period of February 2nd to May 4th, 95 ICU patients diagnosed with COVID were analyzed. There was predominance of male (64.2%), median age of 64.9 years, previous diagnosis of hypertension, diabetes and obesity in 51.6%, 27.4% and 30.5% respectively. AKI was diagnosed in 54 (56.8%) patients and 32 (59.2%) of them required HD. Mortality rate was 17.9%. Patients with AKI, compared to no-AKI patients were statistically significant more frequently hypertensive and diabetic, worse SAPS3 and SOFA scores and need for organ support therapies. Laboratory tests depicted more anemia, lymphopenia, and higher levels of inflammatory markers as well as longer length of stay in ICU, hospital and death. Similar findings were seen in those ones who required HD compared to those with conservator treatment. Comparing patients who undergone death to survivors, they were older, more frequently diabetic, worse SAPS3 and SOFA scores and need for organ support therapies, AKI and dialysis. Multinomial logistic regression predicted that hypertension (p<0.01), mechanical ventilation (p<0.01) and use of hydroxychloroquine (p<0.009) were independent risk factors for AKI, hypertension (p<0.01), mechanical ventilation (p<0.01), use of vasopressor (p=0.04), and use of hydroxychloroquine (p<0.009) for HD patients; and age >65 years (p=0.03) and AKI (p=0.04) for death. Conclusions: In our study, AKI was a common complication of ICU COVID patients, it was associated to hypertension, Mech ventilation and use of hydroxychloroquine. As well as age >65 years, AKI was an independent risk factor to death.

PO0673
Incidence of New-Onset Proteinuria in AKI Associated with COVID-19 Is Not Greater Than It Is in AKI from Other Causes
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Background: The epidemiology, clinical presentation, management and outcomes of COVID-19 comes from early reports from China and Europe with AKI prevalence ranging widely from 0.5% to 29%. However, knowledge about this pandemic is still evolving. As well as age >65 years, AKI was an independent risk factor to death.

PO0674
AKI Perspectives and Practices in Latin America (LA) During COVID-19: Analysis from GlomCon Latin America Working Group
Javier Soto-Vargas,1 Desirée García Antonio,2 Diana Aguirre,2 Denisse Arellano-Mendez,3 Franco H. Cabeza Rivera,2 Julio A. Gutierrez-Prieto,2 Blanca Martinez-Chagolla,4 Sonia Rodriguez Ramirez,2 Carmen Avila-Casado.2 GlomCon Latin America Working Group 1Especialidad de Nefrologia, Hospital General Regional 46, Guadalajara, Mexico; 2University Hospital Vall d’Hebron, Barcelona, Spain; 3Hospital Clínic de Barcelona., Barcelona, Spain; 4Hospital Universitario Virgen Macarena, Sevilla, Spain; 5Hospital de la Paz, Madrid, Spain; 6Hospital Universitario Infantia Sofia., San Sebastian de los Reyes, Spain.

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PO0675
AKI due to COVID-19 in the Intensive Care Unit: Analysis of a Brazilian Center
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PO0676
AKI in Patients with COVID-19 Infection: Preliminary Data from AKI COVID-19 Registry of the Spanish Society of Nephrology
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Background: SARS-CoV-2 coronavirus pandemic has significant impact on the general population, and chronic hemodialysis patients presented a poor prognosis with a mortality rate around 25%. Data from severe acute kidney injury(AKI) and acute renal replacement therapy(RRT) is scarce. We present the preliminary results of AKI COVID-19 Registry of the Spanish Society of Nephrology.

Methods: The online Registry began operating on May 21th. It collects epidemiological variables, contamination and diagnostic data, signs and symptoms, treatments and outcomes. Patients were diagnosed with SARS-CoV-2 infection based on PCR of the virus.

Results: One week after the AKI COVID registry started, 54 patients with AKI and RRT from 11 Hospitals. Age was 64±9 years and 55% men, 65% hypertension, 31% diabetes mellitus, 14% cardiovascular disease, 26% chronic kidney disease, 6% neoplasms, 29% obesity, 8% chronic obstructive pulmonary disease, and
6% smokers. Previous treatment: 10% immunosuppressive, 20% ACEI, 25% ARBs, 14% antidiabetics, and 16% anticoagulants. Clinical characteristics: 92% common respiratory symptoms, 96% pneumonia, 90% required intensive care unit (ICU) and 87% mechanic ventilation. 32% albuminuria, 18% hematia, and 50% AKI with preserved urine output. Time from COVID-19 symptoms start to AKI 12.3±8days, time ICU 19.8±5days. ACR: CVAE: 15.7: 81.8% lymphopenia. RRT was needed in 91% 13.4±12days: 55% received continuous RRT, and 72% anticoagulation. Kidney biopsy was not performed. Mortality 46.3% (60 patients), and 4% remained under RRT. Time from ICU to renal function recovery 25±14 days. 65.2% death patients had hypercoagulable state. No differences were observed in comorbidities, chronic treatments, renal clinical characteristics, dialysis modality and mortality. Decreased lymphocyte count was associated with worse patient prognosis (dead 495±260 vs. survivors 789±460, p=0.023).

**Conclusions:** The mortality in AKI with RRT and COVID-19 is alarming. Several factors associated with COVID-19 disease is more frequent in males. Interestingly, half of the patients preserved urine output. Severe lymphopenia was associated with mortality. More data from the AKI COVID-19 registry will help us to enlighten the prognosis and risk factors associated to mortality.

**Funding:** Government Support - Non-U.S.

**PO0677**

**AKI in People Living with HIV Hospitalized with COVID-19**

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**Background:** People living with HIV (PLWH) have an increased burden of kidney disease and interdependence factors as a risk place them at increased risk for acute kidney injury (AKI) in the setting of COVID-19. The aim of our study was to characterize the incidence, risk factors and outcomes of AKI among hospitalized PLWH with COVID-19.

**Methods:** We performed a retrospective study of adult PLWH hospitalized with laboratory confirmed COVID-19 in a large healthcare system in Bronx, New York, from March 10-May 11, 2020. Data collected included demographics, comorbidities, antiretroviral therapy (ART), initial laboratory data, and predmission CD4 count and HIV viral load. AKI was defined and staged using KDIGO criteria. Fisher and Wilcoxon tests were used to determine differences among those with and without AKI.

**Results:** During the study period, 77 PLWH were hospitalized with COVID-19. The majority were Black or Hispanic, 50% were men, 53% had hypertension, 31% diabetes mellitus, 22% chronic kidney disease (CKD) and 14% end-stage kidney disease (ESKD). Mean age count was 470 cells/μL and 85% had a suppressed HIV viral load (<40 copies/μL). After excluding 11 with ESKD, AKI incidence was 50%. Those with AKI were older [63 (SD 9) vs 55 (SD 13) years, p<0.005], more were black (56% vs 37%, p=0.01) and more had CKD (42% vs 9%, p=0.001) compared to those without AKI. There were no significant differences in CD4 count, HIV viral load, or use of tenofovir-containing ART between those with and without AKI. By AKI severity, 11/33 (33%) were stage 1, 4/33 (12%) stage 2 and 18/33 (55%) stage 3. Mechanical ventilation (33% vs 0%, p=0.0004) and in-hospital mortality (42% vs 3%, p=0.0002) were more common in those with AKI. Of 6 patients who required renal replacement therapy, 4 died and 2 remained RRT dependent. Admission white blood cell count, neutrophil/lymphocyte ratio, D-dimer, ferritin, C-reactive protein and lactate dehydrogenase levels were significantly higher in those with AKI.

**Conclusions:** The incidence of AKI in PLWH hospitalized with COVID-19 was high and associated with poor outcomes. We did not identify HIV-specific or COVID-related risk factors for AKI in the setting of COVID-19. Admission inflammatory markers may be predictive of AKI in PLWH with COVID-19.

**PO0678**

**AKI Is Related to Mortality in COVID-19 Patients Without Underlying Kidney Disease**

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**Background:** Due to its high infectivity and mortality, coronavirus disease 2019 (COVID-19) has become a global public health issue. The kidneys act as critical metabolic organs, therefore, whether COVID-19 can induce renal damage is of utmost importance but remains controversial, and the prognosis of COVID-19 encountering acute kidney injury (AKI) is unknown. Moreover, the efficacy of different treatments that COVID-19 patients with AKI (COVID unrelated-AKI (COV-)) are treated with is unknown. The mortality in AKI with RRT and COVID-19 is alarming high. Several factors associated with COVID-19 disease is more frequent in males. Interestingly, half of the patients preserved urine output. Severe lymphopenia was associated with mortality. More data from the AKI COVID-19 registry will help us to enlighten the prognosis and risk factors associated to mortality.

**Funding:** Government Support - Non-U.S.

**PO0679**

**Acute Peritoneal Dialysis with Percutaneous Catheter Insertion for COVID-19-Associated AKI in Intensive Care: Experience from a UK Tertiary Centre**

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**Background:** During the COVID-19 pandemic in 2020, high rates of acute kidney injury (AKI) in critically unwell patients are being reported, leading to increased demand for renal replacement therapies (RRT). There are considerable challenges providing RRT for large numbers of patients with COVID-19 and alternatives to continuous veno-venous hemodiаlіsіs tہrехnіqұ (CVVHD) in intensive care units (ICU) are needed in both high and low-resource settings. Peritoneal dialysis (PD) can be initiated immediately after percutaneous insertion of the catheter, but there are concerns about impact on ventilation and RRT efficacy. We describe our recent experience of percutaneous catheter insertion and peritoneal dialysis in patients in ICU with COVID-19 infection.

**Methods:** Patients were selected according to local protocol and catheters inserted percutaneously using Soldinger technique by two experienced operators. Sequential Organ Failure Assessment score (SOFA) and ventilation requirements were recorded at time of insertion, and at 24 hours after insertion. Procedure complications, proportion of RRT provided by PD, renal recovery and RRT parameters during PD were assessed.

**Results:** Percutaneous PD catheters were successfully inserted in 32/39 (82.1%) patients after median of 10.0 (IQR 13.0, 19.0) days on ICU. No adverse events following insertion were reported, SOFA scores and ventilation requirements were comparable before and after insertion and adequate RRT parameters were achieved. Median proportion of RRT provided by PD following catheter insertion was 90.2% (IQR 77.5, 100).

**Conclusions:** PD provides a safe and effective alternative to CVVHD in selected patients with AKI and COVID-19 infection requiring ventilation on intensive care.

**Clinical Parameters of Patients Prior to and after Peritoneal Dialysis Catheter Insertion**

The relationship between AKI and outcome of study population

- IQR: interquartile range; PD: Peritoneal Dialysis; PaO2 : FIO2 ratio (arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen (FiO2 expressed as a fraction)); SOFA: Sequential Organ Failure Assessment

**PO0680**

**Adding Heparin to Citrate in Continuous Renal Replacement Therapy May Extend Filter Life-span in COVID-Related AKI**


**Background:** COVID may predispose patients to thrombosis and lower filter lifespan. Association between D-dimer level (DD) and filter clotting in Continuous Renal Replacement Therapy (CRRT) has not been described.

**Methods:** All patients who needed CRRT in Hospital das Clinicas (Brazil) during March to May 2020 (COVID related-AKI (COVID+), n=37) and August to September 2019 (COVID unrelated-AKI (COV-), n=18) were studied. Anticoagulation in CRRT in COVID+ was done with citrate 3mmol/L (ACD, n=19), or citrate 4mmol/L plus non-fractioned heparin 10U/Kg/h (ACD/Hep, n=18), while in COV- with citrate 3mmol/L only. Data are expressed in median [IQR]. We performed Spearman’s correlation between DD and time-free of filter clotting (TFC), and Kaplan-Meier curve to study filter survival by anticoagulation method and COVID.

**Results:** ACD/Hep group presented lower filter clotting in 72h when compared to other groups (ACD/Hep: 35% vs ACD: 100% vs COV-: 80%; p< 0.05). Analyzing
filter clotting per patient-day, ACD/Hep also presented less clotting than ACD group (ACD/Hep: 41% vs ACD: 10%; p < 0.05). In COVID patients, median TFC was 33.5 h (17.0; 72.0); ACD: 29.0 h (13.6; 68.5), ACD/Hep: 40.0 h (17.0; 62.0), p = NS. Clotting time from obese patients did not differ from non obese patients (obese: 31.0 h [18.5; 57.2] vs non-obese: 36.0 h [16.8; 72.0], p = ns). Median DD in all COVID patients was 3,519 [1420-13,883]. Patients with DD below median (<3,500) had higher TFC (ACD high DD: 19.0 h [9.0; 27.5], ACD/Hep high DD: 34.0 h [17.0; 62.0], ACD low DD: 57.0 h [27.0; 66.8], ACD/Hep low DD: 67.0 h [26.0; 72.0]; Figure 1). There was statistically significance in correlation between DD and TFC in ACD patients, but not in ACD/Hep group.

Results: We excluded patients with renal failure requiring renal replacement therapy (RRT) (RRRT) or diagnosis of COVID19 as a previous history of thrombosis. We were left with 69 patients, whom we analyzed the first three RRT treatments of each patient. The average age was 59.48 years, 81.2% male, 18.8% female. 15% of patients were African American, 5% Caucasian, 31% Hispanic, and 5% Asian as other. The average BMI was 30.2. 40% of patients had diabetes mellitus, 49% hypertension, and 14% CKD or ESRD. We analyzed a total of 162 RRT treatments. Of these 162 treatments, 49% of patients received bivalirudin, 27% heparin, and 23.4% did not receive AC. We found that 84.5% of patients receiving bivalirudin completed their CRRT treatment, and receiving heparin completed treatment, and 59.3% of patients not on AC completed treatment.

Conclusions: Patients with a confirmed diagnosis of COVID 19 that are critically ill and receive CRRT are more likely to finish their CRRT treatment, and therefore achieved improved clearance, if they were given some form of AC to prevent clotting.

PO0683

Association of Ventilatory Time and AKI in a Bronx Cohort of COVID-19 Patients

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Background: The relationship of lung-kidney interactions in COVID-19 has not been well described. AKI has been associated with increased mechanical ventilation times. Recent publications have shown a strong association of COVID-19-AKI with mortality and a high incidence of AKI occurring peri-intubation. We hypothesized that mechanical ventilation (MV) time would be increased in patients with COVID19-AKI and longer in those with severe AKI.

Methods: We analyzed a cohort of incident COVID19 patients who required MV. Patients with end stage renal disease were excluded. AKI was defined using KDIGO criteria (0.3 mg/dL increase or greater than or equal to 50% increase from the baseline Cr) between the start of MV and baseline Cr. AKI stage was defined as per KDIGO. The total MV time was measured in days from date of initial intubation, including subsequent intubation/extubation events, until successful extubation or death. Censored data was not included. Linear regression models were utilized to evaluate associations.

Results: We analyzed 316 patients. 62% were male, 37% were black/African American and 33% were Hispanic/Latino. Hypertension was prevalent in the cohort (N=212) and over 50% were obese. Median MV time was 4.67 days (IQR 1.76, 9.95). AKI occurred in 89% (N=283) of the cohort. Stage 3 AKI developed in over 50% (N=161) of patients. In models adjusted for age, hypertension, diabetes and disease related group weight, patients with AKI had 3.46 more days of MV, however this finding did not reach statistical significance (95%CI 0.92-6.00). This association however was significant and increased linearly with stage of AKI (p for trend <0.001).

Conclusions: This is one of the first studies to evaluate the association of COVID19-AKI and MV time. Even after adjusting for severity of illness, patients with increased stage of AKI had longer MV times. This may be due to pathophysiological kidney-lung interactions seen in non-COVID19 disease and/or direct effect of COVID19 on the kidneys. As few patients in our cohort were spared from kidney injury, inferences comparing those with and without AKI are difficult to discern. We plan to explore this question in a larger cohort to determine whether COVID19-AKI alone is associated with ventilatory time.

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PO0684

Can the AKI Alert Staging Tool Help Manage Patients Admitted During the COVID Pandemic?

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Background: Basildon & Thurrock University Hospital has the second highest rate of hospital admissions with AKI stage 3 in the United Kingdom based on Renal Registry Hospital Episode Submission Data. Acute kidney injury (AKI) is common in hospitalized patients and carries a high risk of mortality. Given the limitations of resources both personnel and equipment, a retrospective study was done to see if the AKI alert staging tool could help predict and direct resources to those patients who would benefit most from specialist intervention.

Methods: Data was reviewed from January - May 2020. This corresponded to the peak of admissions and by the end of the period, the hospital was on course to returning to pre-pandemic activity. Relevant data including admission laboratory tests and imaging was collected. The admission stay was analysed for duration, the need for transfer to an intensive care environment to receive ventilator support and/or renal replacement therapy. Discharge destination was reviewed and whether the patient was discharged home, to another facility or did not survive the admission. For comparison we looked at the same period in the preceding year as this would represent the most matched population.

Results: Over 5000 AKI alerts were generated for this period for 4390 unique admissions. This compares to 3910 AKI alerts for 1098 unique admissions for the identical period in the previous year. The vast majority were for AKI stage one alerts none of which were in COVID positive patients. A significant proportion of patients with AKI Stage 2 and 3 alerts were positive for COVID. Those that were admitted to Intensive Care with Stage 3 AKI almost always required intubation and renal replacement therapy. Mortality was higher in this group.

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Conclusions: The AKI alert system helps identify patients who are unwell and can benefit from Nephrologist input at an early stage. The Alert algorithm excludes haemodialysis patients, therefore this population was excluded. During the COVID-19 pandemic there was a clear increase in AKI admissions and alerts creating a substantial demand on renal services. Specialist intervention should be directed to AKI alert stage 2 patients where intervention can help prevent progression into AKI stage 3 and subsequent ICU admission. AKI stage 1 patients who are COVID negative can be managed without specialist input.

PO0685
Characteristics and Outcome of AKI Needing Dialysis with COVID-19

Background: COVID-19 infection has varying grades of mortality worldwide. Multi-organ injury, not uncommonly associated with AKI, portends a poor outcome. We studied AKI needing haemodialysis (HD) in the context of COVID-19 infection.

Methods: From March 15th to May 25th 2020, for consecutive COVID-19 infections AKI needing HD in a large dialysis network age, gender, payer type, days:admission to HD start, urine output, S. Cr, comorbidities, length of stay & outcome, dialysis session details: blood flow rate(BFR), dialysis flow rate(DFR), ultrafiltration volume were reviewed. We compared survivors and non survivors using Mann Whitney/ Wilcoxon 2 sample test for medians and Fisher exact 2 tailed for association.

Results: n = 20. Mean age: 56.7 ± 3.93 years. M:F 17:3, 9 survived, 11 expired. HD sessions=51; CRRT: 4, duration: 22 ± 25.4 hours. 47 sessions: Duration: 4.87 ± 1.11 hours, BFR: 195 ± 43 mL/min, DFR: 389 ±99 mL/min, UF: 437mL/hour. No clotting reported.

Conclusions: AKI needing HD in COVID-19 infection is associated with significant multiorgan injury and high mortality, mostly age and male predominance. No significant clinical characteristics were predictive of survival in a sample size

Comparison of survivors and non survivors of COVID-AKI needing HD

PO0686
Circuit Clotting on Continuous Venovenous Hemofiltration in COVID-19 Patients at New England’s Largest Health Safety-Net Hospital
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Background: The pandemic of COVID19 led to a surge in critically ill patients with severe kidney failure requiring continuous renal replacement therapy (CRRT). Primary reports rapidly showed a hypercoagulable state associated with cytokine storm representing a challenge to conduct CRRT. We report our experience to face clotting on continuous venovenous hemofiltration (CVVH) with COVID19 patients.

Methods: We reviewed data on all admitted patients with COVID19 diagnosis and requiring CVVH at Boston Medical Center between March, 15th and May 7th, 2020. The study was approved by the institutional IRB.

Results: Twenty six patients were admitted to ICU with COVID19 disease and developed acute kidney injury requiring CRRT. The majority of patients were males (73%), and mean age was 67.6 ± 15.4 (95% CI [62-73]) years. 11 patients (41.2%) had COVID19 diagnosis initiation, patients showed marked inflammatory state with a median CRP of 239mg/dL (IQR 123-391.5), fibrinogen 609mg/dL (431-693), d-dimer 4,036 ng/mL (1,777-15,558). CVVH was conducted in prefiltration mode, with a median therapy rate of 3L/h (2.5-3.1) and a mean blood flow of 280 mL/min. The median cartridge half-life from CVVH initiation was 11.8 hours (3.5-20). Twelve patients (46%) experienced CVVH circuit clotting within the first 2 hours, including 6 patients (23%) with severe recurring clotting. Curative systemic anticoagulation by heparin was used in 12 patients (46%) based on hospital protocol. Its use was associated with mild improvement in cartridge half-life: 13h with curative heparin versus 10.5h with no low dose preventive anticoagulation (non-significant). Of note, heparin was held prior to CRRT initiation for dialysis catheter placement and was reinstituted without bolus, which could lead to early coagulation of the filter in patients with hypercoagulable state. The fatality rate was 76.9% with a median time to outcome of 2.5 days (1-8.7) days.

Conclusions: Conducting CRRT in patients with multiorgan failure secondary to COVID19 is challenging. Our experience suggests only a mild non significant improvement of clotting prevention with heparin anticoagulation at the time of cvvh initiation. Further studies are warranted to determine the optimal anticoagulation regimen.

PO0687
Clinical Characteristics and Short-Term Outcomes of Severe AKI in COVID-19 in Bronx, New York
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Background: After the first reported case of COVID-19 in the U.S., New York City quickly became the epicenter of the pandemic. AKI has been reported in patients with severe COVID-19. The Bronx consists of a predominantly minority population with a high burden of comorbidities that may be at increased risk for AKI in the setting of COVID-19. We aimed to characterize risk factors and short term outcomes in patients hospitalized with COVID-19 and severe AKI.

Methods: We performed a retrospective study of 113 adults hospitalized with COVID-19 in a large healthcare system in the Bronx who required nephrology consultation for AKI from March 11-March 30, 2020. We extracted data on demographics, comorbidities, admission vital signs and labs, need for mechanical ventilation, renal replacement therapy (RRT), in-hospital death and discharge. AKI was defined by KDIGO criteria. Chi-square analyses and Wilcoxon tests were used. Data was censored on April 12, 2020. All patients had ≥14 days of follow up.

Results: Mean age was 63 (SD 12) years old; 69% were men and 33% were Black and 23% were Hispanic. Forty-five patients (39.8%) had chronic kidney disease, 58(51%) had diabetes mellitus and 87(77%) had hypertension. The majority presented with AKI within 24 hours of admission, 75% had Stage 3 AKI. Ninety-two (81%) patients had proteinuria and 53(47%) had hematuria. Intensive care unit (ICU) was required in 62(55%), 64(57%) required mechanical ventilation, 56(49%) required RRT and 18(16%) were not candidates for RRT. In-hospital death occurred in 68(60%) and 22% were discharged. Of those who required RRT, in-hospital death occurred in 35(62.5%) and only 6 patients were discharged, 5 of whom remained RRT dependent. Heavy proteinuria (3+4+) and initial C-reactive protein (CRP) were higher in those with AKI who died [21.1 (IQR 14.3-29.6) versus 6.6 (12.3-16.3), p=0.001].

Conclusions: Severe AKI in the setting of COVID-19 is associated with increased utilization of ICU, mechanical ventilation, and RRT. Outcomes are poor in those with Stage 3 AKI, underscoring the need for palliative care involvement and early goals of care discussions. Elevated initial CRP and heavy proteinuria may be useful to risk stratify patients with COVID-19 and severe AKI at increased risk for mortality.

PO0688
Clinical Factors Associated with AKI in Patients with COVID-19 from a University Hospital in Brazil
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Background: Critically ill patients with COVID-19 frequently presents Acute kidney Injury (AKI) associated with increased mortality. However, there is paucity of data from Brazil. So, we analyzed factors in associated with COVID-19 hospitalized at Hospital Sao Paulo-Federal University of Sao Paulo. Diagnosis and classification of acute kidney injury (AKI) were by KDIGO. We examined the rates of renal function, mechanical ventilation (MV), renal replacement therapy (RRT), medications and in-hospital mortality.

Methods: We conducted an observation with frequencies and association with binary logistic regression study in patients with COVID-19 hospitalized at Hospital Sao Paulo-Federal University of Sao Paulo. From March 15th to May 7th, 2020. The study was approved by the institutional IRB.

Results: We observed a total of 172 in-patients with COVID-19. Patients were predominantly male (61.5%). We observed hypertension in 55%, diabetes 34%, smokers 27%, obesity (19%). Eighty-nine (52%) patients needed intensive care unit (ICU), 70 (99%) cases of AKI were in ICU (31% of general ward admissions; p<0.001). In the ICU there were 78% needed mechanical ventilation, 36% in RRT, amine vasoactive 65% and mortality in 48%. AKI patients were older (61±15, 55±15; p<0.01), higher creatinine in admission (2.6±1.6, 1.3±0.7; p<0.002), higher RWD (14±7.1, 13±3.1; p<0.08), needed of MV (88%) and vasoactive amine (90%), RRT (88%) and higher mortality (87%). We used creatinine, RWD, in-hospital death and discharge as dependent variables.

Conclusions: AKI is associated with high rates of RRT and death. Higher age and need of mechanical ventilation were associated with AKI in COVID-19 patients.

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PO0689

Community and Hospital-Acquired AKI in COVID-19

Background: AKI is a frequent complication of COVID-19. We describe characteristics of patients with COVID-19 who developed both, community-acquired AKI (CA-AKI) and hospital-acquired AKI (HA-AKI) in a Mexico City reference COVID-19 center.

Methods: We included data from all consecutive patients hospitalized between March 16th - 29th 2020, with pneumonia and positive SARS-CoV-2 by RT-PCR test. Only data from patients who finished follow-up (n=636) was analyzed. AKI was defined according to KDIGO and ESKD patients (n=6) were excluded. Clinical and demographic characteristics of those with CA-AKI, HA-AKI, and non-AKI were compared by non-parametric ANOVA.

Results: Of 630 COVID-19, AKI was detected in 164 (26%), 81 (49%) CA-AKI, and 83 (51%) HA-AKI. Among AKI, 84 (51%) were Stage 1, 38 (23%) Stage 2, and 42 (26%) Stage 3. Stage 3 was more frequently observed in HA-AKI (p<0.001). RRT was provided to 15 (9.1%) at a median 3 days from diagnosis. Fluid overload was the main indication for RRT initiation. In general, AKI was associated with higher severity of COVID-19 evidenced by several risk scores, ICU admission, mechanical ventilation, and vasopressor therapy. Recovery from AKI was more frequent in the CA-AKI group 66% vs 44% (p<0.001), and often associated to volume depletion and poor fluid management. Among patients with AKI, 92 (56%) died, 49% in the CA-AKI vs. 63% in the HA-AKI group (p<0.001). There were no differences in RAAS inhibitor use between groups.

Conclusions: CA-AKI and HA-AKI are frequent renal manifestations in COVID-19. AKI is associated with more severe COVID-19 and significantly higher mortality. Although more comorbidities were present in CA-AKI, outcomes were better for CA-AKI vs. HA-AKI in spite the latter group being younger, as it represents ICU patients. Although more comorbidities were present in CA-AKI, outcomes were better for non-parametric ANOVA.

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PO0691

Kidney Injury in ICU Adults with Severe COVID-19
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Background: The SARS-CoV-2 infected humans through the angiotensin converting enzyme (ACE-2) receptor. Kidney, which highly expressed ACE-2, became one of the main targets attacked by SARS-CoV-2. In this cross-sectional study, we aimed to explore renal injury in ICU adults with severe coronavirus disease 2019 (COVID-19).

Methods: Fifty-three severe COVID-19 adults, admitted into ICU (Tongji Hospital, Wuhan, China) from Feb-9.2020 to Mar.24.2020, were finally included in analysis. Baseline demographic, clinical characteristics, laboratory examination data and prognosis were all recorded.

Results: Mean age of 53 patients was 67.5±15.2 years, including 34 men and 19 women. The predominant comorbidities were: hypertension in 26 patients (50.0%), diabetes mellitus in 11 patients (21.2%), cardiovascular diseases in 5 patients (9.6%) and chronic kidney disease in 2 patients (3.8%). The mean serum creatinine at admission was 67.2±26.7 μmol/L, while the baseline urine routine before hospitalisation was uninformed. In the period of whole ICU stay, most patients presented abnormal urine routine: 93.2% of patients had proteinuria (+/-9.1%, 1+ 40.9%, 2+ 31.8% and 3+ 11.4%, respectfully) and 97.7% had hematuria. 20 of 53 patients (37.7%) with mean age of 72.9±9.9 years diagnosed as hospital-acquired acute kidney injury, according to KDIGO stage classification. AKI diagnoses were made in 22 (41.5%) patients, of whom 52.5%, 7.35% and 8.4% reached AKI stage I, II and III, respectfully. AKI was diagnosed after 25.0±12.8 days since onset of Covid-19 and after 7.8±5.6 days since ICU admission. The mean duration of AKI course was 7.9±7.1 days. Finally, 16 of 20 patients with AKI (80.0%) died in ICU. The survival time of AKI patients was 32.9±14.6 days since onset of Covid-19 and 15.7±9.4 days since ICU admission. The in-hospital all-cause mortality of AKI patients was higher than non-AKI patients (80.0% vs 29.4%, p<0.001). Only one (5.0%) patient recovered from AKI during ICU stay (serum creatinine reduced ≤50%).

Conclusions: Kidney injury including abnormal urine routine and increased serum creatinine presented in almost all severe Covid-19 patients. AKI event could predict poor prognosis with severe Covid-19. We should increase awareness of kidney injury in patients with severe COVID-19.

PO0692

Association of Antiplatelet and Anticoagulation Therapy with Dialysis-Inducing AKI-D in Critically Ill Patients with COVID-19
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Background: Critically ill patients with COVID-19 have a high incidence of thrombotic complications and dialysis-requiring acute kidney injury (AKI-D). COVID-19 hypercoagulability has been implicated as a possible contributor to AKI-D. Our hypothesis is that pre-existing antiplatelet (APT) or anticoagulation therapy (ACT) is associated with a lower incidence of AKI-D in critically ill patients with COVID-19.

Methods: Records of patients with COVID-19 admitted to the ICU from March 13th - April 1st 2020 were reviewed. Exclusion criteria included ESRD status, and ICU discharge or death prior to 14 days of follow-up. Groups were divided based on APT or ACT prior to ICU admission. AKI-D was defined as initiation of renal replacement therapy within 2 weeks of any kind of follow-up day 14. Groups were compared using 2-tailed Fisher’s exact test and unpaired t tests.

Results: A total of 149 records were reviewed, and 98 patients were included (47 died and 4 discharged). Twenty-three patients (23.5%) were on APT or ACT and 39 (40%) required RRT. Table 1 compares characteristics by study group. Hypertension and cardiac conditions were significantly different between groups. Twelve (52%) of patients on APT or ACT required RRT and 27 (36%) not on either required RRT (p=0.22).

Conclusions: Pre-existing APT or ACT was not associated with AKI-D in critically ill patients with COVID-19. 2 weeks of follow-up. Our study confirmed a high incidence of AKI-D but was limited by significant differences in cardiac conditions between study groups. Future larger studies examining this association in groups with comparable cardiac conditions are needed.

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COVID-19: AKI and Outcomes

**Background:** Acute Kidney Injury (AKI) occurs in 3-37% of COVID patients; recovery is poorly described.

**Methods:** All patients who recovered from AKI in Clinics Hospital (São Paulo, Brazil) during April 2020 (COVID-related-AKI (COV+), n=35) and September 2019 (COVID-unrelated-AKI (COV-), n=25) were studied for 1.5 month each. Recovery-AKI was represented by spontaneous serum creatinine (sCr) drop in patients not submitted to dialysis, or by withdrawal of dialysis in those who needed the therapy. Serum creatinine, urea (sU), sodium (sNa), bicarbonate (bic), and fluid balance (FB) were analyzed during the first five days of recovery (5-Dr). Data are expressed in mean ± SD. Repeated measures ANOVA was used to compare different days on each parameter, and t test was used to compare groups. Categorical data were analyzed using Fisher’s test.

**Results:** Among 88 COV- patients, 25 recovered from AKI, while 35 in 102 COV+ patients recovered during the time studied (80% COV+ were in KDIGO 3 classification). In COV+ group, COVID-AKI time was predictive of AKI duration: earlier AKI (≤ 4 days from COVID symptoms) lasted 5.6 ± 4.0 days (vs 11.9 ± 9.2 days in later AKI presentation, p<0.01). Both COV+ and COV- patients recovered when sCr was dropped without sU drop. COV+ patients presented negative overall FB during 5-Dr, while COV- patients presented positive FB (p=0.05). COV+ patients had bicarbonate increase in COV+ (from 24.3 ± 3.6 to 27.0 ± 4.9 mmol/L, p<0.05), and in COV- it did not. Among diuretic users, the same pattern of FB was seen between groups (194.9 ± 3163 in COV+ vs 163.5 ± 1080 ml/24h in COV-), and COV- showed increased sNa through 5-Dr (p<0.05), while COV- reduced sNa through 5-Dr (p=0.05). Diuretic users had bicarbonate increase in COV+ (from 24.3 ± 3.6 to 27.0 ± 4.9 mmol/L, p<0.05), but not in COV-. In diuretic non-users, both groups have risen sNa through 5-Dr, but only COV+ reached statistical significance. Diuretic use at AKI-recovery was higher in COV+ patients (57% vs 28%, p=0.05).

**Conclusions:** Later-onset COVID-related AKI seems to be more prolonged. Diuretics should be carefully used in AKI-recovering COV+ patients, once hypernatremia and metabolic alkalosis are more common than in other AKI etiologies.

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Impact of Replacement Therapy Modality on Prognosis of SARS-CoV2 Infection
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Background: Prognosis of SARS-CoV2 infection among patients with Chronic Kidney Disease (CKD) is poorly known. In particular, the impact of replacement therapy (RRT) modality on prognosis is undetermined. Patients with kidney transplant exhibit treatment-induced immunomodulation, while on dialysis are usually older and exhibit higher frailty. We aim to determine the impact of RRT modality on the prognosis of SARS-CoV2 infection among patient with advanced CKD.

Methods: We conducted a retrospective cohort study using our institution’s Clinical Data Warehouse. Health records of all patients with at least one hospitalization or consultation in our nephrology department were screened based on ICD-10 codes. Inclusion criteria were: hospitalization in any of our institution’s hospitals for SARS-CoV2 infection (national Public Health agency criteria). Patients were divided into 3 groups: «active kidney transplants» and «dialysis». A Cox model stratifying on age and medical history of coronary artery disease was used to determine adjusted Hazard Ratio (HR) for death or intensive care unit (ICU) admission.

Results: We included 72 patients: 47 in the «transplant» group and 25 in the «dialysis» group. First hospitalization was on 20/02/28 and last hospitalization on 20/05/19. Median follow-up was 21.5 days. Death or ICU admission occurred in 21 (29%) patients («transplant» group: 15 (32%), «dialysis» group: 6 (24%), p=0.45). In multivariable analysis, adjusted HR of death or ICU admission was 1.70 [95%CI:0.59-4.86] for transplant vs. dialysis (p=0.32).

Conclusions: In our study, among patients hospitalized for SARS-CoV2 infection, no significant difference in risk for ICU hospitalization or death was found between CKD patients on dialysis or with active kidney transplant. A trend for higher risk was noted among patients with active kidney transplant. Further studies are required to confirm these findings.

PO0698
Low-Molecular-Weight Heparin Is a Superior Anticoagulant to Unfractionated Heparin for Renal Replacement Therapy in Patients with AKI due to Coronavirus Disease 2019
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Background: Severe coronavirus disease 2019 (COVID-19) not only causes acute pulmonary pathology leading to acute respiratory distress syndrome needning intubation, but also leads to acute kidney injury (AKI) requiring renal replacement therapy (RRT). Due to hemodynamic instability, these patients (pts) often need either continuous RRT (CRRT) or prolonged intermittent RRT (PIRRT). Accelerated Veno-Venous Hemodialysis (AVVHD), a form of PIRRT with typically 40-50 liter of dialysate used over 8-10 hours has been successfully used to treat hemodynamically unstable pts. In the past, we have published extracorporeal circuit clotting (ECC) to be low (5%) even without anticoagulation. However as hypercoagulability is extreme with COVID-19, we noticed a marked increase in ECC. Unfractionated heparin (UFH) was the initial anticoagulation of choice during the early phase of the pandemic but is currently not considered in preventing ECC, prompting a trial of low molecular weight heparin (LMWH).

Methods: We conducted a single-center retrospective study to evaluate the efficacy and safety of LMWH vs UFH in preventing ECC in pts with AKI due to COVID-19 who received AVVHD from 3/25/20 through 4/30/20 at a large academic medical center. Data collected included pt demographics, type of anticoagulation and thrombolytic use, treatment characteristics including clotting frequency as well as bleeding complications. ECC was defined as any event that required an unexpected interruption in treatment or the use of thrombolytics.

Results: A total of 58 pts received 408 AVVHD treatments. The average pt age was 58 years, 65% were male, 66% were black and 66% were obese with body mass index >30 kg/m2. 188/408 (46%) of AVVHD treatments received anticoagulation with UFH while 165/408 (40%) of treatments received LMWH. ECC occurred in 30% of AVVHD treatments who received UFH vs 15% in the LMWH group, a relative risk reduction of 50% (P = 0.001). 47.1% pts who were on UFH had ECC on the first RRT treatment compared to 13.6% on LMWH (P = 0.01). Only 1 pt experienced a major bleeding event in the UFH group and none with LMWH.

Conclusions: Anticoagulation with LMWH is superior to UFH in reducing ECC in pts receiving AVVHD for AKI due to COVID-19 without an increased risk of bleeding.
COVID-19: AKI and Outcomes

Poster

Patients admitted to KCH from 3/1 to 5/15/2020

Total % of AKI Mortality
COVID-19+ (with HIV) | 43.3% (32/74)
COVID-19+ (without HIV) | 24.4% (19/78)
COVID-19- | 9.1% (9/99)
HIV-uninfected COVID-19 | 9.1% (9/99)

P<0.05 for developed AKI (Mortality Rate) (49.147 359 vs 9.469 24 8.51)

PO0701
Mortality of AKI in Human Immunodeficiency Virus with and without Co-Infection with COVID-19

Ije Oyewo,1 Siddharta D. Rajacharya,1 Ernie Yap,1 Mary C. Mallappallil,1,2 Kings County Hospital Center, Brooklyn, NY; SUNY Downstate Medical Center College of Medicine, Brooklyn, NY.

Background: Since the start of COVID-19 pandemic, concerns have been raised about specific populations being at potential higher risk for developing more severe diseases, and patients living with HIV (PLWH) are among them. SARS-CoV-2, a newly isolated virus from the Corona Virus family, is enveloped, positive-sense single-stranded RNA virus that causes multi-organ failure, especially acute kidney injury (AKI) which is proved to be associated with significantly elevated mortality rate. It dysregulates human immunity especially on T lymphocytes which is shared by HIV as the mechanism of immunity especially on T lymphocytes which is shared by HIV as the mechanism of diseases, and patients living with HIV (PLWH) are among them. SARS-CoV-2, a newly isolated virus from the Corona Virus family, is enveloped, positive-sense single-stranded RNA virus that causes multi-organ failure, especially acute kidney injury (AKI) which is proved to be associated with significantly elevated mortality rate. It dysregulates human immunity especially on T lymphocytes which is shared by HIV as the mechanism of immunity especially on T lymphocytes which is shared by HIV as the mechanism of

Methods: Retrospective chart review of all admitted patients to Kings County Hospital (KCH), a municipal hospital in Brooklyn, New York City between 3/1 to 5/15, 2020, from the electronic medical record. Patients were reviewed in groups of COVID infection without history of HIV, HIV patients admitted without COVID infection and patients with history of HIV who were admitted because of COVID infection. The rate of AKI and mortality were extracted and analyzed using Chi-squared test in SPSS.

Results: A total of 1,092 patients with confirmed COVID-19 diagnosis were admitted in the review time period, out of which 22 were diagnosed with COVID-19 and HIV. In the COVID-19 without HIV diagnosis group, 458 patients developed AKI and 213 patients died, with a mortality rate of 47.3%; in the COVID-19 with HIV group, 9 patients developed AKI and 4 expired, mortality rate is 44.4%. There’s no significant difference between these two groups (p=0.86). Compared to these two groups, 21 out of 93 PLWH without COVID infection had AKI during hospitalization with 2 patients deceased, and a mortality rate of 9.5% which is significantly lower (p=0.03).

Conclusions: Data from our hospital between 3/1 and 5/15/2020 shows the mortality rates of patients with HIV and COVID-19 co-infection with AKI and COVID patients without HIV who developed AKI are not statistically different, but significantly higher than patients with HIV who developed AKI.

PO0702
Phenotype and Outcomes of AKI Associated with COVID-19 in New Orleans

Munir Mohamed,1 Ivo Lukitsch,2 Aldo E. Torres Ortiz,1 Joseph B. Walker,1 Cesar F. Hernandez-Arroyo,1 Muhamed Almasri,2,3 Castauno Caraballo,2,3 1Department of Nephrology, Ochsner Health System, New Orleans, LA; 2Ochsner Clinical School, The University of Queensland, Brisbane, QLD, Australia.

Background: Acute kidney injury (AKI) is a manifestation of COVID-19 (CoV-AKI). However, there is paucity of data from United States, particularly in a predominantly African American (AA) population. We report the phenotype and outcomes of AKI at an academic hospital in New Orleans.

Methods: We conducted an observational study in patients hospitalized at Ochsner Medical Center over 1-month period with COVID-19 and diagnosis of AKI by KDIGO. We examined the rates of renal replacement therapy (RRT) and in-hospital mortality as outcome measures. Adjudication of cause of AKI was independently performed via manual chart review by 3 study team members.

Results: Of 664 admissions with COVID-19, 69 were excluded due to ESRD or kidney transplant. Thus, 575 patients entered the cohort (173 [28%] to an intensive care unit (ICU). Patients were predominantly AA (71%). AKI was diagnosed in 161 patients (28% overall, 61% of ICU admissions), median age 65 [34 – 96], predominantly male (62%) and hypertensive (83%). Median follow up was 25 days. Inhospital mortality rate for those with AKI was 50% (80/161). De novo AKI was diagnosed in 65%, whereas AKI over preexisting chronic kidney disease occurred in 35% of the cohort. Ninety-one (57%) patients arrived with AKI, whereas the remaining 43% acquired AKI during the hospitalization [median hospital day of AKI onset: 4 (2 – 10)]. RRT was required in 89/161 (55%) and 77/105 (73%) patients for all AKI cases and the ICU subset, respectively. The mortality rate for those with AKI-RRT was 72% (64/90). Hemodynamic instability leading to ischemic acute tubular injury (ATI) and rhabdomyolysis accounted for 66% and 7% of the etiology, respectively. Reversible prerenal azotemia occurred in 9%. In 17%, no obvious cause of AKI was identified aside from the COVID-19 diagnosis. Three (1.8%) patients had de novo collapsing glomerulopathy.

Conclusions: CoV-AKI is associated with high rates of RRT, ICU care and death. Hemodynamic instability leading to ischemic ATI is the predominant cause of AKI in this setting, but other etiologies contribute to the overall AKI burden.

PO0703
Presentation on Admission and Outcomes in COVID Patients Admitted with AKI

Richard J. Durrance,1 Payal Ram,1 Paul Catella,2 Demetrios Papademetriou,2 George N. Corissidis,1,2 Icahn School of Medicine at Mount Sinai, Elmhurst Hospital, Elmhurst, NY; Elmhurst Hospital Center Department of Nephrology, Elmhurst, NY.

Background: COVID-19 infection secondary to the SARS-CoV-2 virus was defined by the WHO as a global pandemic. While the disease initially affects the respiratory system, a multi-system organ dysfunction of varying degrees has been described. Renal failure has been recognized as a significant part of the pathophysiology. Elmhurst Hospital Center (EHC) was described as the “epicenter of the epicenter” in New York City. A retrospective chart review was undertaken of COVID positive adult patients (polymers chain reaction testing of a nasopharyngeal sample) admitted to EHC from 3/7/20 - 4/7/20. Demographics, clinical characteristics, biomarkers, and outcomes were examined. AKI was determined by the KDIGO definition. Exclusion criteria: <18 years old, pregnant, ESRD, patients expired within first 5 days.

Results: The average age was 59 years, 77.95% were Male; 55% had hypertension (HTN), 40% had diabetes (DM). Hispanics made up the most significant portion of the demographic with 62.05%, followed by Asians (24.1%). AKI occurred in 44.1% of patients and was associated with HTN (p=0.011) but not DM (p=0.289). AKI was associated with an increased use of mechanical ventilation (p=0.001), and increased mortality (p=0.001). Hypertension (p=0.007), older age (p=0.003), and DM (p=0.018) were significantly associated with mortality. Ethnicity was not associated with mortality (p=0.231). Admission CPK did not have a significant association with AKI (0.065) or death (p=0.19).

Conclusions: Both HTN and DM are associated with increased mortality. AKI is significantly associated with increased respiratory failure requiring mechanical ventilation and mortality. Diabetes and admission CPK were not associated with AKI.
PO0704
Refractoriness of Hyperkalaemia and Hyperphosphatemia in Dialysis-Dependent AKI Associated with COVID-19
Akanksha Ramanand,1 Vinip Varghese,1,2 Yuin Yang,1 Muner Mohamed,2 Juan Carlos Q. Velez,2 Ochsehr Nephrology,3 Ochsehr Clinical School- The University of Queensland, New Orleans, LA; 2Department of Nephrology, Ochsehr Health System, New Orleans, LA.

Background: There have been anecdotal accounts of an unusual incidence of persisting hyperkalaemia (hyperkP) and hyperphosphatemia (hyperSP) in patients with COVID-19 and acute kidney injury (AKI) (CoV-AKI) despite renal replacement therapy (RRT). However, an observation bias could not be discarded. Thus, we examined the rate and severity of hyperkP and hyperSP in patients with CoV-AKI actively treated with RRT.

Methods: Among 161 patients with CoV-AKI, we selected those who underwent RRT by sustained low efficiency dialysis (SLED) for ≥ 2 days (n=64). A database of patients with AKI on SLED who underwent urinary sediment microscopy (Sedi-AKI cohort, 2017-2019, n=60) served as control (non-CoV-AKI). We examined the rate of hyperkP [serum potassium (sK) ≥ 5.5 mmol/L], severe hyperkP [sK ≥ 6.5 mmol/L], hyperSP [serum phosphate (sP) ≥ 4.5 mg/dL], moderate hyperSP [sP > 7.0-10.0 mg/dL] and severe hyperSP [sP > 10.0 mg/dL] as % SLED-days with an event.

Results: Median age were similar: 60 (39-84) and 58 (22-88) years for CoV-AKI and non-CoV-AKI, respectively. Black race (77% vs. 30%, p=0.001) and male sex (78% vs. 61%; p=0.04) were more common in CoV-AKI. Ischemic ATI was the presumed cause of AKI in 85% and 82% of the CoV-AKI and non-CoV-AKI, respectively. Along the duration of SLED, the incidence of hyperkP was greater in CoV-AKI [mean 19 ± 2% vs. 14 ± 0.5% in 5% SLED-days, p=0.002]. The proportion of patients with a 1 event of severe hyperkP was greater in CoV-AKI [33% vs. 7%, p=0.004]. The incidence of hyperSP were similar between groups [mean 56 ± 4% vs. 53 ± 5% SLED-days, p=0.49]. However, the proportion of patients with 1 event of moderate and severe hyperSP were greater in CoV-AKI [86% vs. 60% (p=0.001) and 50% vs. 18% (p=0.002)]. In CoV-AKI, sK and sP correlated with lactate dehydrogenase (LDH) [R=0.305 (p=0.044) and R=0.307 (p=0.043), respectively] but not with creatine kinase; and hyperSP events correlated with shorter SLED runs (hours/run) (R=–0.286, p=0.055).

Conclusions: HyperkP and hyperSP refractory to RRT (by SLED) were more frequent in CoV-AKI compared to other forms of AKI in the pre-COVID-19 era. Because of the correlation of sK and sP with higher LDH and shorter SLED runs, intracellular ion release from cell injury due to cytokine “storm” and RRT interruptions may play a role.

PO0705
Risk Factors for AKI in Patients Hospitalized with COVID-19
Mridula Nadanam, Yu-Lun Liu, Sadaf S. Khan, Shani Shastri, Duwayne L. Willett, Nilum Rajora, Catherine Chen, Susan Hedayati. The University of Texas Southwestern Medical Center, Dallas, TX.

Background: We evaluated risk factors and prevalence associated with AKI in our early experiences with patients hospitalized with COVID-19, 32% of whom required ICU level care, at the University of Texas Southwestern and Parkland Hospitals in Dallas, Texas from 3/13/20-5/07/20.

Methods: Patients admitted with COVID-19 confirmed by SARS-CoV-2 PCR test were screened for AKI. Univariate and multivariate logistic regression was used to perform forward selection and identify independent factors associated with AKI.

Results: COVID-19 was confirmed in 145 patients, of whom 62 (43%) had AKI. Patients with AKI were older, mean (SD) age (17) vs. (54) years without AKI, p=0.03, and were more likely to have hypertension, 74% vs. 47%, p=0.002, and diabetes mellitus, 6% vs. 31%, p=0.001. CKD was present in 42% of those with AKI vs. 7% of those without, p=0.001. Race, ethnicity, and ACEI/ARB use did not differ between groups. Patients with AKI had higher CRP, mean (IQR) 102 (44-161) vs. 59 (21-116) mg/L, p=0.009, and LDH on presentation, 365 (263-493) vs. 317 (228-385) U/L, p=0.04. Ferritin, IL-6, and D-dimer was similar between groups. A higher percent with AKI received steroids, 42% vs. 16%, p=0.001. Tocilizumab was administered in 15% of AKI vs. 5% of non-AKI groups, p=0.08 while rates of hydroxychloroquine and remdesivir use did not differ. Renal replacement therapy was required in 8 patients with AKI, of whom 7 received CVVHD and 1 HD. There were 8 (13%) deaths in those with AKI vs. 5 (6%) in those without. Factors associated with AKI are listed (Table 1).

Conclusions: During the first weeks of COVID-19 outbreak at our hospitals, 43% of patients had AKI. Underlying CKD, diabetes, steroid use and illness severity were independently associated with AKI. Follow-up is needed to determine the long-term impact on kidney function and recovery.

PO0706
The Impact of COVID on CRRT Filter Lifespan
Lewis Mann, Mony Fraer, Sarat C. Kuppachi, Lama A. Noureddine, Lisa M. Antes, Sreedevi koppsieti Jenigiri, Maria T. Story, Meenakshi Sambharia, Jayesh B. Patel, Kandi O’Connor, Benjamin R. Griffin. University of Iowa, Iowa City, IA.

Background: Patients with COVID are more likely to have systemic thrombotic events. Although it has been theorized that those on CRRT also have an increased rate of filter loss due to clotting. If COVID-positive patients are more likely to clot their filter than other patients on CRRT, a more aggressive anticoagulation strategy may be worthwhile. This could result in longer filter lifespan, less circuit down time, which would result in improved clearance, lower costs, less risk of iatrogenic blood loss, and less wasted nursing time. If there is no difference in filter lifespan between COVID positive and negative patients, then more aggressive anticoagulation would result only in added risk without a clear benefit.

Methods: We analyzed COVID data on patients in a related unplanned prospective randomized trial, in which patients are assigned to either pre-filter CVVH or CVVHD. The standard treatment protocol at the University of Iowa is to use citrate anticoagulation with a blood flow rate of 200 mL/min and a dose of 25 mL/kg/hr. The primary outcome is average filter life, and secondary outcomes are mortality, intensive care unit LOS, hospital LOS, and renal recovery.

Results: A total 30 patients using a total of 98 filters from March 25 to May 20, 2020 were evaluated (Table 1). The average filter life in COVID-positive patients was 37.4 +/- 35.8 compared to 33.1 +/- 26.7 in COVID-negative patients (p = 0.55). However, COVID-19 patients were more likely to receive heparin anticoagulation in addition to citrate.

Conclusions: Contrary to other reports, in this retrospective, unadjusted analysis of CRRT patients, the presence of COVID-19 did not decrease average filter life. Further research is needed regarding the appropriate anticoagulation strategy in COVID-19 positive patients.

Table 1: Patient characteristics

PO0707
Single-Center Experience of AKI in COVID-19-Infected Patients in West Kent Hospital, United Kingdom
Matthew James, Tord H. Hogsand, Kieran Jankowski, Jeetendra R. Rathod, Nihal Chitalia, Jonathan Kwan. Darent Valley Hospital, Dartford, United Kingdom.

Background: The outcome of renal function and in COVID-19 positive patients is unclear. We studied the epidemiology of acute kidney injury (AKI) in the COVID-19 positive patients.

Methods: Between 9th March 2020 and 26th April 2020 data was prospectively collected on 253 adult COVID-19 positive inpatients, of whom 71% were male, median age 71 ± 16 years. Common co-morbidities were Hypertension (54%), Cardiovascular Disease (34%), Diabetes Mellitus (12%), Chronic lung disease (8%), and Dementia (6%). CRRT was required in 26% (21/80) patients. The primary outcome was hospital mortality. Secondary outcomes were intensive care unit mortality, hospital mortality, and mortality of patients who were dialysis dependent before admission.

Results: Of the 253 patients, 58.9% were male with (mean ± sdev) age 71.9 ± 16.4 years. Common co-morbidities were Hypertension (54%), Cardiovascular Disease (34%), Diabetes Mellitus (12%), Chronic lung disease (8%), and Dementia (6%). CRRT was required in 26% (21/80) patients. The primary outcome was hospital mortality. Secondary outcomes were intensive care unit mortality, hospital mortality, and mortality of patients who were dialysis dependent before admission.

Conclusions: COVID-19 infected patients have a high mortality rate without a clear benefit.
wise AKI mortality was AKI1 25.7% (27), AKI2 10.4% (11) and AKI3 20% (21). 66.6% had mortality rates of 45% (11) and 20% (21) died with normal creatinine. Mortality in CKD patients as co-morbidity was 64%. All renal transplant patients survived without haemofiltration patients. 23% (25) AKI patients died with normal creatinine. Mortality in patients with COVID-19 infection. AKI was seen in 42.6% patients with COVID-19 infection. More than 60% required mechanical ventilation with 62.5% (15) of these developed AKI with mortality patients. 75% (6) patients with CPAP died. A further 24 (9.75%) of this high mortality.

Conclusions: Elderly patients were most commonly infected with COVID-19 infection. AKI was seen in 42.6% patients with COVID-19 infection. More than 60% COVID-19 infected patients died if they had AKI and were on any form of mechanical ventilatory support or had CKD as co-morbidity.

PO0708
Severe AKI in SARS-COV-19 Patients from a Tertiary Hospital in Rhode Island
Harshitha Kota,1 Kevin Mitchell,1 Jie Tang,1,2 Brown University, Providence, RI; 2University Medicine Foundation Inc, Providence, RI.

Background: The clinical features & outcomes of COVID-19 patients who developed severe AKI are still being elucidated.

Methods: 42 patients with COVID-19 infection who developed KDOQI stage 3 AKI were identified from March 1 to May 15, 2020, at Rhode Island Hospital, a large tertiary teaching hospital. Their clinical presentations and outcomes are presented. The data in table 1 were presented as mean (± SD), median (IQR), or # (%).

Results: The baseline characteristics are outlined in table 1. Among them, 88% were admitted to ICU, 83% were intubated and needed pressor support. 71% received renal replacement therapy (80%) on CVVHDF). The mean duration of RRT and ICU stay were 6 and 14 days, respectively, 33% participants received treatment for COVID-19, among them 14 (33%) received Remdesivir(RDV), 6 (14%) received convalescent plasma(CP), 4 (10%) received hydroxychloroquine(HCQ), and 25 (60%) also received azithromycin. The mortality rates were 15% in the RDV group, 67% in the CP group, and 75% in the HCQ group. The mortality was 67% in those without any treatment. At the 60-day follow-up, 11 (26%) were discharged alive, 21 (50%) died. Those who died were older (mean age 71 vs. 61), having higher Charlson Comorbidity Index (4.7 vs 3.0), more likely to have diabetes (71% vs. 61%) and coronary artery disease (38% vs. 24%).

Conclusions: The mortality rate of SARS-COV-19 patients who developed severe AKI is high in our cohort. Future larger scale studies are needed to elucidate the causes of this high mortality.

Funding: Clinical Revenue Support

Table 1 Baseline and Presenting characteristics of the cohort

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Marital</th>
<th>BMI</th>
<th>BP</th>
<th>DM</th>
<th>CRP</th>
<th>LDH</th>
<th>WBC</th>
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<td>Male</td>
<td>White</td>
<td>Yes</td>
<td>25</td>
<td>120/80</td>
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<tr>
<td>70-80</td>
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<td>Black</td>
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<td>30</td>
<td>130/90</td>
<td>Yes</td>
<td>6.5</td>
<td>50</td>
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PO0709
The Clinical Presentation of AKI Complicating COVID-19: Observations from Elmhurst Hospital, New York City
Nasser M AlNazzari, Demetrios Papademetriou, George N. Cortisidis, Payal Ram, Ellena A. Linden, Aaron S. Stern. Icahn School of Medicine at Mount Sinai, New York, NY.

Background: Early in March, NYC Hospitals became inundated, especially safety net public hospitals. The physicians at Elmhurst Hospital Center (EHC) encountered countless cases of respiratory failure often accompanied by AKI. Autopsy studies from China described an interstitial nephritis, with macrophage infiltrates and complement deposition along with fibrotic changes. We report our experience with COVID-19 and AKI.

Methods: We reviewed the charts of 137 SARS-CoV-2 positive patients (PCR of a nasopharyngeal sample) admitted to EHC 3/7/2020 - 4/7/2020. We categorized patients as having KDOQI defined AKI vs no AKI within the first seven days of admission. Co-morbidities, renal associated markers and inflammatory markers were anaylsed. Clinical outcomes were assessed. Exclusion criteria: <18 years old, pregnant, ESRD, mortality prior to day 7 of hospitalization. Welch T test and Chi square were used for AKI vs non-AKI.

Results: Age was similar in both groups as was gender (male 74% vs 79%) and incidence of diabetes. Early AKI developed in 35% of whom 55% needed RRT; 85% of the AKI patients required mechanical ventilation vs 11.2% of the non-AKI group. Inflammatory markers (WBC, CRP, LDH); urine protein and urine white cells (but not CPK) were significantly higher in the AKI group. Procalcitonin and D-dimers as maximum levels became significant. We found that 20% of those not with early AKI developed late-onset AKI. Mortality was 76.7% in the AKI and 17.9% in the non-AKI group.

Conclusions: Early AKI developing in the first week of hospitalization was associated with overwhelming respiratory failure. The accompanying higher inflammatory markers, elevated urine WBCs and protein could implicate intestinal nephritis as an underlying pathology as described earlier.

<table>
<thead>
<tr>
<th>AKI (n=68)</th>
<th>Non-AKI (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Cr</td>
<td></td>
</tr>
<tr>
<td>1.45 ± 1.08</td>
<td>1.16 ± 1.42</td>
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<tr>
<td>D-dimer</td>
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<td>1.05 ± 0.98</td>
<td>1.04 ± 0.78</td>
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<tr>
<td>Procalcitonin</td>
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<tr>
<td>25 ± 15</td>
<td>20 ± 14</td>
</tr>
<tr>
<td>WBC</td>
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</table>

PO0710
Incidence of AKI in Hospitalized Patients with COVID-19
Lili Chan, Kumanndep Chaudhary, Aparna Saha, Kinsuk Chauhan, Akhil Vaid, Barbara T. Murphy, John C. He, Girish N. Nadkarni, Steven G. Coca. Icahn School of Medicine at Mount Sinai, New York, NY.

Background: Preliminary reports indicate that acute kidney injury (AKI) is common in coronavirus disease (COVID-19) patients and is associated with worse outcomes. AKI in hospitalized COVID-19 patients in the United States is not well-described.

Methods: This is a retrospective observational study of patients aged ≥18 years with laboratory confirmed COVID-19 admitted to the Mount Sinai Health System between February 27 and April 15, 2020. We describe the frequency of AKI and dialysis requirement, AKI recovery, and adjusted odds ratios (aOR) for mortality while adjusting for age, gender, race, comorbidities, and admission labs and vital signs.

Results: Of 3,235 hospitalized patients with COVID-19, AKI occurred in 1406 (46%) patients and 280 (20%) with AKI required dialysis. The proportion with stages 1, 2, and 3 AKI overall was 35%, 20%, 45%, and 20% received dialysis (Figure 1A). In the 815 patients admitted to the intensive care unit (ICU), 553 (68%) had AKI and 34% required dialysis. The median peak serum creatinine was 2.2 (IQR 1.6-3.7) mg/dL in those that did not receive dialysis and was 8.6 (IQR 6.5-11.4) mg/dL in those that did receive dialysis. Urine studies were available for 581 (18%) patients of whom 338 (60%) patients had AKI. 535 (96%) of all patients had any urinary abnormalities of proteinuria, hematuria, or leukocytoria. Independent predictors of severe AKI were chronic kidney disease, systolic blood pressure, and potassium at baseline. In-hospital mortality in patients with AKI was 41%. The aOR for mortality for AKI was 9.6 (95% CI 7.4-12.3), 56% of patients with AKI who were discharged recovered kidney function back to baseline (Figure 1B).

Conclusions: AKI is common in patients hospitalized with COVID-19, associated with worse mortality, and nearly half of patients do not recover kidney function.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: From 2/17 to 5/29, 2020, Dialysis Clinic Inc. had identified 422 COVID+ patients from 90 clinics in 20 states. We compared their characteristics relative to the uninfected source clinic population (N=6,993) and tracked outcomes over the 15-week period.

Results: Comparative characteristics are shown in the table (*P<0.05). Hospitalization occurred in 295 (70%) with 75 deaths, 159 discharges and 61 still hospitalized. Ten patients died <30 days post-discharge. Another 11 deaths occurred in 116 non-hospitalized patients. Overall, 96 of 422 died (22.7%). While more black patients were infected, death rates were higher in white than black dialysis patients (31.5% vs. 18.8%, p=0.008).

Conclusions: Chronic dialysis patients with COVID have higher death rates than the general population. Infected patients tended to be older, with more comorbidity, particularly DM/CVD, and utilized respiratory inhalers/assistance. Group home residents were overrepresented with COVID while home dialysis patients were disproportionately spared.

PO0712

ESKD Patients Hospitalized with COVID-19: Early Outcomes in Bronx, New York
Molly Fisher,1,2 Milagros Yunis,1 Michele H. Mokrzycki,1,2 Ladan Golestaneh,1,2 Maria Coco,1,2 Montefiore Medical Center, Bronx, NY; 3Yeshiva University Albert Einstein College of Medicine, Bronx, NY.

Background: It is unclear whether end-stage kidney disease (ESKD) patients with COVID-19 are at increased risk for adverse outcomes due to impaired immune responses attributed to uremia. Alternatively, a weakened immune state could mitigate the cytokine surge observed in non-ESKD patients with COVID-19. The aim of our study is to describe the clinical characteristics and short term outcomes in ESKD patients requiring hospitalization for COVID-19.

Methods: We performed a retrospective study of 114 consecutive ESKD patients hospitalized at two major hospitals in the Bronx with COVID-19 from March 9, 2020 to April 12, 2020 in the midst of the coronavirus surge in New York City. Clinical and laboratory data were extracted from the medical record and short term outcomes were reported.

Results: The mean age was 63 years (range 30-87); 61.4% were men and 88.6% were Black or Hispanic. Most had hypertension (89.5%) and diabetes mellitus 66% and 30.7% were nursing home residents. Intensive care unit admission was required in 13(11.4%) patients and 17(14.9%) required mechanical ventilation. In-hospital mortality occurred in 23(20%) patients and was similar to mortality observed in non-ESKD patients. Mortality was 59% in those who required mechanical ventilation. At the time of data censoring, 47% had been discharged and 32% remained hospitalized. Initial procalcitonin, ferritin, lactate dehydrogenase and lymphocyte percentage were significantly higher in those who died.

Conclusions: Short term mortality in Bronx ESKD patients hospitalized with COVID-19 was similar to non-ESKD patients. Mechanical ventilation was associated with high mortality. Initial elevated inflammatory markers may be predictors of mortality in ESKD patients with COVID-19. To date, this is one of the largest studies describing outcomes in hospitalized ESKD patients with COVID-19. Further studies describing long-term outcomes in this population following COVID-19 are needed.
PO0714
Implementation of Strategies for Prevention and Control of SARS-CoV-2 Infection at Dialysis Units in Latin America: Analysis from GlomCon Latin America Working Group (LGlonCon)
Denise Arellano-Mendez,1 Julio A. Gutierrez-Prieto,1 Javier Soto-Vargas,1 Blanca Martinez-Chagollaga,2 Franco H. Cabeza Rivera,1 Desiree Garcia Anton,1 Dolores Negreira,3 Carmen Ayala-Casado,5 GlomCon Latin America Working Group1 Unidad Medica de Atencion Ambulatoria 254, IMSS, Morelia, Mexico; 2Hospital Central del Estado de Chihuahua, Chihuahua, Mexico; 3Hospital General Regional 46, IMSS, Guadalajara, Mexico; 4Hospital General “Dr. Miguel Silva", Morelia, Mexico; 5University of Mississippi Medical Center, Jackson, MS, "Hospital General de Mexicali, Mexicali, Mexico; 6Multi-Organ Transplant Program, University Health Network, Toronto, ON, Canada; 7Pathology Department, University Health Network, Toronto, ON, Canada.

Background: Patients on dialysis belong to the high-risk group to develop severe COVID-19 infection due to their multiple comorbidities. International societies have issued recommendations for the control and prevention of SARS-CoV-2 infection at dialysis units but implementing them may not always be feasible as many healthcare systems in Latin America (LA) have limited resources. This study aims to reflect the experience of nephrologists in LA at taking care of these patients and if the recommendations were adopted in their practices.

Methods: Descriptive analysis extracted from an online survey carried out among nephrologists, renal pathologists and other health workers treating kidney diseases between 1 May 2020 and 31 August 2020. Sixteen Spanish speaking LA countries divided into 6 categories. We present the results for the ESRD category.

Results: 430 responses were obtained, 360 were considered for analysis. 276 (86.5%) of the participants were nephrologists and 178 (64%) of them practiced in dialysis units. 163 (92.6%) already implemented strategies to control and prevent COVID-19 in their units. 125 (71%) received training on it and 128 (72.7%) reported personal protective equipment availability. The most common implemented strategies were: education sessions about COVID-19 for patients and caregivers (68.5%), designated isolation areas or shifts (68.2%) for patients with suspected or confirmed COVID-19 and a 7-feet separation between hemodialysis (HD) machines (61.9%). 49 (28%) of the nephrologists reported an outbreak among patients and 60 (34.2%) among medical staff. Patient absenteeism to their HD sessions due to fear of infection, a decrease in the frequency and the duration of the time of the sessions was reported in 41.7%, 30.2% and 36%, respectively. 29 (16.5%) of the respondents considered that those practices were associated with patient mortality.

Conclusions: Most dialysis units in LA are partially implementing the recommended strategies for control and prevention of COVID-19 but this seems to be insufficient since at least one third of them already faced outbreaks among patients and medical staff.

PO0715
Implementing COVID-19 Infection Control Procedures in Outpatient Dialysis in an Urban US Population
Ibironke W. Apata, Jason Cobb, Jose E. Navarrete, Janice P. Lea. Emory University School of Medicine, Atlanta, GA.

Background: Emerging data reveal disparities in the burden and severity of disease among racial and ethnic minorities in the US. Emory Dialysis consists of 4 outpatient dialysis facilities, serving an older, urban and predominantly African-American population. These facilities are in counties with the highest number of COVID-19 cases in Georgia. We describe infection control measures implemented to prevent COVID-19 transmission, and the clinical characteristics of patients with COVID-19 in the facilities.

Methods: Based on CDC’s recommended guidance, we implemented the following infection control procedure between February and April 2020: 1) screening; triaging all patients, and separating patients with symptoms of COVID-19; 2) monitoring staff for COVID-19 symptoms; 3) limiting healthcare personnel in the facilities; 4) universal masking in the dialysis units; 5) conducting PPE re-trainings; 6) assessing facility preparedness; 7) separating high risk patients (nursing home residents); and 8) cohorting patients with COVID-19 to a dedicated dialysis shift.

Results: Of the 745 patients followed at the Emory dialysis facilities, 18 (2.4%) were diagnosed COVID-19 between March 25—May 7, 2020. Among the 18 patients, 17 were receiving in-center hemodialysis and 1 was on peritoneal dialysis. The median age was 66.8 years (range 43–84) and 11 (61.1%) were female. Nine (50%) were residents of a skilled nursing facility. Sixteen (88.9%) patients had a diagnosis of hypertension, 10 (55.6%) had diabetes, and 10 (55.6%) had cardiac disease. Eight patients (44.4%) required hospitalization and 4 patients (22.2%) died from COVID-19 related complications. Two patients (11%) were dialyzing at adjacent dialysis stations and the timing of their symptoms suggested possible transmission in the dialysis facility. In response, education, infection control audits and PPE re-trainings were conducted to bolster infection control practices.

Conclusions: In a high-risk patient dialysis population, we successfully implemented recommended infection control measures to mitigate the spread of SARS-COV-2 in our facilities. Dialysis facilities must stay vigilant and monitor for possible transmission of COVID-19. Regular audits of infection control practices remains critical.
PO0718
Clinical Characteristics and Outcomes in ESKD Patients with COVID-19 Infection in an Urban Community Hospital in Brooklyn, New York, During the Global Pandemic
Carlos M. Zapata, Yanina E. Rodriguez, Olawale Akande, Laurie Ward, Premila Bhat. Wyckoff Heights Medical Center, Brooklyn, NY.

Background: The impact of coronavirus disease 2019 (COVID-19) on individuals with End Stage Kidney Disease (ESKD) receiving maintenance hemodialysis (MHD) is unknown. This study aims to describe clinical characteristics and outcomes in a cohort of patients with ESDK receiving MHD hospitalized with confirmed COVID-19 infection in an urban community hospital during the New York City peak of the global COVID19 pandemic.

Methods: Cases with a diagnosis of ESKD and COVID-19 based on positive PCR testing results were identified from retrospective review of electronic health records for patients hospitalized between March 4, 2020 and April 30, 2020. Electronic health records were reviewed in order to obtain demographic data, presenting symptoms, laboratory values, medical management, and outcomes.

Results: 29 patients with ESKD on MHD with confirmed COVID-19 infection were identified. 16 (55%) were over age 60 years, 20 (69%) were male and 14 (48%) were Hispanic. 18 (62%) had Diabetes and 26 (89%) were overweight or obese (BMI ≥25). All had hypertension. 68% were on Statin and 40% on ACE inhibitor or ARB at the time of admission. 25 (86%) were dialyzed via arteriovenous fistula or graft. The most common presenting symptoms were dyspnea (85%), cough (60%) and fever (28%). All chest radiographs showed abnormalities, with diffuse infiltrates on 21 (72.4%) and focal infiltrates on the remainder. All patients who required renal replacement therapy during hospitalization received conventional HD. 10 patients required mechanical ventilation during hospitalization (34%); all of these patients died. Overall, 13 patients (45%) died and 16 patients (55%) were discharged after a median of 6 and 7 days hospitalization, respectively. Three patients (10%) were readmitted during the period of observation. No significant associations were found between age, sex, race, or diabetes and mortality. Mechanical ventilation was the most consistent predictor of death.

Conclusions: 45% mortality was observed in a small cohort of patients with ESKD on MHD with confirmed COVID-19 infection hospitalized during the peak of the global COVID-19 infection. This high mortality rate reinforces the need for social distancing and infection control measures to reduce transmission in this high risk population.

Funding: Clinical Revenue Support

PO0719
Clinical Outcomes of Patients with ESKD Hospitalized with COVID-19
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Background: Patients with end-stage kidney disease (ESKD) comprise a vulnerable population to infections. COVID-19 has been responsible for high mortality worldwide. To-date, there is limited data regarding the impact of COVID-19 in the ESKD population. We report clinical outcomes of ESKD patients with COVID-19 admitted to an academic hospital in New Orleans.

Methods: We conducted an observational study in patients with ESKD and COVID-19 hospitalized at Ochsner Medical Center over a 7-week period. We compared rates of need for mechanical ventilation, shock, need for intensive care (ICU) and in-hospital mortality as outcome measures between patients with and without ESKD.

Results: Among 851 admissions (67% black) with COVID-19, 49 (6%) patients had diagnosis of ESKD. Patients with ESKD were mostly male (61% vs 49% in non-ESKD vs 49% in non-ESKD, p=0.16) were admitted (BMI) were 32 vs 27 kg/m2 (p = 0.11) for those admitted to ICU vs wards, respectively. Thirteen of them (27%) vs 293 (37%) in the non-ESKD group, p=0.16) were admitted (BMI) were 32 vs 27 kg/m2 (p = 0.11) for those admitted to ICU vs wards, respectively. Thirteen of them (27%) vs 293 (37%) in the non-ESKD group, p=0.16) were admitted for COVID19 infection. This high mortality rate reinforces the need for social distancing and infection control measures to reduce transmission in this high risk population.

PO0720
Clinical Symptoms in 44 Hemodialysis Patients Who Survived and Recovered from COVID-19 in Relation to Age and Hospitalization: An International Experience
Mauro Prioz,1 Szymon Brzozko,2 Marta Serwanska-Switew,2 Werner Kleophas,3 Thilo Krueger,4 Joao M. Frazao,5 Fatima Silva,6 Wisam H. Al-Badr,1 Atef Z. Altaher1 Rosnawati Yahya,7 Maciej Drozdz,8 Partha Das,9 Claudio A. Montero,1 Stefan H. Jacobson,9 DaVita Colombia, Bogota, Colombia; DaVita Poland, Wroclaw, Poland; DaVita Germany, Dusseldorf, Germany; DaVita Portugal, Lisbon, Portugal; DaVita Saudi Arabia, Riyadh, Saudi Arabia; DaVita Malaysia, Kuala Lumpur, Malaysia; DaVita International, London, United Kingdom; DaVita Kidney Care Brazil, Brasilia, Brazil; Karolinska Institutet, Stockholm, Sweden.

Background: A novel coronavirus (SARS-CoV-2) is now rapidly spreading throughout the world. Patients undergoing long-term in-center hemodialysis (HD) are highly vulnerable given kidney failure, comorbidities, and the need for frequent visits to a dialysis facility.

Methods: A total of 610 patients on maintenance HD at DaVita clinics in 6 countries were tested for presence of infection with SARS-CoV-2 using polymerase chain reaction (PCR) between March 28 and May 18. Of these, 115 HD patients (19%) were positive. Information up to May 25, 2020, show that 44 patients have recovered. Clinical symptoms during infection with SARS-CoV-2 are reported from these 44 recovering survivors (Germany 13 patients, Poland 12, Portugal 12, Colombia 2, Saudi Arabia 3, and Malaysia 2) to be classified into 4 categories: symptoms, mild, moderate, or severe symptoms. Hospitalizations and time to recovery were also analyzed. Statistical comparisons were made using Chi-2 analysis and Kruskal-Wallis tests.

Results: Of the 44 patients recovering from COVID-19, 22 were ≥70 years and 22 were <70 years. Symptoms in relation to age, hospitalization, and time to recovery are shown below.

Conclusions: The majority of HD patients (66%) who recovered from COVID-19 had no or mild clinical symptoms during the infection. There were no significant differences in the occurrence of symptoms from SARS-CoV-2 in relation to age, hospitalization, or time to recovery. Additionally, old and frail HD patients with confirmed COVID-19 may have mild symptoms of the disease.

Percentage of HD Patients Who Recovered From Clinical Symptoms During Infection With SARS-CoV-2

PO0721
Comparison of Psychological Distress and Demand Induced by COVID-19 During the Lockdown Period in Patients Undergoing Peritoneal Dialysis and Hemodialysis: A Cross-Section Study in a Tertiary Hospital
Zhiyun Zang, Zi Li, Xiaoxiao Xia, Xiaofang Wu, Department of Nephrology, West China Hospital, Sichuan University, Chengdu, China.

Background: Since the outbreak of COVID-19 in December 2019, it has spread rapidly and widely, bringing great psychological pressure to the public. In order to prevent HD and PD patients from being infected by COVID-19, patients were required to stay at home during the lockdown period. In order to prevent the psychological distress and the psychological demand induced by COVID-19 in the patients undergoing dialysis and compare the difference between hemodialysis (HD) and peritoneal (PD) patients during the lockdown period.

Methods: Questionnaires were given to the dialysis patients in West China Hospital of Sichuan University. The Impact of Event Scale (IES) was used to investigate the clinical symptoms in 44 hemodialysis patients who survived and recovered from COVID-19 during the epidemic period of COVID-19. IES scores and the psychological support during the epidemic period of COVID-19.

Results: 232 eligible respondents were enrolled in this cross-section study, consisting of 156 PD patients and 76 HD patients. The median IES score for all the enrolled patients was 8.00 (2.00-19.00), which belonged to the subclinical dimension of post-traumatic stress symptoms. PD patients had a significant higher IES score than PD patients (11.50 vs 8.00) (p<0.05). PD patients already got more psychological support from the medical staff. There was no significant difference in the further demand of psychological support between the two groups. In the multivariate regression analysis, we found that dialysis vintage, the impact of COVID-19 on the severity of illness and daily life, the IES scores and the psychological support during the epidemic period of COVID-19.

Conclusions: HD patients had more severe trauma-related stress symptoms than PD patients. When major public healthy events occurred, careful psychological estimate and sufficient psychological support should be provided to the dialysis patients, especially to the HD patients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
COVID-19: Dialysis Patients

PO0722

COVID-19 Incidence and Outcomes in Hemodialysis Patients in Mexico
Juan M. Ardavin Iturato, Alicia Pineduia, Juan Carlos Rodríguez, Medica Santa Carmen Staff Nephrologists Medica Santa Carmen, Mexico, Mexico.

Background: HD pts are at high risk for COVID-19. High incidence and death rate were reported in China and Europe with more than 20% of asymptomatics. We report incidence, features and outcomes of COVID-19 in HD patients in a network of 8 clinics in Mexico. A protocol was started on Mar 15 with hygiene measures; symptoms triage; separation by age; use of PPE and isolation of suspected cases. We use a more inclusive case definition, different from Mexico Health Ministry’s (SSA). All cases are referred for PCR but most aren’t tested.

Methods: Retrospective analysis of cases (suspect or PCR(+) from mar 15 to may 22 2020 compared to controls. T-test and Chi2 were used. Hospitalization, IMV and deaths were registered. Overall mortality from mar - may 2020 compared to same period of 2019. We compared the number of cases using our case definition with that using the SSA’s. Incidence of COVID-19 in staff was also analyzed.

Results: Total 1267 pts; Of 102 suspects 25 (24%) had PCR and 16 (64%) were (-). 13 (12%) non-tested were discarded based on alternative dx. 2 pts with (-) PCR were cases based on CT. Total 75 cases (10 (+)PCR, 65 w/o test) were analyzed and compared to controls. No differences in HD vintage, DM, CVD, HD session length, VA, BUN or Kt/V. Less age, fem gender, HTN, more sessions/wk, ACEi/ARB and lower Hb were found in the cases. 7 (9%) hospitalized and 2 (3%) required IMV. There were 6 (8%) deaths, only 1 (1.3%) attributed to COVID-19. Overall mortality minimally higher than that of the same period of 2019 (1.5% vs 1.30%). 31% of cases had only 1 symptom. Only 1 PCR(+) and 14 PCR(-) cases fulfilled SSA’s case definition. Among 231 staff members, 31 (13.6%) had tested (+) PCR(+) and 20 non tested.

Conclusions: Incidence of probable or confirmed COVID-19 was 5.9%; probably overestimated suggested by scarce testing and low mortality. ACEi/ARB use more frequent in cases, adjusted for HTN and age. Our protocol helps prevent in-clinic contagion. A more comprehensive probable case definition appears more useful for HD patients.

PO0723

COVID-19 Infection in Patients with ESRD Requiring Hemodialysis
Anna Anisimova, Valeria Ripa, Biruk Almaz, Nirav Mistry, Fariborz Rezai, St. George’s University School of Medicine, True Blue, Grenada; Saint Barnabas Medical Center, Livingston, NJ.

Background: This case series assesses characteristics and outcomes of patients with confirmed novel coronavirus (SARS-CoV-2, COVID-19) infection and end stage renal disease (ESRD) requiring hemodialysis during the COVID-19 pandemic.

Methods: This is a single center retrospective study of 24 ESRD patients on hemodialysis who were admitted to Saint Barnabas Medical Center, a 597-bed acute care hospital in Livingston, New Jersey, and with a confirmed COVID-19 diagnosis between February 1st to April 5th, 2020. The characteristics, clinical course, and outcome were assessed and compared. In addition, a subgroup analysis was made between patients who expired (n=8) versus those who lived (n=16).

Results: The overall mortality rate was 33.3% vs. 21% in the general population with COVID-19. Among the 4 (16%) patients who required ICU admission and prolonged pressor support and invasive mechanical ventilation, 2 (50%) patients were successfully extubated and discharged from the hospital while the other 2 (50%) patients died. There were no statistical differences in laboratory values between patients who survived versus patients who died except C-reactive protein (CRP), p=0.002.

Conclusions: We report a mortality rate of 33.3% in our case series of 24 patients with ESRD on dialysis with concurrent COVID-19 infection. There was a statistical difference in CRP value between patients who died versus survived. Fifty percent of intubated patients were successfully extubated and discharged.

PO0724

COVID-19 Infection Patterns in an Academic Inner City Dialysis Unit
Vipin Synthasam, Sarah M. Ahmad, Sandeep Aggarwal, Ihab M. Wahba, Yonghong Huan, University of Pennsylvania, Philadelphia, PA.

Background: COVID-19 remains a major public health emergency and in-center dialysis provides multiple opportunities for its spread. Elderly immunocompromised host is pose a significant risk for infection as well as poor outcomes. We present a retrospective analysis of COVID-19 cases in our dialysis unit.

Methods: Retrospective analysis was done as a part of a quality improvement project using unidentified patient data including: demographics, distribution of dialysis shift, patient zip code, transportation mode (self, ride share or public transport), residence type (home, long term care facility or homeless shelter), etiology of ESRD and dialysis vintage. T-test and multivariate analysis (including logistic regression for binary and categorical data) were conducted using SPSS v23.

Results: There were 70 patients in the unit and 10 became positive for COVID-19. 65 (92%) of all patients were African American. Between COVID-19 positive and negative patients, there was no significant difference in age (62±15 vs 63±14 years p=0.2), dialysis vintage (7.6±8.7 vs 5.2±4.7 years p=0.31), male gender (7/10 (70%) vs 40/70 (58%) p=0.31). 3/10 (50%) of the positive patients were MWF 2nd shift. On multivariate analysis, this effect approached significance (p=0.05); however, there was no information from the positive patients positive status with demographic characteristics, dialysis vintage, residence type, zip code distribution, or transportation modality. Of note, universal masking and temperature screening were implemented on March 5, 2020 in this unit and no new cases were noted after May 2, 2020.

Conclusions: Our analysis did not show any clear factor associated with COVID-19 infection among our dialysis patients although clustering approached statistical significance. Small sample size and demographic distribution are shortcomings of our study; larger scale epidemiological studies and data analysis are required for better understanding the risk of COVID-19 infection amongst in-center dialysis patients.
COVID-19: Dialysis Patients

Background: Patients on regular dialysis are at an increased risk to COVID-19 due to their multiple comorbidities and exposure in the health care setting. The risk for virus transmission within a dialysis unit is also high emphasizing the importance of implementing infection control measures. The objective of this report is to describe the COVID-19 outbreak in a dialysis unit including interventions done.

Methods: Review of the epidemic course with contact tracing was done from March 14 to May 14, 2020 in the dialysis unit of a tertiary hospital in the Philippines. Results: Of 167 patients, 20 became COVID-19 suspects. Eight were positive -3 were exposed from the first confirmed case, 2 were handled by a COVID-19 infected healthcare worker (HCW) who was asymptomatic at time of contact while 2 asymptomatic patients tested positive during mass testing. Two of 67 HCWs tested positive were exposed to patients. Key interventions are (a) enhanced screening by mass testing using NPS/OPs RT-PCR of patients and HCWs after identifying 6 patients and 2 HCWs infected with COVID-19 (b) instead of cohort, dialysis of COVID-19 confirmed and suspected cases was done in isolation rooms separate from the dialysis unit (d) adequate personal protective equipment for HCWs and masks for all patients and (e) environmental disinfection especially in the waiting area with strict social distancing and daily screening.

Conclusions: The infection control and preventive actions done halted the increase in cases. Maintaining these strategies for the duration of the pandemic allowed further decline in the rate of infection.

COVID-19 Suspects, Cases and Interventions

Contact Tracing in the Unit

Effect of COVID-19 on Dialysis Practices on the Ground: Early Results from an International DOPPS Program Survey

Murilo H. Guedes,1,2 Brian Bieber,3 Patricia De Sequeira,2 Pablo A. Urena Torres,1 Giuliano Brunori,1 Xinling Liang,4 Li Zuo,5 Michel Y. Jiaquin,6 Roberto Pecoits-Filho,7 Jeffrey Perl,8 Ronald L. Pisoni,9 Bruce M. Robinson,10
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Background: The COVID-19 pandemic caused unprecedented disruption to dialysis patient care globally. Facility surveys were distributed to assess the impact of COVID-19 pandemic on hemodialysis (HD) and peritoneal dialysis (PD) practices.

Methods: Medical Director (MD) and Nurse Manager (NM) Surveys (MDS, NMS) are being distributed in May/June 2020 to 723 clinics enrolled in the Dialysis (in-center HD, PD) or Peritoneal (PDOPPS) Dialysis Outcomes and Practices Study in Canada, China, Japan, the United States, 7 European countries, 5 Gulf Cooperative Council countries, and China metropolitan areas (Beijing, Guangzhou, Shanghai). Surveys content includes the number of COVID-19 cases, testing, and clinical management, screening, infection control, staffing, patient transportation, and psychological support.

Results: As of 27 May 2020, we have 80 MDS (China, Europe, US = 33, 38, 5) and 101 NMS (45, 46, 9) responses from DOPPS sites. The following percentages are presented sequentially for China, Europe, and US. Among MDS, 0%, 6%, 67% reported at least one confirmed COVID-19 case among dialysis patients, and 85% confirmed COVID-19 case among dialysis patients, and 100% of MDS reported being on the late phase of the COVID-19 curve. 19%, 23%, 23% reported in all regions, shortages of human and medical resources were common, as were changes to dialysis delivery/practice including more skipped sessions, greater use of potassium binders, and preferentially recommending home dialysis. Over the next month, we expect hundreds more responses, and will compare approaches in PD and HD clinics. These data will inform guidance for dialysis care as the COVID-19 pandemic ensues.


Demographic and Clinical Characteristics of Patients with CKD and SARS-CoV-2 Undergoing Hemodialysis Treatment

Laura C Fuentes-Mendez, Angela M. Cordoba Hurtado, L. M. Perez-Navarro, Rafael Valdez-Ortiz, Maribel Merino. Hospital General de Mexico Dr Eduardo Liceaga, Ciudad de Mexico, Mexico.

Background: Patients on HD or PD are likely to be at increased risk of COVID-19 and its complications because they have multiple comorbid conditions. There is a lack of evidence about the optimal management and even clinical manifestations because clinical presentation is highly variable. The delayed diagnosis is because it’s not recognized by the treating centers and the confusion with patients with fluid overload or uremic syndrome can be fatal in this population.
Factors Associated with SARS-CoV-2 Infection (COVID) Severity and Mortality in Chronic Dialysis Patients

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Background: From 2/17 to 5/29, 2020, Dialysis Clinic Inc. had 422 maintenance dialysis patients diagnosed with COVID from 90 clinics in 20 states. While prognostic factors in the general population have been reported, there is limited information regarding the US dialysis population.

Methods: Over a 15 week period of observation, 96 patients died (22.7%) and 116 (27.5%) were not hospitalized (for up to 30 days post-COVID diagnosis), likely with milder illness. We compiled univariable associations with p<0.1 into stepwise logistic regression models (forcing in age, sex, race) to determine factors associated with 1) Death from COVID; and 2) Moderate/severe illness (hospitalized or died without hospitalization <30 days post-COVID diagnosis).

Results: Candidate variables are listed in the table, with retained significant factors marked (a or b at p<0.05). Notably, 42% of all deaths occurred at age >75 years, increasing to 74% of all deaths at age >65 years. Wheelchair use also associated with higher death risk.

Conclusions: Dialysis patients with low albumin and vintage ≥1 year associated with increased illness severity. It was surprising that a history of pneumonia vaccine associated with more severe illness - whether this reflects “treatment by indication” bias vs. pulmonary immune activation by vaccination vs. chance finding is unclear. PVD also tended to increase illness severity but more importantly, was significantly associated with risk of death, independent of older age.

<table>
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Impact of Undertaking Safeguards to Limit Exposure and Prevent COVID-19 Infection in Ambulatory Dialysis: A Single-Center Experience


Background: Dialysis patients are considered at high risk to develop serious COVID19 complications. Taking extreme measures are necessary to prevent COVID19 transmission at the dialysis center. We are presenting outcomes of our COVID19 prevention project from our largest dialysis center in Qatar.

Methods: Our project was done at FBJKC (largest dialysis center in Qatar with about 60% of all hemodialysis (HD) and 90% of all peritoneal dialysis (PD patients in Qatar)) between March 1st and May 25th 2020. We gradually implemented a bundle of measures and algorithm (attached) to properly triage and limit COVID19 exposure inside the center. New infection control protocol with specifications to COVID19 were implemented, including a new policy for reusing N95 masks in high risk areas. We tracked number of patients and staff who were infected during that period and source of infection.

Results: Our dialysis census during that period was 480 HD and 170 PD patients. Only 6 HD patients turned positive for COVID19 (0.9%) and 2 PD patients (1.2%) (compared to 1.3% general population in Qatar by May 25th). We had 3 dialysis staff infected out of 114 (2.6%). Our investigation showed that all cases of COVID19 (both in patients and staff) were likely contracted outside the center. All staff and patients exposed to positive cases of COVID19 inside the center turned out negative. Our infection control classified most exposures at low risk, especially after we fully implemented our precautions.

Conclusions: Preventive actions implemented inside a large dialysis center led to prevention of COVID19 transmission. Increase positive COVID19 cases (in staff and patients) were related to countrywide growth of infection.

Outcomes of COVID-19 in ESRD Patients on Hemodialysis

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Background: Patients with ESKD have a dysregulated immune system and a higher annual mortality rate compared with the general population. We aimed to describe the clinical characteristics and compare the outcomes of patients with and without ESKD, among those hospitalized with COVID-19 disease.

Methods: We reviewed the health records for all patients hospitalized with Covid-19 between March 1, 2020 and April 27, 2020 from 13 hospitals in New York. Patients < 18 years or admitted to inpatient obstetrics service were excluded. ESKD diagnosis was defined using ICD-10 code and manual adjudication. Patients were followed up through May 27, 2020.

Results: Of 10,482 patients admitted with COVID-19, 419 (4.0%) had ESKD. Among patients with ESKD, 408 (97.4%) were on hemodialysis and 11 (2.6%) were on peritoneal dialysis. When comparing baseline characteristics of the two groups, patients with ESKD were older, were predominately of Black race, and had greater proportions of comorbid conditions. The primary outcome was that patients with ESKD had a higher odds of in-hospital death than those without ESKD (rates, 31.7% vs 25.4%; OR 1.4, 95% CI 1.1 - 1.7). After adjusting for age, sex, race/ethnicity, the odds of
in-hospital death remained higher in the ESKD group (adjusted OR 1.5, 95% CI 1.2 - 1.8). The ESKD group did not have a significantly higher odds of needing mechanical ventilation than the non-ESKD group in both the crude analysis and after adjustment for age, sex, race/ethnicity. The odds of having a length of stay of >7 days was higher in the ESKD group compared to the non-ESKD group, in both the crude analysis and the adjusted analysis (OR 1.62, 95% CI 1.3 - 2.1; adjusted OR 1.6, 95% CI 1.3 - 2.1). The independent predictors for death for non-ESKD patients were age, male gender, cancer, CHF, elevated BUN, low albumin and being on a ventilator. The independent predictors of death for ESKD patients were age, lymphopenia, low albumin and being on a ventilator. Black race was associated with lower risk of death.

Conclusions: ESKD patients had a higher rate of mortality compared to non-ESKD patients hospitalized with COVID-19. Black race was associated with a lower risk of death among ESKD patients compared to white patients.

PO0735
Outcome of Hospitalized ESRD-COVID-19 (C19) Infected Patients
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Background: Emory University affiliated hospitals serve the metro Atlanta area, where a significant number of C19 cases have occurred. In this report we describe the outcomes of AKI and ESRD patients with confirmed C19 admitted to our health-system.

Methods: All patients seen by Emory Nephrology at 2 tertiary referral and one county hospital were categorized as ESRD if they required dialysis prior to C19 infection, or AKI if they developed acute kidney injury as a result of C19 infection. Outcomes of interest included patient survival and discharge from the hospital. Admission to Intensive Care Unit (ICU) and use of mechanical ventilation were recorded. Comorbid conditions and outpatient use of medications were analyzed.

Results: From 3/1/20 to 5/26/20, 474 consecutive patients were seen in COVID-19 related consultation. 287 patients were considered PUI and eventually tested negative for C19. The remaining 187 patients were C19 positive by nasopharyngeal swab or tracheal aspirate and represent the study population for this report. There were 43 ESRD (23%) and 144 AKI (77%) patients. Age (64 vs 63 years), gender (63 vs 66% males) ethnicity (86 vs 82% African-americans) and comorbid conditions were similar in AKI and ESRD patients. AKI patients were more likely to be admitted to ICU (83 vs 35%) and to require mechanical ventilation (73 vs 20%) compared to ESRD patients (p<0.05). Figure 1 presents the outcomes based on the type of renal disease at presentation. The eGFR of AKI patients at time of admission was 50±34 ml/kg/m². 84 AKI patients required dialysis during their hospitalization (52.5%).

Conclusions: Patients with ESRD C19+ were less likely to require ICU admission or mechanical ventilation. Mortality of ESRD patients was 14% compared with 42% of AKI patients, (p=0.002). ESRD patients with C19 were also more likely to be discharged from the hospital compared to those with AKI. Despite similar demographics and co-morbidities, hospitalized AKI C19 patients had worse mortality than those receiving chronic dialysis.

PO0736
Non-Hospitalized Maintenance Hemodialysis Patients with COVID-19 Have Elevated Inflammatory Markers
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Background: In addition to an aggressive pneumonia, patients hospitalized with COVID-19 have marked inflammatory and hypercoagulable states, with downstream cardiovascular and thrombotic events. Hemodialysis patients have baseline increases in inflammatory markers among hemodialysis patients with COVID-19 who were managed as outpatients.

Methods: Patients in our dialysis program with one positive nasopharyngeal swab PCR for SARS-CoV-2 were consecutively admitted to an outpatient COVID-19 hemodialysis shift. While receiving their usual dialysis prescription, the patients also had weekly measurements of D-Dimer, Fibrinogen, C-reactive protein (CRP), and Serum Ferritin, until they tested negative x 2 for SARS-CoV-2.

Results: 16 consecutive patients were admitted to the COVID-19 isolation shift over 30 days. Their average age was 60 yr, 56% were Black, 25% Hispanic, and 44% female. Causes of ESKD included diabetes (75%), glomerular diseases (19%), and hypertension (6%). No patients received intravenous iron supplementation while on the isolation shift. Table 1 displays the inflammatory marker levels in this group. Note, the 4-fold (D-Dimer), 6-fold (Ferritin) and 21-fold (CRP) increase in these biomarkers from normal levels.

Conclusions: Our initial, unique data show an increase in inflammatory markers in a cohort of non-hospitalized COVID-19 hemodialysis patients. Such an increase may be from the pro-inflammatory impact of COVID-19 in a group with pre-existing high levels of inflammation from uremia and oxidative stress. Additional investigation as to whether elevated inflammatory markers with cardiovascular and thrombotic events (dialysis circuit and vascular access clotting, sudden cardiac death) is needed.

Funding: NIDDK Support, Clinical Revenue Support

Inflammatory Markers among Non-Hospitalized HD Patients with COVID-19

PO0737
Network Analysis of In-Center Spread of COVID-19: A Single Dialysis Center Experience
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Background: The need to continue in-center hemodialysis (HD) during COVID-19 pandemic presents a risk of transmission for patients and staff members. The present study aimed to determine if the periodic interactions among patients and staff resulted in spread of COVID-19 in a HD center during a period of 2 months

Methods: This is a retrospective analysis on a HD center in New York City (172 patients, 32 staff members, 26 chairs, MWF and TTS schedules, and 4 shifts/day). From March 24th to April 24th we recorded every HD treatment (chair, patient, and staff member involved in care). We kept dated records for positive COVID-19 cases (patients and staff). To estimate the patient-to-patient interaction, we obtained the location coordinates of each dialysis chair, calculated the Euclidian distance between them and weighted the interaction by proximity between chairs. We conducted network analysis to assess these interactions.

Results: During the study period, 16 patients and 2 staff members became COVID-19 positive. As shown in Figure 1(a), there were 3 chairs (2, 24, and 25) that had more than 1 positive patient. Clusters in chairs 2 and 25 were ruled out based on a lack of direct contact between the involved patients (at least 2 shifts separating them at all times; no in-between patients became positive); chair 2 had a nonviable temporal direction of transmission. Based on schedule, shift, and a 14-day incubation period, the cluster in chair 24 was dismissed. This was corroborated by network analysis [Fig. 1(b)] where the purple dots represent the COVID-19 positive patients, the blue dots represent negative patients (same shift/schedule), and the edges represent the weighted patient-to-patient interaction. We reasoned that more exposed patients would have had a higher chance of becoming infected. Similar information was found for staff-to-patient interaction

Conclusions: Based on our analysis we consider that for patient-to-patient, staff-to-patient, and staff-to-staff interactions, in-center spread of COVID-19 was unlikely

Funding: Private Foundation Support

PO0738
Outcomes of Patients on Chronic Dialysis Hospitalized with COVID-19
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Background: Preliminary reports find that patients with end stage renal disease (ESRD) on dialysis who test positive for SARS-CoV-2 have fewer symptoms and require less intensive care than expected. However, there are no reports regarding the outcomes of ESRD patients who are hospitalized with coronavirus disease 2019 (COVID-19).

Figure 1(a)infection history; (b)network analysis patient interaction

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: This is a retrospective observational study of patients aged ≥18 years with known COVID-19 admitted to the Mount Sinai Health System between February 27 and May 20, 2020. ESRD patients were identified by International Classification of Disease codes for ESRD. ESRD patients were propensity matched (5:1) to non-ESRD patients by age, gender, race/ethnicity, comorbidities, body mass index, and facility and week of hospital admission. Multivariate analysis was performed to test the association of ESRD with mortality after adjustment for age, diabetes, hypertension, stroke, coronary artery disease, and congestive heart failure.

Results: 122 ESRD patients were admitted during the study period and matched to 610 non-ESRD patients from the same study period. Patients with ESRD were well matched on age, sex, race/ethnicity and most comorbidities except ESRD patients had a higher prevalence of diabetes (55% vs 43%, P=0.02) and hypertension (66% vs 55%, P=0.03). ESRD patients had higher inflammatory markers of ferritin and procalcitonin. There was no significant differences in d-dimer, fibrinogen, C reactive protein, or interleukin-6 (Figure 1A). ESRD patients were significantly less likely to receive mechanical ventilation (3% vs. 10%, P=0.01) or be admitted to the intensive care unit (9% vs. 21%), and had similar in-hospital mortality (9% vs 15%, P=0.5). ESRD status was associated with lower odds of intubation and intensive care admission, but not significantly associated with mortality after adjustments for age and comorbidities (Figure 1B).

Conclusions: While ESRD patients had a higher prevalence of comorbidities and higher inflammatory markers, they had similar in-hospital mortality as matched non-ESRD patients.

PO0739
Outpatient Hemodialysis Unit Preparedness During COVID-19 Pandemic in Several Dialysis Units in New York State
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Background: HD units are clustered close contact environments where prolonged and repeated exposure to blood borne pathogens occurs. Weeks into the CoVID-19 pandemic, wide disparities in rates of death and exposure of staff and patients amongst HD units in the same zip code of an epicenter in New York region emerged.

Methods: Random HD units surveyed as to when and what infection control measures they implemented. Direct input into RedCap and SAS 9.0 analysis of the data conducted.

Results: 15 HD units (average census 18-240) responded. Survey compiled exposure rates from 3/1/20 - 4/30/20. The 1st reported case of CoVID-19 by a facility was 3/2/20. Most facilities reported outbreaks (4-30 cases per facility) by 3/21/20. Missed HD sessions due to CoVID varied from 2-100, hospital stays for such patients varied from 2-20 days and death rates from 0-15 per facility. 4 of 15 facilities reported deaths of family members of exposed patients and impediments in logistics of single person transportation forcing carpooling. Home dialysis programs reported minimal deaths and exposures. 20% of facilities had no infection preventionist and 26% no patient educator. Reported waiting area cleaning and hand sanitizer refill rates ranged from 1-5 times per day. 20% of the facilities have < 6 feet distance between patients. Implementation of infection control practices such as wearing of masks by patients varied widely amongst units. Some started March 1st-March 16th some later due to mixed messages of its importance. Lack of personal protective equipment (PPE)(in 13% of facilities), staff, and housekeeping shortages (6.7-13.3%) compounded the problems. Positive CoVID results had 1-10 staff members absent from the facility with sick call rates from 7-30 days, and no staff death. 46% of the HD units don’t belong to the CDC coalition.

Conclusions: Maintenance of strict hand hygiene, proper air flow, repeated environmental surface cleansing, availability of PPE, and patient and staff education remains a cornerstone in preventing infections from spreading. Lack of leadership support and failing to share best practices between dialysis units in the US remains prohibitive but must be encouraged and standardized.

PO0741
Impact of the COVID-19 Pandemic on In-Center Intermittent Hemodialysis Treatment Adherence
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Background: Studies have shown that 7.9% of patients miss one to two hemodialysis session per month and 35% miss hemodialysis at least once every three months.1 During current COVID-19 pandemic there has been a decrease in utilization of emergency medical services due to fear of contagion. We hypothesized that patients undergoing in-center hemodialysis might have increased compliance with their dialysis prescription to avoid emergency department visits or hospitalizations. We therefore evaluated the effects of the COVID-19 pandemic on patient adherence to their dialysis prescription.

Methods: This is a retrospective analysis of in-center hemodialysis patients treated in the seven American Renal Associates (ARA) dialysis facilities in Dallas, Texas. COVID-19 was declared a pandemic on March 11, 2020 and pandemic related changes were mandated in ARA hemodialysis facilities on March 13, 2020. We used existing clinical data and examined patient compliance with their dialysis prescription between January 1 to March 14, 2020 (pre-COVID) and March 15 to May 18, 2020 (COVID).

Results: The study enrolled 754 eligible patients. Significantly fewer patients missed a single treatment in the COVID vs pre-COVID periods (35.5% vs 49.9%; p<0.001). The percentage of patients who were hospitalized was lower during COVID vs pre-COVID (12.5% vs. 19.6%; p<0.001). The percentage of patients who shortened hemodialysis time was lower during COVID vs pre-COVID (36.2% vs. 40.9%; p=0.06) although not statistically significant. Finally, significantly more patients achieved a weight within 1 kg of their estimated dry weight at the end of the dialysis sessions COVID vs. pre-COVID (28.5% vs. 34.5%, p=0.01).

Conclusions: These data suggest that during current COVID-19 pandemic, hemodialysis patients have become more adherent to their dialysis prescription. Retrospective studies have suggested that patients are avoiding seeking medical care due to fear of contacting the SARS-CoV-2 virus1. Our data suggest that similarly, hemodialysis patients have significantly increased their adherence to hemodialysis prescription in order to avoid hospital visits. Additional studies are ongoing to determine the causes for the observed improved compliance.
PO0742

Accuracy of Lower Temperature Thresholds in Detecting COVID-19 in Hemodialysis Patients

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Background: Patients receiving in-center hemodialysis (HD) are uniquely vulnerable to COVID-19 yet identifying infected individuals may be challenging. They may not present with typical symptoms and low basal body temperature may impair detection of fever. We studied the accuracy of temperature thresholds in detecting COVID-19 in HD patients.

Methods: We retrospectively studied all patients between March 24-May 14, 2020 from a single HD unit (Hôpital du Sacré-Cœur) in Montreal, Canada, where COVID-19 is highly prevalent. All patients who presented with symptoms or contact exposure were tested by nasopharyngeal swab. Promoted by an outbreak, systematic testing of all HD patients was started on April 18th. Basal temperature was defined as the average pre-dialysis temperature from weeks -1 to -3 before testing. Diagnostic performance was determined for various temperature thresholds defined a priori.

Results: Of 205 in-center HD patients, 34 developed COVID-19 during the study period. Of those, 21 (61%) were hospitalised, 4 (11%) required intensive care and 9 (26%) died. Baseline characteristics are presented in Table 1. Less than a third had typical clinical circumstance. A substantial proportion of dialysis patients may have had asymptomatic SARS-CoV-2 infection.

PO0743

Assessment of a Laboratory-Based SARS-CoV-2 Antibody Test Among Hemodialysis Patients: A Quality Improvement Initiative

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Background: The coronavirus disease 2019 (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Assessment of newly developed anti-SARS-CoV-2 antibody tests in hemodialysis patients is needed.

Methods: As part of a quality improvement (QI) initiative, nasopharyngeal swabs and predialysis blood samples were collected on the same day from adults receiving routine dialysis care at clinics managed by a large dialysis organization in the Miami, Florida, region (April 23-30, 2020). Polymerase chain reaction (PCR) tests for SARS-CoV-2 (Fulgent Genetics, Temple City, California) and chemiluminescence immunoassays (Diazyme Laboratories, Inc, Poway, California) were performed according to manufacturer protocols. For antibody tests (IgM and IgG), a reading of >1 arbitrary unit/ml was scored as positive.

Results: Of 715 participants in the QI initiative, 38 had symptoms consistent with COVID-19 prior to or during the initiative. Among these, COVID-19 was confirmed in 14 and ruled out in 20, with 4 being inconclusive. Among the 34 patients with known COVID-19 status, the sensitivity and specificity of the antibody test were 57.1% and 85.0%, respectively, when both IgM and IgG were considered. The remaining 677 patients had no record of symptoms consistent with COVID-19 or any known exposure. Of these, 38 (5.6%) tested positive for anti-SARS-CoV-2 antibodies; none of the antibody-positive patients with available PCR results (N=33) tested positive for SARS-CoV-2 using PCR.

Conclusions: The operational characteristics of the laboratory-based antibody test make it sufficient to rule in, but not rule out, SARS-CoV-2 infection in the appropriate clinical circumstance. A substantial proportion of dialysis patients may have had asymptomatic SARS-CoV-2 infection.

PO0744

Clinical and Psychosocial Impact in Mexican Hemodialfiltration Population During the COVID-19 Pandemic, Twice Weekly Sessions: Is This Safe?

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Background: There is evidence that in patients with residual kidney function (RKF) could benefit switch thrice versus twice weekly schedule. In patients without RKF, the evidence is limited. We evaluated the clinical and psychosocial impact of the Covid-19 pandemic in Mexico City.

Methods: At the beginning of the Covid-19 pandemic, the on-line postdialiltration hemodiafiltration (OL-HDF) sessions were adjusted from 3 to 2 times per week. 2 months later, we determine hemoglobin, urea, serum creatinine, sodium, potassium, calcium, phosphate, albumin, ferritin and C reactive protein. Likewise psychological evaluation using Hamilton test were carried out and characteristic of sessions were collected. We divide in two groups according to thrice versus twice weekly schedule.

Results: 25 patients were evaluated, 16 (64%) were female, mean age was 42.04±16.02 years, 21 (84%) did not have RKF. The length session between thrice vs twice were 181.74±9.94 vs 196 ± 9.19 (p=0.01). When we analyzed the anuric patients (24.43±10.91 vs 26.5± 12.48 L, p=0.04) and no difference in Kt/V (1.67±0.34, p=0.35). We found significance difference between groups in serum creatine (8.68±3.55 vs 10.04±2.94, p=0.03) in the rest of molecules we did not find difference. 32 and 44% of the patients developed depression and anxiety, respectively. 36% of patients lost their jobs and 80% use public transport. There was a moderate correlation between anxiety episodes and economic limitation due to Covid-19 (r = -0.40 p = 0.04). There was no significant inverse correlation between pharmacological adherence and economic limitation (r = -0.29 p = 0.29).

Conclusions: Change of the schedule in patients without RKF did not show significant differences in terms of biochemical parameters. On the other hand, improvement in replacement volumes. We considered a safe strategy to reduce the risk of transmission among our population. Pharmacological and attending adherence to sessions was not modified despite the psychological findings due to the Covid-19 pandemic.
PO0745
Clothing of Catheters in Patients with Renal Failure with COVID-19
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Background: We are an inner-city hospital in New York that had a surge of patients diagnosed with COVID-19. Many of these patients had acute kidney injury (AKI) and required renal replacement therapy (RRT). NYC Health + Hospitals/Kings County has 40 adult intensive care unit (ICU) beds. ICU capacity expanded to a potential of 150 beds during the COVID-19 surge. The surge included patients transferred from other NY inner-city hospitals for critical care and RRT. Sequential obstacles were faced in providing hemodialysis (HD) to this expanded pool of AKI patients. Additional machines, supplies, staffing and organization were helpful. Clinicians noted that COVID-19 complications included hypercoagulability and we observed an increased frequency of clotting of hemodialysis catheters (HDC).

Methods: We examined the percentage COVID-19 tested renal failure patients with clotting of HDC access during the period March 1, 2020 to May 15, 2020. We collected data on 146 patients during the above period who had HD. We then compared those who were COVID-19 positive confirmed by testing to those who were not COVID-19 by testing. HDC clotting was identified by the use of alteplase. We compared our findings of the two groups to historical controls during a similar time period prior to the COVID-19 surge, between January 1 to February 29, 2020.

Results: We had 3,665 admissions between March 1 and May 15, 2020, of which 1,075 patients had a confirmed COVID + test during the admission. Of these, 773 patients were noted to have AKI from diagnosis codes in the electronic medical record. Of the 146 patients who needed HD (including patients with AKI and CKD) 97 were COVID-19+ and 49 were negative. HDC clotting identified by the use of alteplase was noted in 27% of those who were COVID-19+ compared to 10% of those who were COVID-19 negative. (P value= 0.02 by Chi-square using SPSS Version 24). The percentage of patients with clotting of catheters in the non-COVID-19 group was comparable to historical controls.

Conclusions: Significantly more COVID-19+ patients had HD catheter clotting compared to non-COVID-19 patients. Increased clotting was noted as a barrier to providing optimal HD therapy. For this and other reasons, we initiated an urgent start acute peritoneal dialysis program to mitigate the challenges in delivering HD to COVID-19 patients.

PO0746
Contingency Planning for COVID-19: Feasibility of Twice Weekly Hemodialysis in a Large Canadian Cohort
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Background: Reducing hemodialysis treatments from three times weekly to twice weekly is a potential strategy to lessen potential exposure/transmission of COVID-19 while allowing hemodialysis units to operate with fixed/reduced resources. As part of contingency planning at a large Canadian center, all facility-based hemodialysis patients were reviewed in advance for candidacy of a reduced “twice weekly” schedule.

Methods: All prevalent patients receiving at least thrice weekly, facility-based hemodialysis - affiliated with the QEII Halifax, Nova Scotia, Canada - were systematically reviewed in a stepwise manner, using accepted criteria for implementing twice weekly hemodialysis (Fig. 1).

Results: Of 473 patients assessed, only 18 (4%) fulfilled criteria for twice weekly hemodialysis (Fig. 1). Of these patients, average age was 63 ± 12 (SD) years, 61% were diabetic, 95% Caucasian; and at least 67% receiving dialysis for 6+ months prior to assessment. 83% of qualifying patients missed 0 treatments in the preceding month, and none missed >1 treatment. Average for serum albumin was 36 ± 4 g/L, Urea reduction ratio, 72.7, and residual urea clearance, 5.7 ± 2.7 mL/min/1.73m².

Conclusions: Although feasible, a twice weekly hemodialysis strategy applied to a small proportion of our patient population, potentially reflecting an ‘intention to defer’ strategy for initiating dialysis.
PO0749

Mental Health Status During the COVID-19 Pandemic of Hemodialysis Patients
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Background: Patients receiving hemodialysis (HD) treatment are a particularly vulnerable population as previous studies have shown that they are at higher risk to develop anxiety, depression, and diminished health-related quality of life. During the COVID-19 pandemic patients and health professionals are under insurmountable psychological pressure which may lead to various psychological problems. The aim of this study was to assess the effect of this pandemic on mental health and quality of life in low-income HD patients.

Methods: Observational, cross-sectional study done in low-income HD patients and matched healthy controls from March-April 2020. The survey collected basic demographic and laboratory data. To assess mental status 3 different scales were used: Generalized Anxiety Disorder (GAD-7), Insomnia Severity Index (ISI), and the Kidney Disease Quality of Life (KDQOL-36). An evaluation of media interest was added.

Results: 152 HD patients and 33 control subjects were included. The median age was similar in both groups (HD 31±17 vs 48±10 yrs p=NS). Literacy was significantly higher in the control group. The control group showed significantly higher interest media (p=0.03); 60.5% of HD patients showed none or low emotional impact with this pandemic (42% in control group p=0.02). Severe anxiety was more prevalent in the control group (22.6 vs 8% p=0.01). The ISI scale showed also significantly higher sleep impairment in control subjects (42.6 vs 20.5%, p=0.04). In the HD group, the prevalence of GAD symptoms was higher in females than men (p=0.005), and one of the most influential factors associated with GAD symptoms was to live in a rented home. Patients ≥50 years had significantly higher GAD symptoms (0.01). Unemployed HD patients showed the lowest K-DQOL scores.

Conclusions: HD patients had less emotional impact, lower GAD-7 and ISI scores, symptoms than healthy controls. To live in a rented home and unemployment were important risk factors associated with a higher prevalence of anxiety and sleep disorders.

Funding: Government Support - Non-U.S.

PO0750

Monitoring Trends of COVID-19 Among ESKD Patients in a Large Dialysis Organization
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Background: Monitoring real-time acceleration, plateaus, and deceleration of infection rates is important for healthcare planning during a pandemic. We implemented methodology to continuously monitor daily cases and changes of COVID-19 case rates among individuals with ESKD receiving care in a large dialysis organization.

Methods: We identified patients with ESKD receiving dialysis in a Fresenius Medical Care North America (FMCNA) dialysis facility who tested positive for COVID-19. We fit a loess curve to the daily cumulative number of identified cases and computed the first and second derivative of the fitted curve to assess rate of change and change in rate of change, respectively, over time. We used these visualization techniques to monitor trends in case rates at the national and state levels.

Results: By May 15, 2020, there were 5,513 confirmed COVID-19 cases among patients receiving dialysis in an FMCNA facility. Mean age was 63.6 years, 57% were male, and 71% of confirmed cases had diabetes. Nationally, during the peak infection period in early April, new cases routinely exceeded 150 per day and there was a steady acceleration in growth of cases until the second week of April. As of May 15, 2020, among states with sufficient data, 2 states demonstrated continued acceleration, 10 demonstrated deceleration, and 13 plateaued in rate of growth.

Conclusions: The timing of the acceleration in growth of COVID-19 cases among individuals with ESKD followed national trends in the general population. Varying patterns of plateauing and deceleration of cases at the state level were observed in the ESKD population. Real-time monitoring of disease rates in high-risk populations, such as individuals with ESKD, is needed to plan for continuously changing healthcare demands during a pandemic.

Funding: Commercial Support - Fresenius Medical Care
Results: Of 834 chronic HD patients, 26% (222) were diagnosed with COVID-19. Mean age of those with COVID-19 was 72±9 years old, 86% were Black, 77% had diabetes and all had hypertension. Of these patients, 59% (13/22) required hospitalization and 18% (4/22) died. IgG Ab testing was performed on 19 out of 22 COVID-19 patients. All 19 patients tested positive for IgG Ab with an average Ab titer of 7±1.2. 20 days after the first SARS-CoV-2 RNA test, 68% (13/19) patients remained positive on repeat RNA testing. 3 patients tested positive for SARS-CoV-2 RNA on repeat surveillance testing despite testing negative on 2 prior consecutive nasal or nasopharyngeal specimens (Fig. 1).

None of these 3 patients were symptomatic at the time their repeat swabs were positive for SARS-CoV-2 RNA.

Conclusions: All HD patients with a confirmed diagnosis of COVID-19 developed IgG Ab to the SARS-CoV-2 virus, but the SARS-CoV-2 RNA was detectable in the swab specimen for a prolonged duration of time. In a few cases, the SARS-CoV-2 RNA became detectable after 2 consecutive negative RNA specimens. It is unknown if the IgG antibodies confer immunity against the SARS-CoV-2 virus. Additionally, the significance of persistent viral RNA shedding in patients who have recovered from COVID-19 remains to be elucidated.

PO0754 Rates of Asymptomatic Carriage and Antibody Positivity for SARS-CoV-2 in a Large Haemodialysis Cohort

Background: Haemodialysis patients represent a unique challenge in the COVID-19 pandemic, balancing infection risk while safely providing life-sustaining haemodialysis. Asymptomatic infection rates in haemodialysis patients are unknown. Aims: 1 - To define rates of asymptomatic swab positivity in a cohort of prevalent haemodialysis patients 2 - To define rates of antibody positivity in patients known to have been historically swab positive 3 - To define rates of antibody positivity in patients without prior symptoms or clinical suspicion of COVID-19.

Methods: A programme of COVID-19 screening using a validated nasopharyngeal PCR analysis was carried out across a prevalent cohort of 1253 haemodialysis patients. Concurrently all patients were offered antibody testing for Anti-SARS-CoV-2 IgG/IgM (Roche) and a total of 848 tests were completed.

Results: 1 – Routine screening over a 4 week period from 4/5/20 to 1/6/20 confirmed 7 cases of asymptomatic swab positivity (0.6%). 2 – In our cohort there were 197 confirmed swab positive cases of COVID, and of the 153 survivors 124 were antibody positive (81%). 10 patients were highly clinically suspicious of COVID and managed as such; of those 3 were antibody positive (30%). 3 – Of the remaining swab negative patients who had antibody testing (n=710) 82 were antibody positive (11.5%).

Conclusions: In a large inner-city London haemodialysis where the population prevalence of COVID has been high, we demonstrate 1 – low asymptomatic rates of virus carriage at this later stage in the pandemic 2 – significant proportions of swab positive patients seroconverting to be antibody positive 2 – suggestion that 11.5% of patients had previous been asymptomatic carriers and had seroconverted to be antibody positive.
Figure 1: Example of COVID-19 outbreaks risk map in European dialysis clinics network. Red, yellow, green circles represent respectively high, middle, low risk classes.

PO0758

Distribution of SARS-CoV-2 Positive Tests, Dialysis Stations, and Household Poverty Within Cook County, Illinois

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Background: The frequency of evaluations in hemodialysis (HD) care affords opportunities to assess profiles that may characterize onset of the 2019 coronavirus disease (COVID-19). We aimed to characterize the trajectories of clinical/laboratory assessments before COVID-19 diagnosis in HD patients.

Methods: We assessed data from HD patients with known COVID-19 dialyzed at Fresenius Kidney Care in the United States between 02 Mar and 09 Apr 2020. We trained a model to predict outbreak in each clinic in a 2-week prediction horizon (i.e. two or more COVID-19 cases). In addition to sentinel distance-weighted risk estimates, the model included 73 variables (i.e. regional-level epidemic data from open source datasets and clinical practice data from the EuCliD® database). We generated the training set on data available on 04/01/2020 and tested prediction accuracy at 4/15/2020 and 4/20/2020.

Results: In the training set there were 58 (9.1%) clinics with two or more patients with COVID-19 infection in the two-week prediction window. In the validation samples there were 27 (4.2%) and 12 (1.9%) clinics with two or more patients with COVID-19 infection during the two-week prediction window. The performance of the model was suitable in both testing windows (AUC=0.86 and 0.80 respectively). The model is used to construct risk maps highlighting geographical clusters of clinics at risk (figure).

Conclusions: A sentinel surveillance system together with the wealth of information collected in EuCliD® and state of the art modeling strategies allows prompt risk assessment and timely response to COVID-19 epidemic challenges throughout networked European clinics.

Funding: Commercial Support - Fresenius Medical Care

Figure 2: Trajectories 30 Days Before COVID-19 Diagnosis in HD Patients

PO0757

Trajectories of Clinical and Laboratory Characteristics Before COVID-19 Diagnosis in Hemodialysis Patients

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Background: The frequency of evaluations in hemodialysis (HD) care affords opportunities to assess profiles that may characterize onset of the 2019 coronavirus disease (COVID-19). We aimed to characterize the trajectories of clinical/laboratory assessments before COVID-19 diagnosis in HD patients.

Methods: We assessed data from HD patients with known COVID-19 dialyzed at Fresenius Kidney Care in the United States between 02 Mar and 09 Apr 2020. We computed mean daily values for 40 variables 90 days before a positive rRT-PCR test (COVID-19+). Nonparametric smoothing splines were used to fit data of individual trajectories and estimate the mean change over time.

Results: There were 1294 HD patients with COVID-19 (mean age 64±14 years, 60% male, 47% white race, 69% had diabetes, and 24% had coronary artery disease). Mean pre-HD body temperature (primarily oral) increased by about 1° Fahrenheit (F) over 10 days before COVID-19+ test and approached 99.5°F at diagnosis (Fig 1A). Mean interdialytic weight gain decreased by about 0.75 kg (Fig 1B) over 14 days before COVID-19+ test, concurrent decreases of about 20 minutes were seen in HD treatment time. Mean neutrophil-to-lymphocyte ratio had mild increases (Fig 1C), while mean platelet counts decreased by about 40x10^3/L over 14 days before COVID-19+ test (Fig 1D). Trajectories of many variables (vitals, heparin, hematology, nutrition, bone, anemia) were observed to change before COVID-19+ test, yet alternations were generally minor.

Conclusions: The trajectories of several clinical/laboratory parameters appeared to change before COVID-19 diagnosis in HD patients. Many changes were small and may not be independently useful in identifying onset of COVID-19. Mean pre-HD body temperature before SARS-CoV-2 infection was 97.4° F and should be considered in screening. Findings may have utility in prediction model development. Further comparisons to patients without COVID-19 are needed.
PO0759
Kidney Patient Mortality due to COVID-19 in Ecuador: The Experience in Guayas Province
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Background: Ecuador is a country of seventeen million population located in the west coast of South America. In late February 2020, Ecuador had its first Covid-19 case in the city of Guayaquil, followed by massive growth of infections in Guayas Province (14,000 of 39,000 cases), the current epicenter. Due to the lack of official information in this population, and the significant impact in mortality saw in other countries, a need for data is warrant.

Methods: There are approximately 15,000 patients on renal replacement therapy in Ecuador, 94% of them on hemodialysis. At Guayas Province, the estimation of 5200 people on hemodialysis accounts for the 34% of the country's patients. A simple telephone-based questionnaire was performed at the first week of May, directed to the owner, medical director, or head of nurses of each center in the Guayas Province.

Results: From the 35 centers in Guayaquil, it was possible to collect data from 29 locations (82.5%) -mostly private centers-, that represents approximately 4719 patients, 89.8% from the total of patients in Guayas Province. Just 2 / 8 public centers provide information. Results are summarized in Table 1.

Conclusions: The 11.91% Covid-19 mortality in Guayas Province was high, especially if the expected monthly mortality is around 0.8-1.1%; the lethality was very high; and this could be explained by the fact that renal patients are considered as high-risk patients in this disease. The low mortality in PD patients could be attributable to the lockdown and stay-in-home measures. It is necessary to implement specific protocols in order to avoid high mortality, if a second peak of Covid-19 is expected.

Results from Guayas Province in Covid-19 pandemic.

<table>
<thead>
<tr>
<th>Mortality (RD):</th>
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<td>11.91%</td>
<td>4719</td>
<td>5-200</td>
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<tr>
<td>Lethality</td>
<td>5.9%</td>
<td>22/360</td>
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<tr>
<td>Mortality (PD)</td>
<td>2.8%</td>
<td>(n=628)</td>
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<tr>
<td>Mortality (FCS)</td>
<td>2.4%</td>
<td>(n=912)</td>
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</table>

HD Hemodialysis, PD Peritoneal Dialysis, TX Kidney transplant patients. Range represents the % variation between centers

PO0760
Clinical Characteristics, Management, and Outcomes in COVID-19-Positive Dialysis Patients from Three London Renal Centres, United Kingdom
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Background: Dialysis patients, with frequent co-morbidities, advanced age and frailty, visiting treatment facilities frequently are perhaps more prone to SARS-CoV-2 infection and related death - the risk-factors and dynamics of which are unknown. The aim of this study was to investigate the hospital outcomes in SARS-CoV-2 infected dialysis patients.

Methods: This prospective, observational, multi-centre study collected data on SARS-CoV-2 infected HD patients between 29/02/2020 and 15/05/2020. Data was collected on demographics, comorbidities, WHO performance status, classical symptoms, laboratory parameters, hospital management and outcomes. Treatment was predominantly supportive, unless patients were part of an approved clinical trial. The study was approved by NHS Research Ethics Committee 20/SW/0077 and Heath Research Authority IRAS 283130.

Results: Of 1737 HD patients at the 3 renal centres, 224 (13%) were COVID-19 positive over the study period. The characteristics of the COVID-19 HD patients were: mean age 65.8; 59% male; 38% Caucasian; 81% hypertension; 54% diabetes; 25% chronic lung disease; 29% ischaemic heart disease and 22% cerebrovascular disease. The most common symptoms at presentation were fever (62%) and cough (53%). About 143 (64%) patients were managed as an inpatient and 81 (36%) as an outpatient. Of 97 patients that required mechanical ventilation: 6 died, 1 patient was discharged and 2 are still under clinical care. Overall 51 patients died (23%), 154 (69%) were discharged alive and 19 (8%) were still under clinical care as of 15/05/2020. Preliminary analyses suggested that those that died were significantly older (p=0.0028), more likely to have ischaemic heart disease (p=0.003), cerebrovascular disease (p=0.019), smoking history (p=0.006), WHO performance status 3-4 (p=0.004), higher neutrophil:lymphocyte ratio at presentation (p=0.0001) and higher CRP at presentation (p=0.0021).

Conclusions: This large cohort of COVID-19 positive haemodialysis demonstrates a high case fatality ratio, which increased significantly with age, cardiovascular disease, smoking history, frailty and markers of inflammation.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0762
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Background: The impact of COVID-19 disease on previously healthy children has been minimal, yet there is limited data on the impact of COVID-19 on children and adolescents with kidney transplants.

Methods: We used the existing infrastructure of the Improving Renal Outcomes Collaborative (IROC) learning health system to develop and rapidly implement a web-based registry for collecting clinical and outcomes data about COVID-19 disease in pediatric transplant recipients. We distributed the registry to 32 U.S. pediatric kidney transplant centers and requested clinical and outcomes data from all recipients suspected of having COVID-19 disease. Here, we present an interim analysis of the first 6 weeks of registry data.

Results: Between April 6 and May 27, 2020, 18 IROC centers entered data on 99 pediatric kidney transplant recipients who had PCR based testing for COVID-19. 54 patients were tested due to symptoms of COVID-19 (most commonly fever and cough), 7 asymptomatic patients had a known COVID exposure. 34 patients were tested per hospital policy (e.g. pre-anesthesia), and 4 did not have a reported testing indication. Overall, 10/99 (10%) tested positive for COVID-19, 6 of whom had any symptoms, 3 had a known exposure with a COVID+ individual, and 1 was diagnosed by a pre-anesthesia screen. Thus far, the clinical course and outcomes are known in 8/10 COVID+ patients: 5 received outpatient supportive care alone, 2 were admitted to intensive care and 1 was admitted to a non-COVID ICU, a non-COVID medical ICU, and a non-COVID transplant unit. Transplant outcomes were excellent in all COVID+ patients. There were no cases with respiratory failure, acute kidney injury, or allograft rejection/failure. There were no deaths due to COVID-19 disease.

Conclusions: In this interim analysis of the IROC learning health system, pediatric kidney transplant recipients had a relatively low incidence of COVID-19 disease and excellent short-term outcomes.

PO0764
Clinical Outcomes of Hospitalized Kidney Transplant Recipients with COVID-19 in a Predominantly Minority Population

Background: COVID-19 has been associated with increased morbidity in kidney transplant recipients. We aimed to identify risk factors for mortality in hospitalized kidney transplant recipients with COVID-19.

Methods: We retrospectively reviewed the medical records of 75 kidney transplant recipients admitted for COVID-19 at our institution. Result: Among the 75 patients, 28 (37%) died at a median 8 days (range, 1-36) after admission to the hospital. The Table summarizes the demographics and initial labs values of both groups. Most of our patients were Hispanic (54%) and African American (32%) and 97% had hypertension and 65% had diabetes mellitus. There was no difference between the two groups in terms of sex, type of transplant, time from transplant, immunosuppressive medications, medical comorbidities, presenting symptoms, temperature, or pulse oximetry values on admission. Non-survivors were older and had higher BMI. On admission most patients were lymphopenic, had low CD4/CD8 counts and had higher inflammatory markers (ferritin, d-dimer, CRP, procalcitonin, interleukin-6 levels). Non-survivors had statistically significant higher procalcitonin, IL-6 and pro-BNP levels on admission. More non-survivors required ICU stay (64% vs. 13%, p < 0.001), intubation (57% vs. 11%, p < 0.001) and renal replacement therapy (32% vs. 17%, p=0.17) compared to survivors. There was no difference in secondary bacterial infections, CMV viremia, DVT or stroke between the two groups. In a multivariate analysis, BMI (OR 1.15, CI 1.04-1.30, p = 0.017 per unit increase), higher procalcitonin (OR 4.16, 95% CI 1.09-18.87, p=0.046) and proBNP level (OR 1.017, 1.002-1.034, p=0.039, per 100 unit increase) on admission were associated with increased mortality.

Conclusions: COVID-19 is associated with increased mortality (37%) in our kidney transplant recipients and higher BMI, procalcitonin and proBNP levels at admission are associated with mortality.

PO0763
Living Organ Donor Perspectives on Organ Donation During the COVID-19 Pandemic
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Background: Due to the COVID-19 pandemic, transplant programs across the U.S. postponed living donor surgeries and transplants. We examined perspectives of former and prospective living organ donors on the risks and excess burdens of organ donation during the COVID-19 pandemic.

Methods: In late April 2020, we disseminated an IRB-approved survey to a national online forum of over 1300 living donors and those in workup for donation. Using visual analog scales, respondents rated sources of information about COVID-19, burdens on donors due to the pandemic, and what factors should determine whether living donation should proceed during the pandemic (0=unimportant, 100=very important).

Results: After 4 weeks, there were 101 respondents from 35 U.S. states; 63% were between 31-50 years old, 95% were non-Hispanic white, and 90% were female. Respondents included 68 living donors (72% kidney) and 33 people in work-up to donate (73% kidney). The most and least important sources of information about COVID-19 were personal doctors (median importance 88, IQR 73-100) and social media (median 26, IQR 12-54), respectively. Nearly half (41%) were unsure of their transplant program’s policy for living donation during the pandemic, and 58% reported that the decision to donate during COVID-19 should depend on factors such as transplant candidate health (median 100, IQR 90-100) and availability of COVID-19 tests (median 84, IQR 70-95).

Conclusions: Many living organ donors were uncertain about their transplant program’s approach for donation during the pandemic. Donors were concerned about the health of transplant candidates and financial stressors, and prioritized availability of COVID-19 testing to determine when living donation should proceed during the pandemic.

Funding: NIDDK Support
COVID-19 and Kidney Transplantation: Results from the TANGO International Transplant Consortium

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Background: Chronic immunosuppression and comorbidities may expose kidney transplant recipients to an increased risk of developing critical coronavirus disease 2019 (COVID-19), but data in transplantation have been limited so far to single centers. To determine the clinical presentation, outcomes, and mortality risk factors in transplant patients with COVID-19, we analyzed retrospective data from a large international transplant consortium (TANGO Study).

Methods: Retrospective cohort study included kidney transplant recipients admitted with COVID-19 in 11 centers participating in the international TANGO consortium. We included all adult (≥18 years) kidney transplant recipients with a functioning kidney allograft who were admitted to a hospital between March-April, 2020. Epidemiological, demographic, clinical, laboratory, treatment, and outcome data were extracted from electronic medical records using an ad hoc designed data collection form.

Results: Among 9,697 kidney transplant recipients followed at 11 transplant centers, 145 (1.5%) were hospitalized due to COVID-19. 65% were male and more than half were over 60 years old (55%). Median time since transplant was 5 years (2-10) and 16% were transplanted less than one year from the presentation. Prevalent comorbidities included hypertension (95%), obesity (41%), heart disease (25%) and lung disease (19%). Common symptoms of the onset of illness were fever and dyspnea (71%), followed by myalgia (54%) and diarrhea (33%). Management of anti-rejection therapy varied across centers: antimetabolites were withdrawn in 69% of patients and calcineurin inhibitor in 26%. Other treatments used during hospitalization included hydroxychloroquine (83%), antibiotics (76%), tocilizumab (13%) and antivirals (10%). During a median follow-up of 13 days (IQR: 7 - 21) after diagnosis of COVID-19, mortality was 30% and occurred at a median 10 (5-16) days after admission. Acute kidney injury (AKI) occurred in 46% and respiratory failure requiring intubation in 29% of cases. No rejection events were observed.

Conclusions: Our large international consortium indicates that kidney transplant recipients with COVID-19 have increased mortality (30%) upon hospitalization compared to the general population with a high rate of AKI (46%) and significant respiratory failure (29%).

Atypical Clinical Presentation of COVID-19 in a Kidney Transplant Recipient with Tacrolimus Toxicity

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Introduction: Kidney transplant recipients represent a unique challenge to manage amidst the Coronavirus disease 2019 (COVID-19) pandemic as they have reduced innate ability to fight the viral infection due to immunosuppression. However, calcineurin inhibitors such as tacrolimus, may offer an advantage in reducing the effects of cytokine storms in transplant patients with viral pneumonia. We present an atypical case of COVID-19 in a kidney transplant recipient with toxic levels of tacrolimus levels presented with mainly fever and diarrhea.

Case Description: A 76-year old African American male kidney transplant recipient presented to the Emergency Department (ED) after five days of fever (temperature of 101.8°F), nausea, vomiting, diarrhea and urinary frequency on March 27, 2020. His vitals were noted with a temperature of 96.9°F, respiratory rate of 40/ min, and heart rate of 166 beats/min, blood pressure of 110/75 mmHg and pulse oxygen saturation was 85% at ambient air. Admission labs were significant for a rise of serum creatinine to 3.1 mg/dL, from a baseline of 1.5 mg/dL, lactic acid of 4.4 mmol/L, and a tacrolimus level of 26.9 mcg/L. He was transferred to the ICU following increased oxygen demands and elective intubation for impending respiratory failure on hospital day 2. His blood pressure transiently improved with a decrease in lactic acid to 1.4 mmol/L and serum creatinine down to 1.6 mg/dL following IV fluid resuscitation. On hospital day 4, he continued to require high ventilator support and initiated on vasoconstricting agents for hemodynamic support. His serum tacrolimus level continued to increase to 32.9 mcg/L with concordant increase of serum creatinine to 2.1 mg/dL with oliguria. Tacrolimus levels sustained super therapeutic levels >8 mcg/L despite cessation of the drug.

Discussion: It is possible that Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection may cause hepatic dysfunction and diarrhea, which reduced drug metabolism and lead to toxic levels of tacrolimus—perpetuating cytokine storm. It is important that in this particular transplant patient population to closely monitor drug levels due to SARS-CoV-2 infection on its metabolism, as well as preventing toxic levels, which further reduces the body’s innate immunity and may indirectly worsen cytokine storm.

Late Rejection of Failed Renal Allograft Precipitated by COVID-19 in a Hemodialysis Patient (HD)


Introduction: We present a case report of an HD patient with a failed allograft that had been stable off immunosuppression who presented with acute allograft rejection in the setting of COVID-19 infection.

Case Description: 50 y/o male with a history of hypertension, living-related kidney transplant in 2005 ESRD after his allograft failed in 2018. The patient’s allograft remained stable off immunosuppression on HD until 3/2020, when the patient presented with severe allograft tenderness with no fever or evidence of urinary tract infection. An abdominal CT was consistent with allograft rejection. Abdominal pain resolved after IV steroids and initiation of low dose tacrolimus. He was discharged but returned 4 days later, with recurrent abdominal pain, fever and shortness of breath. CT chest was consistent with COVID19 pneumonia with a positive swab. His condition was complicated by acute respiratory failure and cytokine storm. Despite receiving Anakinra for COVID-19, our patient died.

Discussion: Failed allograft rejection for patients who initiate HD usually occurs within the first 6-12 months. Unless allograft failure occurs within a year of transplantation, many nephrologists complete withdrawal of immunosuppression in failed grafts after 4 months to decrease the risk of infections. In our case, the development of allograft rejection after stable long-term HD, is very unusual. We propose that the cytokine storm from COVID-19 in our patient provided the appropriate “danger signals” that triggered innate inflammation and augmented effector responses against the allograft's COVID-19 infection triggers a proinflammatory immune response, with IL-6 being a key cytokine that potentially drives T-cell effector responses and inhibits T-regulatory responses to donor allograft.
Results: 31 patients were identified, 30 were admitted. Median age was 58 (IQR 53-68) and 60% were male. 32% Caucasian, 29% African American, 29% multiracial, and 6% Asian. Median time from transplant to COVID-19 testing was 1178 days (IQR 252-2897). The most common symptom was cough, followed by fever, shortness of breath and fatigue. Chest X-ray/CT revealed multifocal patchy opacities. Ten patients required mechanical ventilation. Laboratory markers can be seen in the table. Acute kidney injury occurred in 39% of patients. The majority of patients were on triple immunosuppression (94% on tacrolimus, 90% on mycophenolate, and 74% on prednisone). During the hospital course 87% had the antiviralosibol stopped while 35% had CNI stopped. Treatments utilized included hydroxychloroquine (93%), azithromycin (50%), convalescent plasma (14%), IL-6 inhibitor (10%) and 1 received remdesivir. At a median follow up of 19 days (IQR 8–26) 10 patients died. Risk of death was greater if the patient was admitted to a non-transplant hospital (80% vs 23%, p=0.027), lymphopenic at presentation (47% vs 8%, p=0.013) or had O2 saturation less than 94% (100% vs 57%, p<0.001). During hospitalization mortality was also higher in patients with higher peak serum creatinine (3.2 mg/dl vs 1.5 mg/dl, p=0.013), or if requiring intubation (70% vs 14%, p<0.001). Increase in inflammatory markers including peak D-dimer, peak CRP, ferritin and procalcitonin were also predictive of mortality.

Conclusions: Kidney transplant recipients with COVID-19 should be monitored closely in a transplant center. Mortality is high, particularly in patients presenting with lymphopenia and hypoxemia.

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<tr>
<th>Barriers to LDKT during COVID-19 pandemic</th>
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PO0769

Living Donor Kidney Transplant Practice in the COVID-19 Era: A Survey of US Transplant Programs

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Background: We surveyed U.S. transplant programs to assess practices, strategies and barriers related to living donor kidney transplantation (LDKT) in the context of the COVID-19 pandemic.

Methods: After IRB approval, the survey was launched 5/20 by email and postings to professional society list-servers, using the Qualtrics platform. Data are reported through 5/27/20, and examined by state COVID-19 prevalence.

Results: Staff at 117 unique centers responded, representing 58% of U.S. living donor recovery centers and 75% of LDKT volume in the year before pandemic declaration. Overall, 66% reported LDKT surgery was on hold (82% in high vs. 50% in low prevalence states). 36% reported that evaluation of new donor candidates had paused, 27% reported evaluations were very decreased (>0% to <50% typical) and 23% reported evaluations were moderately decreased (25% to <50% typical). Barriers to LDKT surgery included program concerns for donor (84%) and recipient (75%) safety, patients concerns (54%), restrictions on elective cases (47%) and hospital administrative restrictions (47%). Programs with higher local COVID-19 prevalence reported more barriers related to staff and resource diversion (Figure). Most centers continuing donor evaluations used remote strategies (video 82%; telephone 43%), 61% of centers plan to continue more telehealth after the pandemic. 32% plan to resume some LDKT within 2 wks and 27% within 1 month. When surgery resumes, all will screen for COVID-19 before donation surgery, although timeframe and modalities vary.

Conclusions: COVID-19 has created many barriers to LDKT, especially in areas of highest prevalence. Transplant centers are planning to restart LDKT cautiously. Consensus-building is needed to reduce barriers, guide optimal practice, and facilitate safe restoration of LDKT across centers.

All data presented in median (IQR) unless otherwise noted

PO0770

Collapsing/Sclerosing Glomerulopathy (CSG) and Acute Tubular Injury (ATI) in Patients with COVID-19

Sunil Sherchan, Mohamed Kahia, Jamrose K. Durranii, Isna Puri, Ibrahim A. Mohamed, Yohannes Melaku, Ernie Yup, Robert F. Leonardo, Subodh J. Saggi, Moro O. Salifu, Anthony D. Nicastro, SUNY Downstate Health Sciences University, Brooklyn, NY.

Introduction: AKI in patients with COVID-19 may be due to hemodynamic instability or inflammatory responses. We present two cases of CSG and ATI in patients admitted for COVID-19.

Case Description: Case 1: 25-year-old black obese female admitted with fever, cough, dyspea and serum creatinine of 1.4 mg/dl, discharged next day with home quarantine. Re-admitted 26 days later due to nausea, fatigue, and bilateral foot swelling. Serum creatinine 28 mg/dl and urine protein to creatinine ratio (uPCR) of 10.4 g/g. Case 2: 42-year-old black female with hypertension, diabetes mellitus admitted with fever, dyspea, cough, and diarrhea. Patient found to have diabetic ketoacidosis, serum creatinine 12.7 mg/dl. She developed deep vein thrombosis and pulmonary embolism and uPCR 15.4 g/g. She was started on hemodialysis, and died from sepsis and multi-organ dysfunction.

Discussion: Our experience above is part of a growing literature describing the direct visualization of SARS-CoV-2 in causing ATI and CSG. Pathogenetic pathways remain to be elucidated.

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Discussion: Our experience above is part of a growing literature describing the direct visualization of SARS-CoV-2 in causing ATI and CSG. Pathogenetic pathways remain to be elucidated.
Results: Presenting symptoms and hospitalization rates were similar in waitlisted ESKD and kidney transplant patients with Covid-19. Azithromycin and doxycycline use was similar in both groups. Hydroxychloroquine use was more frequent in kidney transplant patients (62% vs 36%), as were other experimental therapies. Mortality was greater in waitlisted ESKD compared to kidney transplant patients (29% vs 13%). Of the waitlisted ESKD patients who died, most were males, Black or Hispanic, and 81% had T2DM and/or HTN as the cause of their ESKD. None of the non-hospitalized patients died in either group.

Conclusions: Waitlisted ESKD patients on dialysis with Covid-19 are comparatively at higher risk for mortality compared to kidney transplant recipients with Covid-19 despite similar demographics and similar burden of comorbidities. Whether the ability of immunosuppressive therapy to prevent the cytokine storm contributed to better survival among kidney transplant recipients remains to be determined.

PO0773
Kidney Transplant Practices in Latin America During the COVID-19 Pandemic: Analysis from GlomCon Latin America Working Group (LGComCon)
Sonia Rodriguez Ramirez,1 Franco H. Cabeza Rivera,2 Julio A. Gutierrez-Prieto,3 Javier Soto-Vargas,4 Blanca Martinez-Chagolla,5 Denisse Arceloi-Mendez,6 Diana Aguirre,7 Desiree Garcia Anton,8 Carmen Avila-Casado.9 GlomCon Latin America Working Group (LGomCon) 1University Health Network, Toronto, ON, Canada; 2University of Mississippi Medical Center, Jackson, MS; 3Hospital Central del Estado de Chihuahua, Chihuahua, Mexico; 4Hospital General Regional 46, Guadalajara, Mexico; 5Hospital General “Dr. Miguel Silva”, Morelia, Mexico; 6Unidad Medica de Atencion Ambulatoria 254, IMSS, Morelia, Mexico; 7Hospital General de Meixcali, Mexicali, Mexico.

Background: Latin America (LA) is the current epicenter of a global pandemic that has never been seen in the era of transplantation and immunotherapy. We aimed to describe their nephrologists’ practices and experience regarding kidney transplant (KT) management in the context of COVID-19 pandemic.

Methods: Descriptive analysis extracted from an online survey conducted among nephrologists, renal pathologists and other health workers treating kidney diseases between May 20-27, 2020 from sixteen Spanish speaking LA countries divided into 6 categories. We present the results for the kidney transplant category.

Results: 430 responses were obtained of which 360 (84%) were considered for analysis. 139 (49%) respondents routinely participate in the care of transplant patients in their centers that perform up to 50 KT per year (70% of them). The transplant activity was suspended in 90% of the centers at the time of the survey. Bigger centers continued their activity but not at full capacity. For transplant recipient who developed COVID-19, 52% of physicians continued the same immunosuppressive treatment for the ones with mild disease (outpatient). For moderate cases (patient but not requiring mechanical ventilation or vasopressors), 72% decreased maintenance therapy starting with the antiproliferative drug. For severe cases (ICU admission for mechanical ventilation or vasopressors), 74% stopped all the immunotherapy with the exception of steroids. ICU admission and need for renal replacement therapy were reported in less than 5% of their cases. Nephrologists from centers that continued their transplant activity during the pandemic reported that only 32% performed routine COVID-19 tests to donors and 51% recipients before KT surgery.

PO0771
What Do Data Tell Us About Patients Receiving Calcineurin Inhibitors (CNIs) and Contracting a Coronavirus
Jung Hoon Son,1 Ollie Fielding,1 Xiaoyang Wang,1 Chris Kipers,1 Jeffrey I. Silberzweig,1 Frank Liu.2 The PEAK team ‘pulseData, New York, NY; 1The Rogosin Institute, New York, NY.

Background: We hypothesized that patients taking CNIs, cyclosporine and tacrolimus would be less susceptible to coronavirus infections because of antiviral and anti-cytokine-storm effects and compared the occurrence of positive coronavirus test rates in a population receiving a CNI and non-CNI treatment population. This is of high importance as CNIs are being trialed as a treatment for severe acute respiratory syndrome coronavirus 2 (COVID-19) immune response (NCT04343108). Transplant nephrologists recommend continuing CNIs through the COVID-19 pandemic.

Methods: We analyzed longitudinal EHR system data from the Rogosin Institute’s nephrology clinic to identify a population of 5,144 patients with a record of respiratory viral panel (RVP) testing for any coronavirus strain between December 2012 and May 2020. We identified 1,195 patients receiving cyclosporine or tacrolimus and compared positive test rates of any coronavirus strain in those receiving CNIs to those not receiving CNIs.

Results: A total of 51 patients tested positive (1.05%) Of the 1,195 CNI recipients, 21 tested positive (1.76%); of 3,949 patients with no record of CNI treatment, 33 tested positive (0.84%). Given an age distribution difference between the two cohorts (CNI cohort median 58; non-CNI cohort median 66), we therefore calculated an age-adjusted positive test rate for both populations, with results of 1.76% for the CNI cohort and 0.83% for the non-CNI cohort. A z-test comparing the population proportions testing positive had a z-value of 2.71 (p-value 0.003), indicating significant difference. 8.47% of positive tests on an RVP for any of coronavirus, rhinovirus or respiratory syncytial were for a coronavirus in the CNI group vs. 6.48% in the non-CNI group (z 2.37, p 0.009). Using a test on an RVP for any of coronavirus, rhinovirus or respiratory syncytial were for a coronavirus in the CNI group vs. 6.48% in the non-CNI group (z 2.37, p 0.009). Using a logistic regression model to examine the probability of testing positive for a coronavirus (features for age, gender, whether the test was conducted in flu season (Dec-Feb) and whether the patient was receiving CNIs) we found that CNIs were statistically significant (p 0.007).

Conclusions: Based on the data, as far as we can tell being on a CNI does not offer protection from a symptomatic coronavirus infection. It remains to be seen if it decreases severity of the illness because of the potential for cytokine storm effects.

Funding: Commercial Support - pulseData
Conclusions: Kidney transplants programs are almost closed throughout LA during the COVID-19 pandemic. The disproportionate resource allocation to COVID-19 will have unintended consequences for those already carrying the burden of health inequality with the potential to disadvantage marginalized patients further. Reported immunosuppression management is in line with transplant societies' recommendations.

Funding: Private Foundation Support

PO0774
A Machine Learning-Based Predictive Model for Outcome of COVID-19 in Kidney Transplant Recipients
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1Department of Nephrology and Kidney Transplant. Hospital Clinic, Barcelona, Spain; 2Institut d’Investigacions Biomediques August Pi i Sunyer, Barcelona, Spain; 3Faculty of Economics and Management. Free University of Bolzano, Bolzano, Italy. 4Department of Economics and Management. University of Trento, Trento, Italy.

Background: Health systems need tools to deal with COVID-19, especially for high-risk population, such as transplant recipients. Predictive models are necessary to improve management of patients and optimize resources.

Methods: A retrospective study of hospitalized transplant patients due to COVID-19 was evaluated (March 3–April 24, 2020). Admission data were integrated to develop a prediction model to evaluate a composite-event defined as Intensive Care Unit admission or intensification treatment with antiinflammatory agents. Predictions were made using a Data Envelopment Analysis (DEA)-Artificial Neural Network (ANN) hybrid, whose accuracy relative to several alternative configurations has been validated through a battery of clustering techniques.

Results: Of 1006 recipients with a planned or an unscheduled visit during the observation period, thirty-eight were admitted due to COVID-19. Twenty-five patients (63.2%) exhibited poor clinical course (mortality rate: 13.2%), within a mean of 12 days of admission stay. Cough as a presenting symptom (P = 0.000), pneumonia (P = 0.011), and levels of LDH (P = 0.031) were admission factors associated with poor outcomes. The prediction hybrid model working with a set of 17 input variables displays an accuracy of 96.3%, outperforming any competing model, such as logistic regression (65.5%) and Random forest (denoted by Bagged Trees, 44.8%). Moreover, the prediction model allows us to categorize the evolution of patients through the values at hospital admission.

Conclusions: The prediction model based in Data Envelopment Analysis-Artificial Neural Network hybrid forecasts the progression towards severe COVID-19 disease with an accuracy of 96.3%, and may help to guide COVID-19 management by identification of key predictors that permit a sustainable distribution of resources in a patient-centered model.

PO0775
Outcomes of COVID-19-Positive Kidney Transplant Recipients

Background: Kidney transplant recipients (KTR) are at increased risk of infections due to immunosuppression (IS). COVID-19 has posed unique challenges due to its evolving symptomatology and lack of effective treatment options. Current data published about the impact of COVID-19 in KTR comes from severely impacted areas. The aim of our study was to review course and outcomes of KTR at our center.

Methods: Retrospective chart review of KTR diagnosed with COVID-19. Descriptive statistics were summarized as absolute numbers for categorical data and as median with interquartile range (IQR) for skewed distribution.

Results: We had 20 KTR diagnosed with COVID-19. Median age of 53.5 years (74-63), 10 males, and 12 blacks. Median time from KT to presentation was 70.7 months (17.25-158.75), with 1 pt in 1st year post KT. Thirteen (65%) pts were obese with BMI≥30 kg/m2, 2 pts had chronic obstructive pulmonary disease, and 5 had cardiac disease. Most common presenting symptom was cough in 14 pts, followed by fever-13 pts, shortness of breath-9, and diarrhea-6pts. During the study, 15 pts were hospitalized, and 9 of them had chest x-ray findings of bilateral opacities consistent with pneumonia. Inflammatory markers were elevated in all pts but did not correlate with disease outcome. Acute kidney injury was seen in 9 pts, with 3 requiring continuous renal replacement therapy. Four pts required mechanical ventilation. Ten pts had reduction of their IS. Hydroxychloroquine was used in 11 pts, and azithromycin in 4. Four hospitalized pts received convalescent plasma as part of an ongoing COVID-19 trial in our center. Donors were 4-6 weeks post recovery from confirmed severe acute respiratory syndrome coronavirus 2 infection. Enrollment was offered to pts at high risk of progression to severe disease. We had 3 deaths, 2 pts remain hospitalized, and the remaining 15 were either discharged or managed as outpatients. Median follow up time from presentation was 25 days (13-38) for the entire cohort.

Conclusions: In our cohort, 45% of patients presented with acute allograft dysfunction highlighting impact of SARS-CoV-2 infection on kidney function. Our center utilized investigational convalescent plasma in 4 pts successfully while the clinical trial outcomes are awaited. Ultimately, the development of a safe and efficacious vaccine targeting SARS-CoV-2 may better equip us to fight this pandemic.

PO0776
COVID-19 in Kidney Transplant Recipients at New England’s Largest Safety-Net Hospital
Hassan Mahmoud, Sandeep Ghai, Jean M. Francis. Boston University, Boston, MA.

Background: The coronavirus disease 2019 (COVID-19) has led to a global pandemic as announced by the World Health Organization. Kidney transplant patients are thought to constitute a unique high risk group for severe COVID19 infection. Furthermore, disparities in health care have led to COVID-19 disproportionately affecting minority groups including African Americans and Hispanics.

Methods: We identified adult kidney transplant recipients who were admitted with COVID-19 between March, 15th and May 1st, 2020. We evaluated the demographic, clinical and laboratory data of all admitted patients. We also evaluated the presence of co-infections as well as decisions regarding immunosuppressant management.

Results: 23 kidney transplant recipients who were hospitalized for COVID-19 were evaluated. 91% of our patients were of minority groups. 35% of patients required ICU admission, and 30% required mechanical ventilation. 40% of patients had associated coinfections in addition to COVID19. 87% of patients had variable degrees of AKI, 26% of patients with AKI required renal replacement therapy. Mortality rate in our population was 22%. Upon admission to the hospital, our immunosuppressant therapeutic approach included stopping the antimitabolites and continuing with the calcineurin inhibitors (targeting trough level of 4 to 6 ng/dl for tacrolimus and 50 ng/dl for cyclosporine), and prednisone if patients were on steroids.

Conclusions: This report demonstrates higher rate of AKI, coinfection and mortality in kidney transplant patients in the setting of COVID19 as compared to general population.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Identifying Scenarios of Benefit or Harm from Kidney Transplantation During the COVID-19 Pandemic: A Simulation Study

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Background: Clinical decision-making in kidney transplantation (KT) during the COVID-19 pandemic is a challenge: both candidates and recipients may face increased acquisition risks and case fatality rates (CFRs). Given our poor understanding of these risks, many centers have paused or reduced KT activity, yet data to inform such decisions are lacking.

Methods: To quantify the benefit/harm of KT in this context, we conducted a Markov simulation study of immediate-KT vs delay-until-after-pandemic for different patient phenotypes under a variety of potential COVID-19 scenarios (Figure 1), simulating expected life-months gained from transplant over 5 years. A calculator was implemented (http://www.transplantmodels.com/covid_sim), and machine learning approaches were used to evaluate the important aspects of our modeling.

Results: Characteristics of the pandemic (acquisition risk, CFR) and length of delay (length of pandemic, waitlist priority for DDKT) had greatest influence on benefit/harm (Figure 2). In most scenarios of COVID-19 dynamics and patient characteristics, immediate-KT provided survival benefit; KT only began showing evidence of harm in scenarios where CFRs were substantially higher for KT recipients (e.g. ≥50% fatality) than for waitlist registrants.

Conclusions: Our simulations suggest that KT remains beneficial under COVID-19 in many scenarios. Our calculator can help identify patients who would benefit most. As the pandemic evolves, our calculator can update these predictions.

Funding: NIDDK Support

COVID-19 in Patients with CKD in New York City

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Background: Coronavirus disease 2019 (COVID-19) has affected millions of people, and several chronic medical conditions appeared to increase the risk of severe COVID-19. However, limited data are available about the outcomes of COVID-19 in patients with chronic kidney disease (CKD).

Methods: This was an observational study of patients with CKD at three affiliated hospitals in New York City who were diagnosed with COVID-19 by reverse-transcriptase polymerase chain reaction of nasopharyngeal swab specimens collected in the emergency departments between March 3rd and April 21st, 2020. We stratified patients into three groups: pre-dialysis CKD, dialysis, and transplant. Data are shown as median (interquartile range). Logistic regression was used to identify CKD characteristics associated with non-survival.

Results: Of the 372 confirmed COVID-19 patients with CKD, 182 were pre-dialysis, 149 were on dialysis, and 41 had functional kidney transplant. The median age of the pre-dialysis group was 75 (63-85) years, dialysis group 66 (58-74) years, and transplant group 63 (48-71) years. Men comprised 62.4% of the cohort. Baseline serum creatinine was 1.5 (1.2-2.2) mg/dl in the pre-dialysis group. By the end of the observation period, 78.5% of patients were discharged or had died. Of these patients, mortality was highest in the pre-dialysis group (26.9%), followed by dialysis (24.2%), then transplant (9.8%) groups. Almost half of the cohort was receiving ACE-inhibitors or ARBs pre-COVID-19, which was not associated with non-survival. In the pre-dialysis group, the other group phosphorus was associated with non-survival (OR 1.5 per each 1.0 mg/dl of increase in serum phosphorus). Anemia, defined as hemoglobin <10 g/dl, was also associated with non-survival (OR 3.1) in that group. Body mass index (BMI)>25 kg/m² was paradoxically associated with non-survival (OR 2.7) in patients with pre-dialysis CKD.

Conclusions: Our data demonstrate that mortality in this cohort, particularly in patients with pre-dialysis CKD, was substantially higher than in the general population in New York City. Poorly controlled CKD complications, including CKD-mineral and bone disorder and anemia, as well as low BMI were associated with mortality. Ongoing control of CKD complications may serve as an opportunity to improve outcomes of COVID-19 in patients with CKD.

Funding: Other NIH Support - Weill Cornell Medicine Clinical and Translational Science Center (UL1 TR000457)
COVID-19: CKD and Transplant Patients

Table 1. The laboratory results, treatment regimen, and outcomes of the patients

| Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only |
| Underline represents presenting author. |
Kidney Involvement and Outcome of COVID-19 Patients Admitted from a Federal Medical Facility

Yahya R. Ahmad, Matthew Shea, Mohamed M. Abdalbaky, Elijah Kakani, Javier A. Neyra, Amr E. Mohamed. University of Kentucky Medical Center, Lexington, KY; Mansoura University, Mansoura, Egypt.

Background: Correctional facilities face unique challenges with the COVID-19 pandemic. A COVID-19 outbreak was reported in the Federal Medical Center (FMC) in Lexington, Kentucky, a prison for inmates requiring medical and/or mental health care. We aimed to compare clinical characteristics and kidney-related outcomes in inmates from this FMC to other COVID-19 hospitalized patients.

Methods: A total of 86 COVID-19 patients were admitted to our hospital between March 1st and June 1st, 2020. Among those, 37 patients were from the same FMC. We examined demographics, clinical and laboratory characteristics, along with the outcomes of this cohort and compared it to other COVID-19 non-prisoners. AKI was determined by KDIGO criteria.

Results: All inmates were men and their mean age was 59.8±10.6 years. The majority of them were white (60%) and required ICU admission (54%), while 39% of patients required mechanical ventilation. The prevalent comorbidities were hypertension (81%), obesity (62%), diabetes (41%) and coronary artery disease (CAD) (58%). Stage 3 CKD was present in 22% of inmates. The mean eGFR was 58±26 mL/min/1.73m² at time of admission. Significant hematuria and proteinuria were found in 17% and 25% of patients, respectively. Hypertension, heart failure, CAD, COPD, hepatitis C infection, and AKI were more prevalent in the FMC cohort (P = 0.030, 0.001, 0.024, 0.001, 0.017, and 0.011, respectively). The difference in mortality rates was not statistically significant between groups (12% for inmates vs.17% for non-inmates, p=0.520). Incident AKI was higher in inmates vs. non-inmates (68% vs. 38%, p=0.006) and there was no difference in acute groups (12% for inmates vs.17% for non-inmates, p=0.520). AKI was determined by KDIGO criteria.

Conclusions: Incidence of AKI was higher in hospitalized inmates with COVID-19 vs. non-inmates. The need for acute dialysis was strongly associated with mortality in overall COVID-19 hospitalized patients.

Can Urine Biomarkers Predict Severity of COVID-19? A Preliminary Study

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Background: Early detection of coronavirus disease (COVID-19) in patients likely to develop severe manifestations enables appropriate interventions, including rapid intensive care unit admission. This study was conducted to determine whether non-invasive urine biomarkers can predict the clinical severity of COVID-19.

Methods: Design: A retrospective case series. Setting: Single-center study, national center hospital designated for infectious disease. Patients: Fifty-eight patients who tested positive for SARS-CoV-2 in respiratory specimens through real-time reverse transcription-polymerase chain reaction (RT-PCR) were retrospectively studied. Measurements and main results: Urinary β2-microglobulin (β2MG), liver-type fatty acid binding protein (L-FABP) were serially measured. Serum interferon γ and monocytic chemotactic protein-1 were also evaluated.

Results: The 58 patients were assigned into three groups. Patients requiring intensive care were assigned to the severe group (N = 12). Patients treated with oxygen were assigned to the moderate group (N = 33). Other patients were assigned to the mild group (N = 33). Urine tests revealed that low β2MG and L-FABP levels on admission were associated with mild disease, whereas high levels were associated with severe disease. In severe cases, L-FABP tended to be persistently high. The resulting cutoff values were β2MG; Severe vs. Moderate+Mild: 2.457 μg/dL (Specificity 76.9% and Sensitivity 90.0%, AUC 85.9%), L-FABP; Severe vs. Moderate+Mild: 22.00 μg/gCr (Specificity 84.6% and Sensitivity 90.0%, AUC 91.8%). Urinary β2MG and serum IFN-γ/MCP-1 showed a similar trend.

Conclusions: Evaluating urine biomarkers such as β2MG and L-FABP may allow determination of COVID-19 patients with active cytokines and recognition of patients likely to become critically ill and requiring careful observation and early intervention.

Funding: Government Support - Non-U.S.
COVID-19 and Kidney Transplant Outcomes

Background: Recent publications report great variations in the clinical course and mortality of COVID-19 in solid organ transplant (SOT) recipients. It is unclear whether these differences are related to study methods, treatment choices, or variables associated with patient populations.

Methods: We reviewed and summarized 9 published articles of COVID-19 in solid organ transplant recipients. We contrasted difference between study design and compared outcomes.

Results: All studies included kidney transplant recipients while study 6 and 8 included non-renal SOT. Four come from the United States. Results can be seen in the attached table. Most studies had a median age in the 50’s, with hypertension and diabetes being common comorbidities. Tacrolimus, mycophenolate analogs and prednisone were the most common immunosuppression regimen. Presenting symptoms were usually fever, cough, dyspnea, and diarrhea. Immunosuppression was either reduced or discontinued in all studies. The majority of patients received hydroxychloroquine. Azithromycin, remdesivir, leronlimab, lopinavir/ritonavir, darunavir, oseltamivir, and tocilizumab were also used. Mortality ranged from 0% to 30%. All studies described hospitalized patients. A third of reports also included outpatients. The median follow-up was approximately 3 weeks for most studies (range of 7 to 29 days). All but one series with reported patient deaths under 20% either did not include or had follow-up periods of less than 10 days.

Conclusions: Presentation of COVID-19 and immunosuppression strategies are similar among transplant centers. Differing outcomes may be related to small number of cases, potentially varying acuities of illness and follow up periods. Given that cytokine storm occurs late in the course of COVID-19, it is plausible that mortality may increase in studies with short follow up. When excluding short or missing follow up, mortality appears to be between 20-30%, which suggests that transplant recipients have a higher mortality than their non-immunocompromised peers.

PO0789
Thrombotic Microangiopathy (TMA) in a Patient with COVID-19
Bessy Suvin Flores Chang, Rushang Parikh, Rinda Wanchao, Vanesa Bijnol, Kenar D. Jhaveri. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

Introduction: We describe a patient with COVID-19 and clinically significant kidney biopsy proven TMA

Case Description: 69-year-old Caucasian female with medical history of asthma came to the ED with productive cough, fever and dyspnea for 2 weeks. She was afibrile, tachypneic and hypoxic. Initial laboratories showed a normal WBC, hemoglobin level and platelet count. Inflammatory markers were elevated. SARS-CoV-2 infection was confirmed by PCR assay. CXR showed bilateral diffuse patchy opacities. Treated with hydroxychloroquine, enoxaparin and oxygen was started. Patient received anakinra and tocilizumab. On day 12, the patient developed thrombocytopenia, anemia and worsening kidney function concerning for microangiopathic hemolytic anemia. Due to worsening hypoxemia, patient received convalescent plasma. On day 17, she was intubated due to worsening respiratory failure. Findings suggestive of hemolysis were present. Urinalysis showed hematuria and proteinuria. Patient’s kidney function worsened requiring initiation of CRRT. On day 20, the patient underwent a kidney biopsy that revealed severe acute TMA with cortical necrosis. Beta 2 glycoprotein-1 IgM levels were elevated, anti-phospholipid antibodies were absent. A disintegrin and ADAMTS13 level were not low. C3,C4 were in normal range. Heparin induced antibody testing was negative. Coagulation parameters were normal. Kidney doppler was unremarkable. No other systemic findings of macro thrombi were found. Low factor H complement and plasma SC5b-9 complement levels suggesting an activation of the complement pathway were found. Genetic testing of ADAMTS13 pathway was not done. Plasma exchange was not performed, but received a single dose of eculizumab on day 21. Unfortunately, she died on day 23.

Discussion: Coagulopathy associated with SARS-CoV-2 has been widely reported. Profound hypoxia, inflammation, disseminated intravascular coagulation (DIC) has all been implicated as potential causes, but were not present in our patient. To the best of our knowledge, we report the first case of TMA associated with SARS-CoV-2 with presence of diffuse cortical necrosis and widespread microthrombi in kidney biopsy. It is not clear if the virus played a direct pathogenic role or unmasked a latent complement defect leading to widespread endothelial damage and micro thrombi.

PO0790
Renal Artery Thrombosis with Infarction in a Patient with Mild COVID-19
Ryan Mocerino, Neeja D. Kumar. Montefiore Medical Center, Bronx, NY.

Introduction: There has been increased focus on the microvascular and macrovascular complications of COVID-19. Here we present a case of renal arterial thrombosis in a woman with mild symptoms of COVID-19.

Case Description: A 69 year old female with diabetes, hypertension, coronary artery disease, and acute embolic cerebrovascular event post cardiac catheterization in 2016 presented to the emergency department with acute diffuse intermittent abdominal pain and nonbloody emesis. Prior to this, she had been evaluated for cough, shortness of breath and myalgias which were conservatively managed with improvement. Her medications included aspirin, clopidogrel, furosemide, and insulin. Examination was significant for diffuse nonspecific abdominal tenderness without rebound or guarding. Laboratory assessment revealed preserved renal function with creatinine of 1.10 mg/dL and PCR positive for SARS-CoV-2. A computed tomography of the abdomen and pelvis with intravenous contrast revealed a non-occlusive thrombus in the left renal artery with several large wedge-shaped areas of decreased enhancement consistent with multiple left renal infarctions. On interdisciplinary discussion, the patient was managed conservatively with anticoagulation without acute intervention and was discharged home on apixaban.

Discussion: To our knowledge, this is the first description of renal artery thrombosis with renal infarction in the setting of COVID-19 infection. Patients who present with a COVID-19 infection, regardless of disease severity, should be evaluated for coagulopathy and development of thrombi as these may potentially contribute to infarction and end-organ damage. Although it requires a high index of suspicion, renal infarction should be considered part of the differential when evaluating a patient with COVID-19 infection presenting with abdominal pain or acute kidney injury. Initiation of anticoagulation should be considered with consideration of risks involved.

PO0791
A Case of Severe Thrombocytopenia in a Patient with COVID-19 Receiving Continuous Venovenous Hemodialysis
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Introduction: Thrombocytopenia is a rare complication of renal replacement therapy with most of the cases reported in intermittent hemodialysis patients. There is limited data regarding the incidence of thrombocytopenia caused by continuous renal replacement therapy (CRRT). We report a case of thrombocytopenia in patient treated with CRRT for severe AKI from COVID-19 sepsis unrelated to heparin.

Case Description: A 73-year female with history of type 2 diabetes mellitus was admitted for Coronavirus Disease 2019 (COVID-19) pneumonia. Patient developed acute hypoxic respiratory failure requiring mechanical ventilation despite treatment with hydroxychloroquine, azithromycin and convalescent plasma. Hospital course was complicated by septic shock and acute kidney injury with serum creatinine rising from a baseline of 0.8 mg/dl. Continuous venovenous hemodialysis (CVVHD) without any anticoagulation was initiated due to severe fluid overload. Significant thrombocytopenia below 50,000/mm3 was noted 2 days after CVVHD treatment. Patient received multiple antibiotics and heparin drip before CVVHD and platelet counts were above 150,000/mm3. Heparin induced thrombocytopenia (HIT) was ruled out with negative serotonin release assay and platelet counts remain low despite the discontinuation of all potential agents. Disseminated intravascular coagulopathy was excluded based on coagulation tests. Platelet counts finally went up to 160,000/mm3 on subsequent CVVHD holidays and again dropped to 70,000/mm3 after CVVHD was resumed.
Discussion: The rate of rise in platelet count more than 150,000/mm3 in 2 days after cessation of CVVHD supports the diagnosis of thrombocytopenia caused by CVVHD. Although the exact mechanisms remain unclear, previous studies suggested that the mechanical destruction of platelets by the hemofilter or allergic reaction to dialyzer membrane as some of the reasons. Some studies have found that severe decline (more than 50%) in platelet count was associated with increased mortality and decreased rate of renal recovery. Thrombocytopenia on CVVHD unrelated to HIT is an under-acknowledged complication. Understanding the multiple etiologies of thrombocytopenia will help prevent the excessive use of blood products, fluid overload state and the potential clotting issue of CVVHD due to transfusion.

PO0792
Case Study: Kidney Transplant Patient with COVID-19: Impact of Viral Infection on Background Cell-Free DNA in a Donor-Derived Cell-Free DNA Rejection Assay
Supervisor: Bhumidust,1 Joanna Scheinman,1 Erik L. Lum,1 Philippe M. Gauthier,2 Ebad Ahmed,2 Paul R. Billings.2 University of California Los Angeles, Los Angeles, CA; 1 Natera, In, San Carlos, CA.
Introduction: Donor-derived cell-free DNA (dd-cfDNA) assays are clinically validated to detect kidney transplant injury, reporting the donor fraction as a percentage of the total, or background, cfDNA. Various clinical factors can cause a significant increase in recipient cfDNA, contributing to higher background cfDNA and lower donor fraction, which may result in a false negative test result.
Case Description: A 50+ year old woman with end-stage renal disease secondary to polycystic kidney disease presented with 4 days (d) of diffuse muscle pain at 11 months post-kidney transplant. In the emergency department she had a fever to 101°F, bilateral edema, and a positive COVID-19 (SARS-CoV2) test. She remained febrile for 3d before developing acute respiratory distress requiring oxygen supplementation; her creatinine level was 3 mg/dL. Due to worsening of her respiratory status, she was intubated and started empirically on vancomycin, meropenem, and azithromycin; her mycophenolate mofetil was discontinued. She rapidly progressed to septic shock requiring vasopressor therapy. Her renal function deteriorated, and she was started on continuous renal replacement therapy on hospital d7. She received lenitromib on hospital d7 and d14 and convalescent plasma on hospital d11. Tacrolimus was discontinued on hospital d10 and she continued prednisone at 5 mg/d. Depressed dd-cfDNA testing to assess allograft injury and to rule out active rejection was performed. At hospital d20, her dd-cfDNA was 0.07% with an elevated background cfDNA of 28.569 arbitrary units (AU, 575 median value). At the second blood draw at hospital d25, her dd-cfDNA was 0.25% with a background cfDNA level reduced to 7.503 AU (15X median value).
Discussion: In this case, infection with the SARS-CoV-2 virus was associated with a very elevated background cfDNA level, likely due to cellular apoptosis due to the immune process and/or tissue ischemia due to sepsis-associated hyperperfusion. Although this patient was not known to have active rejection of her allograft, the very high background levels complicate the interpretation of results, especially when donor fraction were reported.

PO0793
COVID-19 AKI to ESRD: A New Cohort of Dialysis-Dependent Patients
Eric J. Chacko,1 Jason Cummings,1 Marc Richards.2 Florida Atlantic University, Boca Raton, FL; 2 Florida Atlantic University, Boca Raton, FL.
Introduction: The Covid-19 pandemic has resulted in a massive number of hospitalizations with widespread effects on the global healthcare system. More research is needed to understand the implications of the disease, particularly its effects on renal function. Although initial studies from China suggested otherwise, there is growing evidence for an association between Covid-19 and AKI.
Case Description: A 66-year-old man with history of CKD IIIb presented to the ED with fever and dry cough for several days. On admission the patient was febrile and tachypneic. Labs were showed elevations in BUN, SCr and inflammatory markers. Chest CT revealed bilateral ground glass opacities and NP swab was positive for SARS-CoV2. The patient was initially treated with hydroxychloroquine, levofloxacin, and IV fluids. Clinical state worsened, eventually requiring intubation and vasopressors. Renal function progressed to anuria. Bicarbonate, potassium binders and loop diuretics with IV fluids. Clinical status worsened, eventually requiring intubation and vasopressors.
Discussion: It is theorized that renal impairment in Covid-19 is due to virus entry into host cells via the ACE-2 receptor present in lungs and kidneys. Post-mortem kidney biopsies suggest that renal damage in Covid-19 is mediated through multiple mechanisms including cytopathic effect, myofibroblastic deposition, and microthrombi-related tubular damage. Although our patient recovered after a prolonged hospital course, he remained anuric requiring RHD far sooner than anticipated with natural progression of CKD, including direct cytotoxicity, immunologic deposition, and microthrombi-related tubular injury. A case report of severe ARF (sCr) was 3.2 mg/dL with an albumin of 2.6 g/dL. A urinalysis showed moderate blood and 3+ protein on dipstick along with granular casts. A urine albumin:Cr (UAC) ratio was 0.19 g/g. Despite volume resuscitation, her sCr continued to rise. Workup included renal ultrasound, hepatitis panel, and parvovirus B19, ANA, ANCA, anti-dsDNA, A, C3, and C4 were neg/nl. On day 5, she was afebrile with resolution of her symptoms, but her sCr was further elevated at 5.3 mg/dL and albumin was 1.1 g/dL. Repeat UAC ratio was elevated over lab measurable range. A biopsy showed FSGS and ATN. She was started on 60mg of prednisone/day. Three weeks later, her sCr was 2.9 mg/dL, albumin 2.4 g/dL and her UAC ratio was 3.0 g/g (Fig 1).
Discussion: The optimal treatment for viral related cFSGS is unknown. Because diffuse foot process effacement typically accompanies this lesion, it is tempting to give steroids. However, there is concern that this may exacerbate the infection, and cFSGS may be driven along with chronicity of the virus. Still, steroids may hasten recovery and reduce morbidity associated with the nephrotic syndrome. The rapid improvement in

PO0794
Rhabdomyolysis as a Complication of COVID-19: A Report of Five Cases
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Introduction: COVID-19 virus pandemic has caused more than 5milllion infected and 330 Thousand deaths worldwide. The incidence of acute kidney injury (AKI) is variable, from 0.5% to 32.8%. Rhabdomyolysis (Rb) is a life-threatening emergency, usually manifesting as myalgia, fatigue, pneumonia, and AKI. One of its leading non-traumatic causes are viral infections. We report 5cases of Rb associated with COVID-19.
Case Description: Of a total of 460 positive cases of COVID-19 infection (real-time PCR), at the NationalMedicalCenter20deNoviembre in MexicoCity, 5were diagnosed with Rb and associated AKI(Ck>5,000U/l and KDIGO AKI criteria). Characteristics of patients are presented in (Fig.1). Age range was from 26 to 64 years, only one female, all with BMI: 25-27 kg/m2, time from admission-diagnosis of Rb was on average one week. Most common symptoms were fever, cough, and dyspnea (5/5), as well as abdominal pain (4/5). Only 1/5 was oliguric at diagnosis. Average Ck at diagnosis was 7845 (18165 μg/L) and all cases had high levels of interleukin-6. They were managed with aggressive hydration, 2/5 of them required renal replacement. At the time of this report, 2 had been discharged, 2 remained hospitalized (one still on RRT), and one died.
Discussion: COVID-19 patients can develop AKI primarily due to low oral intake, sepsis, and anaphylaxis. Some patients with COVID-19 have multiple risk factors for Rb development: viral muscle cytotoxicity, continuous hyperthermia, and anaphylaxis storm among others. This shows a high risk of AKI via 3 mechanisms: renal vasoconstriction, tubular obstruction and direct tubular toxicity. Of note, in the described cases, abdominal pain was a common symptom and only one was oliguric. Early identification allowed aggressive treatment, which underscores the importance of having a high index of suspicion. Further observations will be needed to understand the full spectrum of association between COVID-19 and Rb, but is clear that these patients are at high risk for developing AKI by these mechanisms.

PO0795
Corticosteroid Treatment in a Case of COVID-19-Associated Collapsing FSGS
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Introduction: Collapsing FSGS (cFSGS) is associated with viral infections including HIV, parvovirus B19 and CMV. Recent reports describe cFSGS in patients infected with coronavirus (COVID-19). While reports on idiopathic cFSGS suggest early response to steroids, there are little data to guide treatment of cFSGS associated with infection. We present a case of AKI with severe abrupt nephrotic syndrome in a COVID-19 patient with cFSGS on biopsy and a rapid response to steroids.
Case Description: A 51 y/o black woman with no known medical history presented with 8 days of fever and SOB COVID-19 testing was positive. Admission serum creatinine (sCr) was 3.2 mg/dL with an albumin of 2.6 g/dL. A urinalysis showed moderate blood and 3+ protein on dipstick along with granular casts. A urine albumin:Cr (UAC) ratio was 0.19 g/g. Despite volume resuscitation, her sCr continued to rise. Workup included renal ultrasound, hepatitis panel, and parvovirus B19, ANA, ANCA, anti-dsDNA, A, C3, and C4 were neg/nl. On day 5, she was afebrile with resolution of her symptoms, but her sCr was further elevated at 5.3 mg/dL and albumin was 1.1 g/dL. Repeat UAC ratio was elevated over lab measurable range. A biopsy showed FSGS and ATN. She was started on 60mg of prednisone/day. Three weeks later, her sCr was 2.9 mg/dL, albumin 2.4 g/dL and her UAC ratio was 3.0 g/g (Fig 1).
Discussion: The optimal treatment for viral related cFSGS is unknown. Because diffuse foot process effacement typically accompanies this lesion, it is tempting to give steroids. However, there is concern that this may exacerbate the infection, and cFSGS may be driven along with chronicity of the virus. Still, steroids may hasten recovery and reduce morbidity associated with the nephrotic syndrome. The rapid improvement in
proteinuria despite an increase in GFR suggests that steroids played a role in the recovery. A randomized trial would be necessary to determine the safety and efficacy of steroids for COVID-19 related fSGS.

PO0796
Remote Peritoneal Dialysis Training in a COVID-19-Positive Patient
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Introduction: Training patients in peritoneal dialysis (PD) traditionally requires up to fourteen in-person clinic visits to cover all aspects of care. The COVID-19 crisis has created an unprecedented challenge in educating patients to perform PD safely while minimizing exposure to staff. Telemedicine has been well-received by staff and patients in other aspects of PD care. We present a case of a COVID-19 positive patient who was fully trained in PD using telemedicine.

Case Description: The patient is a 21-year-old man with VATER Syndrome who progressed to ESRD with uremic symptoms. He chose PD as his dialysis modality while awaiting a kidney transplant. Prior to his PD catheter insertion, he tested positive for COVID-19. He was deemed an ideal candidate for PD training via telemedicine and agreed to proceed. For the first two training sessions, he presented to the PD clinic and was placed in a designated isolation room with his personal computer. His PD nurse was in an adjoining room and trained him via video conferencing with the option to enter his room if needed. The patient quickly mastered the procedure in this monitored environment. He completed the remainder of the required education remotely in his home via telemedicine.

Discussion: There are several advantages of telehealth in COVID-19 patients. The risk of viral exposure to healthcare staff and other patients is reduced by limiting trips to the PD clinic. Additionally, reducing the burden of travel saves time and expense for the patient. Patient selection for telehealth learning is critical: the ideal patient must be motivated and technologically savvy. The patient, PD nurse, and nephrologist must jointly determine whether proceeding with tele-learning is feasible and safe. Although remote videoconferencing is not the conventional or optimal method for PD education, it can be used successfully to train patients while minimizing exposure of COVID-19 to staff.

PO0797
Calciphylaxis and COVID-19-Associated Thrombotic Retiform Purpura in a Peritoneal Dialysis Patient
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1Weill Cornell Medicine, New York, NY; 2Rogosin Institute, New York, NY.


Case Description: A 62-year-old female presented to the emergency room with leg pain and edema for 4 weeks. She had recently been started on peritoneal dialysis. Examination revealed tender, indurated retiform dusky plaques on thighs and bilateral leg pain and edema for 4 weeks. She had recently been started on peritoneal dialysis. She was transferred to interventional hemodialysis and started on intravenous sodium thiosulfate 25 grams three times weekly.

Discussion: In COVID-19 era, coagulation abnormalities are becoming increasingly evident. Management of calciphylaxis in PD patients is difficult under current circumstances due to limitations in the ability to provide regular infusions and multi-interventional care. We hypothesize that our patient had an underlying predisposition for calciphylaxis given risk factors of secondary hyperparathyroidism and an additional insult (COVID-19) caused a so-called “second hit” resulting in clinically apparent disease. Atypical presentations of COVID-19 due to a combination of procoagulant state, as well as any preexisting risk factors for calciphylaxis, must be kept in mind.
PO0799
Severe Hypernatremia as an Unintended Consequence of COVID-19-Related Social Distancing
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Introduction: COVID-19 is primarily a respiratory infection which can have adverse effects on multiple organ systems. There is limited information concerning the harmful effects of social distancing in patients with COVID-19 who are at risk of undernutrition due to avoidance of medical attention due to fear of contracting the novel COVID-19 disease.

Case Description: A 64-year-old African American female with a past history of HIV-related dementia and seizure disorder was residing with family members, requiring assistance for daily living. She was not able to attend to her hygiene and meals. The family reported that over the past 7-10 days, she had become less interactive, remaining bedbound and resistant oral intake. There was an initial reluctance to bring her to the Medical Center due to the fear of contracting COVID-19 infection, given her status. Despite her condition, the family requested to provide social services, home care, mental status progressively worsened, prompting presentation to the emergency department. The patient had a GCS of 10. The patient was nonresponsive, did not follow commands, and only withdrew from noxious stimuli. Vital signs were prominent for fever 37.7°C and blood pressure was 94/64 mmHg. Pertinent laboratory results included: serum sodium 201 mEq/L, plasma osmolality, 431 mOsm/kg, BUN 107 mg/dL, and creatinine of 4.8 mg/dL. CT head showed no acute intracranial pathology. Her condition required ICU care, including mechanical ventilation. COVID-19 screening was negative to 37 % of cases. Here we report a case of a woman with COVID-19 presenting with rhabdomyolysis and AKI.

Case Description: A 48 y/o Hispanic woman with history of HTN, hyperlipidemia and DM type 2 who presented to the ED complaining of shortness of breath, fever, cough, and myalgias four days before presentation she had been diagnosed with COVID-19 and was self-isolating at home. Her symptoms worsened prompting her visit to the ED. Vital signs showed fever of 103.1 F, pulse 86, respirations 37, blood pressure 106/58 and O2 Sat 85% at room air, 95% with nasal canula at 4 L. PE was normal except for tachycardia. Course was initially uneventful on lung with COVID-19. Admission labs were remarkable for AKI and rhabdomyolysis. Serum creatinine was 3.61, BUN, and total CK 106,193. U/A with blood, 5-10 RBC, 5-10 WBC and many bacteria. FeNa was 0.3%. Toxicology panel was negative. Respiratory viral panel was negative. Inflammation A and B markers were initially elevated 2 L bolus of IV NS then continued with balanced crystalloid solutions for volume expansion over the next 3 days. She received treatment with hydroxychloroquine, azithromycin and ceftriaxone for COVID-19 pneumonia. Her symptoms improved and serum creatinine and CK gradually decreased until back to normal levels.

Discussion: Rhabdomyolysis can be seen associated with viral infections. We presented a patient with COVID-19 and rhabdomyolysis. There are no studies establishing a mechanism for COVID-19 induced rhabdomyolysis. Patients with COVID-19 pneumonia are generally kept with negative fluid balance to avoid overload and worsening of ARDS. On the other hand, volume expansion is mainstay management for rhabdomyolysis. Clinicians should have a high suspicion for rhabdomyolysis in patients with COVID-19 presenting with myalgias and AKI. Early recognition of and appropriate treatment is crucial to improve outcomes.
PO0804
Extracorporeal Cytokine Reduction Using Oxiris Blood Purification in COVID-19
Spencer Hodges,1 Marat Abdullah,2 Mark A. Tidwell,1 Daniel L. Landry,1 1Baystate Medical Center, Springfield, MA; 2Kidney Care and Transplant Services of New England, Springfield, MA.

Introduction: Severe COVID-19 infection can cause "cytokine storm" and end-organ dysfunction. Oxiris, a blood-purification filter, was recently approved by the FDA under emergency use authorization for this indication due to its ability to remove cytokines and endotoxin through its AN-69ST membrane. We describe our experience with the first two cases treated at our institution.

Case Description: Case 1: 58-year-old female patient with a baseline creatinine of 0.8 mg/dL. & history of hemoglobin SC disease was admitted with respiratory failure due to COVID-19 infection. She deteriorated on hospital day (HD) 6 and was intubated. She received broad-spectrum antibiotics and convalescent plasma. On HD 15 she had increasing vasopressor requirement, anuric AKI and was started on continuous renal replacement therapy (CRRT). Due to worsening clinical status on HD18 she was started on the Oxiris hemofilter through the CRRT circuit for 48 hours. Oxygenation improved and there was some improvement in inflammatory markers (IM) (table 1), however, the family withdrew care on HD 20.

Case 2: 29-year-old male with no prior past medical history apart from morbid obesity presented with fever and dry cough in the setting of recent COVID-19 exposure. He was found to be COVID-19 positive and rapidly deteriorated with resultant intubation on HD4. He received hydroxychloroquine, doxycycline, remdesivir and convalescent plasma. Oxiris hemoperfusion was initiated on HD8 due to worsening hyponatremia despite high fluid flow of 250 ml/min and dialysate flow of 25 ml/kg/hour with either systemic heparin or the patients for 48 hours with a scheduled filter exchange at 24 hours. We used a blood-purification filter, was recently approved by the FDA under emergency use authorization for this indication due to its ability to remove cytokines and endotoxin through its AN-69ST membrane. We describe our experience with the first two cases treated at our institution.

Discussion: We present our first 2 cases using the Oxiris hemofilter. We treated the patients for 48 hours with a scheduled filter exchange at 24 hours. We used a blood-purification filter, was recently approved by the FDA under emergency use authorization for this indication due to its ability to remove cytokines and endotoxin through its AN-69ST membrane. We describe our experience with the first two cases treated at our institution.

Table 1: Inflammatory and Respiratory Parameters

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Chest XR

PO0805
Rhabdomyolysis as a Late Complication of COVID-19 Infection
Benjamin Lidgard, Ann M. O’Hare, Sarah F. Sanghavi, Bessie A. Young, University of Washington, Seattle, WA.

Introduction: The 2019 novel Coronavirus (COVID-19) is a betacoronavirus which typically presents with fever, cough, myalgia, and fatigue and can be associated with acute kidney injury (AKI). Recently, several cases of rhabdomyolysis (with and without AKI) have been reported with COVID-19 infection. We present a case of a patient with COVID-19 infection who developed rhabdomyolysis on hospital day 22.

Case Description: A 74-year-old man presented with several weeks of progressive malaise, dyspnea, fatigue, and nausea. He was hypoxic to 87%, febrile (38.8°C) and had diffuse bilateral infiltrates on chest x-ray [Figure 1]. He was intubated on hospital day 1. Testing for COVID-19 by PCR was positive. Creatinine improved from 1.6 to 0.9 mg/dL with 2L of IV fluids. He did not require vasopressors. On hospital day 22, while still intubated, his creatinine increased from 1.4 to 3.8 mg/dL. The level of creatinine phosphokinase (CPK) had was 7393 U/L from 118 U/L on admission, and his plasma free myoglobin was 34,640 mcg/L. Urinalysis was positive for 3+ occult blood, few red blood cells, and many granular casts. His serum creatinine peaked at 6.67 mg/dL on hospital day 26 and subsequently declined to 1.6 by hospital day 33.

Discussion: Rhabdomyolysis is an infrequent complication of COVID-19 infection. While observed, rhabdomyolysis is typically present on admission. This is, to our knowledge, the latest that rhabdomyolysis has been observed in COVID infection. The patient’s inflammatory markers were not re-checked at the time of this event, though worsening inflammation may have provoked this event. Their troponin was mildly elevated, but was not tested. He was not treated with steroids. No bed sores were observed, and the patient had no access to illicit substances. No medications known to cause rhabdomyolysis were given prior to this development. This case report suggests that rhabdomyolysis-related AKI may be a late complication of COVID-19 infection.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

Renal Biopsy
Case Description: Case 1, a 28 years old African American female and Case 2, a 58 years old African American male with baseline CKD III, admitted with COVID-19 infection and had acute kidney injury with significant proteinuria with hypalbuminemia. Patients had kidney biopsies. Please see table for all the details.

Discussion: Possible etiologies of acute kidney injury in COVID 19 are tubular injury due to cytokine storm, direct cytotoxic effect and immune mediated glomerulonephritis. Both the patients had collapsing FSGS in addition to tubular injury suggesting injury to the podocytes. Viral particles were not seen on both the biopsies, and hence direct cytotoxic effect was not considered to be the mechanism of renal injury, although viral level below the detection threshold could not be excluded. Collapsing FSGS has been seen with other viral infections including Parvo-virus infection, Cytomegalovirus infection and HIV. Variant of apolipoprotein L1 (APOL1) gene in African Americans have been shown to be associated with FSGS. These two patients had genetic susceptibility due to APOL1 and COVID infection caused interferon surge leading to a second hit. Teaching Points: Renal biopsy should be considered in patients with COVID-19 and Nephrotic range proteinuria. APOL1 testing should be done in patients with African American descent.

Demographic, clinical, laboratory, biopsy findings and follow up.

SARS-CoV-2 infection in the early post-transplant period after a living donor kidney transplant

Case Description: Three LDKT recipients developed COVID-19 in the early post-transplant period and were detected positive for SARS-CoV-2 at day 7, day 19 and 2 months post-transplant. Patients 1 and 2 had received 1 mg/kg of anti-thymocyte globulin (ATG) as induction and patient 3 had received no induction at the time of transplant. Induction agent was reduced in patient 1 and was stopped in patients 2 and 3. Patient 3 developed acute kidney injury with a peak serum creatinine of 2.4 mg/dL, whereas other 2 patients did not develop kidney allograft dysfunction. All 3 patients recovered from SARS-CoV-2 infection with normal renal function at discharge.

Introduction: Coronavirus disease 2019 (COVID-19) pandemic presented multiple challenges for living and deceased donor kidney transplant programs with the likelihood of exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report the course of COVID-19 and immunosuppression in 3 months of living donor kidney transplantation (LDKT) which has not been described previously.

Case Description: Three LDKT recipients developed COVID-19 in the early post-transplant period and were detected positive for SARS-CoV-2 at day 7, day 19 and 2 months post-transplant. Patients 1 and 2 had received 1 mg/kg of anti-thymocyte globulin (ATG) as induction and patient 3 had received no induction at the time of transplant. Induction agent was reduced in patient 1 and was stopped in patients 2 and 3. Patient 3 developed acute kidney injury with a peak serum creatinine of 2.4 mg/dL, whereas other 2 patients did not develop kidney allograft dysfunction. All 3 patients recovered from SARS-CoV-2 infection with normal renal function at discharge.

Discussion: Limited experience of SARS-CoV-2 infection in early post-transplant period is available in deceased donor kidney transplant (DDKT) with serious morbidity and mortality implications. Lymphopenia described in patients with severe illness due to SARS-CoV-2 can be aggravated by recently used higher dose of lymphocyte depleting agent, especially to cover for delayed graft function in DDKT. As compared to previously reported cases of DDKT, our relatively young recipients of LDKT had a milder course, minimal complications and recovered from SARS-CoV-2 infection. We suggest consideration of recipient age, pretransplant isolation and using induction agent basiliximab or lower dose of ATG for a LDKT program during COVID-19 pandemic.

Introduction: During our current pandemic, physicians must exclude COVID-19 in every patient presenting to the hospital with a febrile illness. However, every patient should have a complete work-up done to not miss other disease processes. Here we describe a case of microscopical polyangitis with symptoms succumbing COVID-19 infection.

Case Description: The patient is a 69 yo female with history of HTN who presented with four weeks of polyarthralgia and fevers; this was accompanied by a dry cough and morning stiffness in her shoulders and hips, for which she heavily used ibuprofen. Vital signs were within normal limits. Physical exam showed clear breath sounds with 2+ pitting edema in the lower legs and no rashes. Labs revealed a WBC of 20,000 cells/μL, with four weeks of polyarthralgia and fevers; this was accompanied by a dry cough and morning stiffness in her shoulders and hips, for which she heavily used ibuprofen. Vital signs were within normal limits. Physical exam showed clear breath sounds with 2+ pitting edema in the lower legs and no rashes. Labs revealed a WBC of 20,000 cells/μL, and a platelet count of 25,000. UA showed moderate leukocyte esterase, trace protein, and large granular leukocytes. Microscopic examination of urine revealed no red blood cells or white blood cells. Hemoglobin was 12.0 g/dL, hematocrit was 35%, and mean corpuscular volume was 89.0 fL. Microcytic anemia was present. A complete blood count revealed no leukocytosis. The ESR was 114 mm/hour, and CRP was 23.4 mg/L. UA showed moderate leukocyte esterase, trace protein, and large granular leukocytes. Microscopic examination of urine revealed no red blood cells or white blood cells. Hemoglobin was 12.0 g/dL, hematocrit was 35%, and mean corpuscular volume was 89.0 fL. Microcytic anemia was present. A complete blood count revealed no leukocytosis. The ESR was 114 mm/hour, and CRP was 23.4 mg/L. A diagnosis of rheumatoid arthritis was made, as well as a diagnosis of possible vasculitis. The patient was started on prednisone 40 mg daily and cyclophosphamide 375 mg in 2 weekly for four weeks and was discharged home in stable condition.

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Underline represents presenting author.

it is 204 mg/L. UA showed moderate leukocyte esterase, trace protein, and large granular leukocytes. Microscopic examination of urine revealed no red blood cells or white blood cells. Hemoglobin was 12.0 g/dL, hematocrit was 35%, and mean corpuscular volume was 89.0 fL. Microcytic anemia was present. A complete blood count revealed no leukocytosis. The ESR was 114 mm/hour, and CRP was 23.4 mg/L. A diagnosis of rheumatoid arthritis was made, as well as a diagnosis of possible vasculitis. The patient was started on prednisone 40 mg daily and cyclophosphamide 375 mg in 2 weekly for four weeks and was discharged home in stable condition.
**Discussion:** Systemic vasculitis remains to be a diagnostic challenge, especially in the era of COVID-19. The overlap in symptoms of COVID-19 and vasculitis is made even more difficult by previous history and histopathological findings coupled with positive ANCA. Despite treatment, almost a quarter of these patients will progress to ESRD. In the era of COVID-19, great care must be taken to diagnose the kidney manifestations of systemic vasculitis.

PO0811
Low-Sodium Disorders and the 2019 Novel Coronavirus Disease (COVID-19)

Jasmee Gill, Xuini S. Guo, Akinwande A. Akinfolarin, Ankit Mehta.

Introduction: COVID-19 have been well characterized with hallmarks of pneumonia and respiratory failure. Hyponatremia is a well reported finding in patients with COVID-19. However only few reports have been directly attributable to the disease. We report three different presentations of hyponatremia in COVID19 patients.

Case Description: 1. 70 year old man with hypertension, diabetes presented with dyspnea. He was clinically septic. Chest X-ray (CXR) showed bilateral interstitial and airspace opacities. Laboratory data revealed, serum sodium 122 meq/L, serum osmolality 264 mosm/kg, urine osmolality 579 mosm/kg and urine sodium 153 mmol/L. A diagnosis of hyponatremia secondary to the Syndrome of Inappropriate Antidiuretic Hormone (SIADH) was made and the patient was treated with oral urea and fluid restriction. 2. 50 year old man with chronic alcohol abuse presented with bilateral calf soreness. CXR revealed increased interstitial markings. Laboratory data showed serum sodium 113 meq/L, serum osmolality 251 mosm/kg, urine osmolality 426 mosm/kg and urine sodium 148 mmol/L. Hyponatremia was attributed to a low solute state. Serum sodium improved with normal saline infusion. 3. 69 year old female with hypertension admitted with vomiting and diarrhea. CXR showed diffuse pulmonary infiltrates. Initial laboratory data revealed serum sodium of 126 meq/L, serum osmolality 260 mosm/kg. Serum sodium recovered as diarrhea resolved. However, eight days after starting therapy with Selinexor, a nuclear transport inhibitor, serum Na declined to 128 meq/L, serum osmolality 260 mosm/kg. SIADH was attributed to Selinexor therapy. Sodium recovered with oral sodium chloride therapy and fluid restriction.

Discussion: Incidence of Hyponatremia due to SIADH in community acquired pneumonia is 8-31% in adult patients. To the best of our knowledge, there have only been two case reports of SIADH in COVID-19 disease from Switzerland. Hence, it is unclear if SIADH is the predominant presentation of hyponatremia with COVID-19. The etiology of hyponatremia in COVID-19 patients is unclear and needs further research.

PO0812
COVID-19 Short-Term Outcomes of AKI and Chronic Hemodialysis


Introduction: Acute kidney injury (AKI), albuminuria and hematuria are common and in some patients in COVID-19 in addition to viral pneumonia, hypercoagulability and hyperinflammation. We present short-term outcomes of 21 COVID-19 patients with AKI and CRRT and the clinical course of 40 chronic hemodialysis (HD) patients with Covid-19.

Case Description: Twenty-one non-CKD Covid-19 infected patients with AKI required mechanical ventilation and CRRT at the ICU, 20 were males, average age was 59.7 years (y), average BMI 29 kg/m2, 33 % had diabetes. The typical scenario was a normal/slightly elevated creatinine level at admission, normalizing after iv fluids, but rising creatinine from day 3-4 and start of CRRT on day 8 (median). Urinary analysis was available in eight patients, of which seven had albuminuria and/or hematuria. So far eight patients (38 %) have died. Dialysis has been discontinued in nine patients (43 %), median time 17 days in dialysis (range 1-35 days), follow up of 1-4 weeks. Patients 3-4 weeks on CRRT and some had a creatinine(Cr) of 7.87mg/dl. Urinalysis revealed active sediment with 55 RBC/hpf, 65 WBC/hpf, and nphretic range proteinuria: 5 gm/gm of creatinine. He was initiated on renal replacement therapy and received convalescent plasma along with Tocilizumab for the treatment of COVID-19. Serologic testing revealed a positive perinuclear (p)-ANCA (1:320), myeloperoxidase (32.5). Kidney biopsy was consistent with a pauci immune glomerulonephritis; cellular crescent present in 40% of glomeruli. He received pulse dose steroids and Rituximab. The patient had a good clinical response and was able to discontinue hemodialysis and serum Cr decreased to 3.5mg/dl. Case Two: 46 year old South Asian male presented with rash from leukocytoclastic vasculitis and was diagnosed with COVID-19. He had an AKI, serum Cr peaked at 4.0mg/dl with proteinuria, leukocyturia, and microhematuria on urinalysis. Cytoplasmic(c)-ANCA and proteinase-3(PR-3) were positive. A kidney biopsy was performed which revealed a necrotizing glomerulonephritis. He was treated with steroids and Rituximab with a positive response, Cr decreased to 2.0mg/dl.

Discussion: It is now well known that SARS-CoV-2 affects organs outside of the respiratory system, with the kidneys being a usual target. The most commonly reported presentation of COVID-19 and the kidneys is AKI, the etiology of which is predominantly acute tubular necrosis (ATN). Collapsing GN is by far the most described glomerular presentation of COVID-19 and the kidneys is AKI, the etiology of which is predominantly acute tubular necrosis (ATN). Collapsing GN is by far the most described glomerular presentation of COVID-19, but collapsing GN can also be seen in the setting of coronavirus disease 2019 (COVID-19). The etiology of collapsing GN in the setting of COVID-19 is unclear and needs further research.

PO0813
ANA-Associated Vasculitis Under a COVID-19 Mask

Rui Song, Srikanth Thiruvuruduoorthy, Jared Hassler, Ziauddin Ahmed, Serban Constantinescu, Avrum Gillespie. Lewis Katz School of Medicine at Temple University, Philadelphia, PA.

Introduction: Ground glass opacities (GGO) on CT scan are the hallmark of COVID-19. GGO can also be seen in ANA-associated lung injury. Additionally, both can present with kidney injury. We report a case of presumed COVID-19 with AKI which was actually severe ANA-associated vasculitis.

Case Description: A 74-year old female with a history of hypertension and diabetes, who presented with a week of chills, cough, dyspnea, and watery diarrhea, and a creatinine of 10.2 mg/dl (baseline creatinine 1.02 mg/dl). A month prior to admission, she was treated for presumed pulmonary eosinophilia, followed by otitis media, and then bacterial sinusitis with oral ciprofloxacin. Despite a negative swab, she was admitted with suspicion of COVID-19 given GGO seen on CT scan and an exposure history at her senior home. She was treated per the COVID-19 protocol: IV methylprednisolone 125mg, azithromycin, ceftriaxone, and furosemide. Serum creatinine went up to 11.5 mg/dl. ANA was suspected as urine microscopy showed granular casts and no dysmorphic RBC or cellular/WBC/RBC casts. After a repeat negative swab and improvement in respiratory symptoms yet worsening renal function requiring hemodialysis, a full serologic workup was performed. Positive results include p-ANCA (1:320), MPO (49), and ANA (1:160 homogenous) without hypocomplementemia. Other autoimmune markers including anti-GBM antibody were negative. A kidney biopsy was performed and showed pauci-immune crescentic glomerulonephritis (GN) with cellular crescents in more than 80% of the glomeruli with minimal interstitial fibrosis and tubular atrophy. Given the frailty of this patient, she was treated with oral prednisone and rituximab instead of cyclophosphamide. She remained on intermittent hemodialysis and tolerated the treatment well.

Discussion: This case emphasizes the importance of detecting pulmonary-renal syndrome in the era of COVID-19. Given the current global pandemic and a high-volume of infected patients coupled with the lack of sensitivity of the SARS-CoV-2 assays, it is possible to miss this relatively rare ANA-associated vasculitis. Patient with rapid proliferative GN feature and lung symptoms should be further worked up to avoid missing an ANA-associated vasculitis. COVID-19 may actually provoke ANA-associated vasculitis and further testing is underway.

PO0814
Antineutrophil Cytoplasmic Antibody (ANCA) Vasculitis with Glomerulonephritis in COVID-19

Yuriy Khain, Vanesa Bjoj, Kenar D. Jhaveri, Nupur N. Uppal. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it inflicts, coronavirus disease 2019 (COVID-19), has become a global pandemic in 2020. To date, only one case of ANCA associated vasculitis (AAV) with COVID-19 has been reported from Iran. We describe the first two cases of AAV and glomerulonephritis in the United States.

Case Description: Case one: 64 year old African American male with a distinct (>10years) history of cryptogenic organizing pneumonia presented to the hospital with hypoxic respiratory failure secondary to COVID-19. He had an acute kidney injury (AKI) with eGFR 9.1 and creatinine(Cr) of 7.87mg/dl. Urinalysis revealed active sediment with 55 RBC/ hpf, 65 WBC/hpf, and nephritic range proteinuria: 5 gm/gm of creatinine. He was initiated on renal replacement therapy and received convalescent plasma along with Tocilizumab for the treatment of COVID-19. Serologic testing revealed a positive perinuclear (p)-ANCA (1:320), myeloperoxidase (32.5). Kidney biopsy was consistent with a pauci immune glomerulonephritis; cellular crescent present in 40% of glomeruli. He received pulse dose steroids and Rituximab. The patient had a good clinical response and was able to discontinue hemodialysis and serum Cr decreased to 3.5mg/dl. Case Two: 46 year old South Asian male presented with rash from leukocytoclastic vasculitis and was diagnosed with COVID-19. He had an AKI, serum Cr peaked at 4.0mg/dl with proteinuria, leukocyturia, and microhematuria on urinalysis. Cytoplasmic(c)-ANCA and proteinase-3(PR-3) were positive. A kidney biopsy was performed which revealed a necrotizing glomerulonephritis. He was treated with steroids and Rituximab with a positive response, Cr decreased to 2.0mg/dl.

Discussion: It is now well known that SARS-CoV-2 affects organs outside of the respiratory system, with the kidneys being a usual target. The most commonly reported presentation of COVID-19 and the kidneys is AKI, the etiology of which is predominantly acute tubular necrosis (ATN). Collapsing GN is by far the most described glomerular presentation of COVID-19, but collapsing GN can also be seen in the setting of coronavirus disease 2019 (COVID-19). The etiology of collapsing GN in the setting of COVID-19 is unclear and needs further research.

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**Introduction:** Rhabdomyolysis is characterized by the release of intracellular muscle contents into the circulation. Of the 1099 patients affected by Covid-19 in China, only 0.2% had rhabdomyolysis.

**Case Description:** A 52 year old African American female with past medical history of Diabetes and hypertension presented to the ER with 7 days of worsening fever, chills, myalgias, nausea, vomiting, dyspnea, loss of sense of taste and smell. Her home medications included metformin and Candesartan-HCTZ, however, she had been off medications for a week. She was seen with the chief complaints of fever, cough, dyspnea, and headache. Her vital signs on presentation were: BP 100/60 mmHg, HR 104 bpm, and oxygen saturation of 92%. Physical examination was remarkable for diminished and diffuse coarse breath sounds. Lab work-up showed serum creatinine of 2.99 mg/dl (baseline 1.19 mg/dl) with an estimated GFR of 26 ml/min. Urinalysis revealed protein > 500 mg/dl, RBC 25, and presence of coarse granular casts. Urine protein-creatinine ratio was 3.2. Serology was negative for ANA, ANCA, and anti-proteinase antibodies, as well as hepatitis and HIV panels. Serum C3 and C4 levels were within normal limits. Viral PCR of nasopharyngeal aspirate was positive for SARS-CoV-2. Home medications lisinopril and hydrochlorothiazide were held on admission, and he was started on intravenous fluids, azithromycin, and hydroxychloroquine. On day 4, serum creatinine trended up to 3.29 mg/dl and potassium was 4 mmol/L but since the patient was oliguric, hemodialysis (HD) was started. Serum creatinine then trended to a high of 15 mg/dl, urea nitrogen to 102 mg/dl and serum potassium level to 6.9 mmol/L despite multiple HD sessions. Meanwhile, his oxygen requirement also increased to 15L. After 10 days of daily HD sessions, serum potassium came down to 4.3 mmol/L but he ultimately required HD post discharge.

**Discussion:** Previous literature has discussed SARS-CoV-2 association with rhabdomyolysis. ACE2 of RAS and proximal tubular cells causing hypokalemia. To the best of our knowledge this would be the first documented case of hemodialysis refractory hyperkalemia seen with SARS-CoV-2 infection. One of the mechanisms for kidney injury is a direct viral induced cytopathic effect, which we believe held true for our patient. As viremia cleared, the kidney function improved though it did not return to baseline. In our case, development of hyperkalemia despite hemodialysis makes it more interesting, but it remains unclear how.

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**PO0187**

**The Role of Point-of-Care Ultrasound in the Management of Dialysis Patients with COVID-19**

**Nathanial C. Reisinger:** 1Abhilash Koratula. 1Medical College of Wisconsin, Milwaukee, WI; 2University of Pennsylvania, Philadelphia, PA.

**Introduction:** Much of the burden for management of outpatient dialysis patients with suspected or confirmed Coronavirus Disease 2019 (COVID-19) has fallen to the dialysis units. Symptom recognition is not straightforward as these patients often have multiple putative etiologies for dyspnea especially given concomitant pulmonary congestion due to fluid overload. In this context, point-of-care ultrasonography (POCUS), particularly lung ultrasound (LUS) is a valuable diagnostic tool for nephrologists taking care of these patients. POCUS is free of ionizing radiation, can be performed at the bedside, and has comparable diagnostic accuracy to chest CT scan for most lung pathologies. We present a case study to illustrate the role of POCUS in dialysis patients.

**Case Description:** A 79-year-old woman with a history of ESKD on maintenance hemodialysis was found to be hypoxemic with an oxygen saturation of 90% on room air. Bedside LUS demonstrated patchy areas of pleural thickening and irregularity as well as confluent B-lines and scattered consolidations consistent with viral pneumonia [Figure]. Focused cardiac US did not reveal any overt signs of fluid overload. She tested positive for COVID-19 and improved with supportive care. She continued to receive dialysis on a separate shift for COVID-19 positive patients.

**Discussion:** In addition to aiding in diagnosis, POCUS limits staff exposure to the virus during transportation and avoids the downtime for radiology room decontamination unlike CT. Most handheld US devices can be completely encased in a standard plastic transducer cover that can be discarded after each use. We propose that dialysis units adopt LUS as a bedside tool to diagnose and monitor the extent of pulmonary involvement in patients with COVID-19 and differentiate from other causes of dyspnea. CT scan can be reserved for those with equivocal LUS findings or underlying chronic lung disease that interferes with interpretation.
Continuous renal replacement therapy (CRRT) while better tolerated is a limited resource. Such patients may not tolerate hemodynamic shifts induced by hemodialysis (HD).

Ventilated patients diagnosed with acute respiratory distress syndrome (ARDS) due to COVID-19 have been particularly challenging for Nephrologists managing patients on continuous renal replacement therapies (CRRTs). This has been well documented in numerous articles and has posed to be a difficult obstacle for those caring for Covid-19 positive patients. This has overall high mortality.

CRRT was continued however multiple issues with filter clotting were encountered. One day later they were intubated for tachypnea and worsening acidosis. They were admitted during this period to the ICU with COVID-19 and AKI showed 7 had normal ferritin levels to 73 pg/mL. Case 2: A 55 year old male on CVVHDF with the M150 filter had a serum ferritin level progressively increasing to 2377 ng/mL and multiple clotting events.

The patient was started on CRRT as thrombocytopenia worsened and there was a concern for heparin-induced thrombocytopenia. He was extubated after 15 days and recovered renal function. Data on 9 other patients therefore, clinicians might have low clinical suspicion for rhabdomyolysis.

Acute peritoneal dialysis (PD) remains a feasible RRT modality in patients on mechanical ventilation. Nevertheless, the hesitance to use PD for fear of increasing intrathoracic pressure (IAP) with dwellings leads to altered respiratory mechanics. Our case demonstrates that acute PD has no adverse respiratory outcomes in a COVID-19 patient.

Case Description: A 42 year-old Hispanic male with end stage renal disease newly initiated on urgent start PD for 1 week presented with acute hypoxic respiratory failure secondary to ARDS from COVID-19. Upon presentation, he was intubated and initiated on lung protective ventilator strategies. Due to high ventilatory requirements (PEEP 15, FiO2 100%) with severe volume overload HD was selected in lieu of PD. He underwent PD run with minimal volume removal due to high daily intake. Due to limited availability of CRRT, he was transitioned to continuous PD via cyclic (fill volume 2L, every 4hr). FiO2 reduced to 40%, peak and plateau pressures did not change, and he was able to maintain adequate ventilation with unchanged tidal volumes while on PD. He eventually received a tracheostomy.

Discussion: COVID-19 has challenged providers with managing critically ill patients in the setting of limited resources. In our case of ARDS with ARF, we transitioned from HD to acute PD in order to facilitate fluid removal in lieu of CRRT. The ICU team feared increased IAP from PD would worsen lung compliance and hypoxemia from atelectasis. A prospective study by Almeida et al showed that acute PD in mechanically ventilated patients was associated with increased IAP, but lung compliance, oxygenation, and PaO2/ FiO2 increased. Our case noted similar observations without adverse event. Acute PD was able to meet the demands on his daily intake without any compromise to ARDS lung protective ventilator strategies.
excessive immune response and cytokine storms which often seen in COVID-19 can promote to high catechol and rhabdomyolysis and therefore it will contribute to rapid worsening on renal function. Early detection and promptly supportive treatment with RRT may help to improve the vital prognosis of COVID-19.

**Introduction:** Continuous renal replacement therapy (CRRT) is a therapy used in critically ill patients and is of particular importance with COVID-19. We present a patient with COVID-19 on propofol for sedation with persistent filter clotting issues found to have severe hypertriglyceridaemia (SHT) corrected with lipopheresis. This case highlights the importance of managing all aspects of CRRT, the highly inflammatory state of COVID-19 and supply chain management during high utilization periods.

**Case Description:** A 41-year-old male with severe obesity and TBD presented to the hospital with shortness of breath and fevers found to have COVID-19. The patient was intubated on presentation due to hypoxemic respiratory failure and admitted to the ICU. The patient was placed on Propofol for sedation. The patient presented with normal kidney function but peri-intubation had a rapid rise in creatinine to 4.00 mg/dL and was started on CRRT. It was noted that the CRRT circuit was continuously clotting within 30 minutes of initiation. The patient was also noted to have rising CPK levels and a concern for Propofol Infusion Syndrome (PRIS) was raised. A triglyceride level was checked and found to be 3286 mg/dL. The patient was initiated on insulin and heparin drips however due to CRRT issues and inadequate clearance a decision was made to perform lipopheresis to rapidly correct SHT. Patient underwent lipopheresis and the triglycerides dropped to 426 mg/dL. The heparin drip was continued and filter life greatly improved. The patient was continued on CRRT and adequate clearance was achieved.

**Discussion:** This case highlights important points for CRRT, COVID-19 and supply chain management. This patient was found to have PRIS however COVID-19 infection, possibly associated with a milder form of respiratory disease and high risk APOL1 genotype, emphasizing the need for ongoing vigilance and further investigation into this phenomenon.

**PO0824**

Severe Hypertriglyceridaemia Leading to CRRT Malfunction in a COVID-19 Patient

Rashid Parikh, Richard L. Barnett. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

**Introduction:** Continuous renal replacement therapy (CRRT) is a therapy used in critically ill patients and is of particular importance with COVID-19. We present a patient with COVID-19 on propofol for sedation with persistent filter clotting issues found to have severe hypertriglyceridaemia (SHT) corrected with lipopheresis. This case highlights the importance of managing all aspects of CRRT, the highly inflammatory state of COVID-19 and supply chain management during high utilization periods.

**Case Description:** A 41-year-old male with severe obesity and TBD presented to the hospital with shortness of breath and fevers found to have COVID-19. The patient was intubated on presentation due to hypoxemic respiratory failure and admitted to the ICU. The patient was placed on Propofol for sedation. The patient presented with normal kidney function but peri-intubation had a rapid rise in creatinine to 4.00 mg/dL and was started on CRRT. It was noted that the CRRT circuit was continuously clotting within 30 minutes of initiation. The patient was also noted to have rising CPK levels and a concern for Propofol Infusion Syndrome (PRIS) was raised. A triglyceride level was checked and found to be 3286 mg/dL. The patient was initiated on insulin and heparin drips however due to CRRT issues and inadequate clearance a decision was made to perform lipopheresis to rapidly correct SHT. Patient underwent lipopheresis and the triglycerides dropped to 426 mg/dL. The heparin drip was continued and filter life greatly improved. The patient was continued on CRRT and adequate clearance was achieved.

**Discussion:** This case highlights important points for CRRT, COVID-19 and supply chain management. This patient was found to have PRIS however COVID-19 infection, possibly associated with a milder form of respiratory disease and high risk APOL1 genotype, emphasizing the need for ongoing vigilance and further investigation into this phenomenon.
and prednisone induction and is on maintenance prednisone. All 3 patients recovered in SLE; ESRD secondary to lupus nephritis. She had been treated with cyclophosphamide typical features of COVID 19 including hypoxia, fever; extensive bilateral interstitial underlying vasculitides who were admitted with respiratory distress due to COVID 19. Excessive and uncontrolled immune response is thought to be one of the important severe manifestations of the disease often associated with high morbidity and mortality. Called SARS-CoV-2. End Stage Renal Disease patients are at high risk for developing outcomes of COVID 19 in patients who had received cyclophosphamide previously. This case illustrates the complexity of dialysis vascular access and some of the potential complications that are associated with it. It also highlights the importance of timely action to rescue any failed access. As outlined by the statement of ASDIN and VASA, dialysis vascular access should always be treated as a priority, and procedures to salvage it ought to be considered essential. This should also be the case in any future unforeseen restrictions to surgical procedures, such as pandemics or natural disasters.

### PO0827


Kevin S. Hsu, Rasha Alawih, Khaled Boubes. The Ohio State University, Columbus, OH.

**Introduction:** Well-functioning dialysis access is of utmost importance as the lifeline of those with end stage kidney disease (ESKD). With the evolution of COVID-19 pandemic, elective procedures were placed on hold. The American Society of Diagnostic and Interventional Nephrology (ASDIN) and Vascular Access Society of the Americas (VASA) issued a joint position statement on March 24, 2020, designating dialysis vascular access procedures to be “essential.” We present a case with a series of complications that could have been prevented had the patient undergone a timely thrombectomy procedure.

**Case Description:** A 62 year old woman with ESKD undergoing hemodialysis through an upper arm arteriovenous fistula (AVF) presented with a thrombosed AVF in early March 2020 (before the ASDIN statement was issued). She was evaluated by the surgical team; however, due to restrictions to surgical procedures at the time, she did not undergo a thrombectomy and had a right internal jugular tunneled dialysis catheter (TDC) inserted instead. This was complicated by a superior vena cava thrombosis a few weeks later. The TDC was then removed and she had a right femoral TDC placed. She was started on anticoagulation. Her right femoral TDC was complicated by tunnel infection, necessitating its removal and subsequent placement of a left femoral TDC.

**Discussion:** This case illustrates the complexity of dialysis vascular access and some of the potential complications that are associated with it. It also highlights the importance of timely action to rescue any failed access. As outlined by the statement of ASDIN and VASA, dialysis vascular access should always be treated as a priority, and procedures to salvage it ought to be considered essential. This should also be the case in any future unforeseen restrictions to surgical procedures, such as pandemics or natural disasters.

### PO0829

**Renal Biopsy Findings in Patients with COVID-19 Infection**

Tuvet Hong T. Tran, Ming Wu, NYU Langone Health, New York, NY.

**Introduction:** COVID-19 infection is caused by severe acute respiratory syndrome-2 (SARS-CoV-2). SARS-CoV-2, using its Spike protein, interacts with angiotensin converting enzyme-II (ACE2) protein expressed in human kidneys. Upon internalization, host cells may go through pyroptosis, a process characterized by membranous pore formation, cytokine storm and cell death. We report light microscopy (LM), immunofluorescence microscopy (IF), and electron microscopy (EM) findings in renal biopsies of patients with COVID-19 to further understand the pathological process.

**Case Description:** 10 patients were biopsied, age range 25-63 years. 7 were confirmed by the real-time chain reaction (PCR) via nasopharyngeal swab. 3 patients were suspected, but PCR-negative. Common comorbidities include hypertension, hyperlipidemia, and obesity. Patients had AKI with elevated creatinine, range 1.2 to 13.48 mg/dL. Kidney ultrasound showed enlargement and increased echogenicity. Biopsies were performed 9-71 days from symptom onset of such as fever, cough, and diarrhea. Tissue was fixed in formalin and processed for LM. Fresh frozen tissue was utilized for IF. Tissue was fixed in parafomaldehyde and processed for EM. All had acute tubular injury and viral particles on EM (Figure). Patients received supportive care. None required ventilation, but 4 required hemodialysis. Survival rate is 100% (8-12 weeks).

**Discussion:** Renal biopsies were evaluated in 7 confirmed and 3 suspected COVID-19 patients. Although PCR is the gold standard, it is known to have a 15% false negative rate. This may be due to low viral loads and antibody testing may be warranted in suspected PCR-negative patients. Coronavirus particles are reported to measure 50-200 nm, and SARS-CoV-2 50-140 nm. Viral particles were seen in all 10 patients. The particles are contained in vesicles or sacs, and can be found in podocytes, endothelial, and tubular epithelial cells. This may contribute to intrinsic injury resulting in AKI seen in patients.

### PO0830

AKI in the Setting of COVID-19: Histopathologic and Ultrastructural Findings in Postmortem Kidney Biopsy

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**Background:** COVID-19 has been associated with a very high risk of AKI. The pathophysiology of the AKI is unclear with conflicting reports regarding the presence of direct infection of the kidney with SARS-CoV2.

**Methods:** Postmortem kidney biopsy was performed in adult patients with confirmed COVID-19 and stage 2-5 AKI. Biopsies were examined using light and electron microscopy. Immunohistochecistry and RNA in situ hybridization were performed for SARS-CoV2.

**Results:** 12 patients (83% male) with mean age of 70±13 years underwent biopsy. Mean baseline and peak creatinine were 1.0 and 5.3 mg/dL, respectively. Renal replacement therapy was required in 8 (67%) patients (Table 1). All 12 patients had a pathologic diagnosis of acute tubular injury with focal acute tubular necrosis (Table 2). There was no glomerulitis, vasculitis, or thrombotic microangiopathy. There were no characteristic viral particles on electron microscopy and there was no evidence of SARS-CoV-2 on immunohistochecistry in the renal biopsy specimens.

**Conclusions:** AKI in patients with COVID-19 infection was associated with acute tubular injury and focal epithelial necrosis in all patients. There was no evidence of direct viral infection. It appears unlikely that SARS-CoV-2 causes renal injury by direct infection.
Kidney Injury Molecule 1 Is a Receptor for SARS-CoV-2

**Background:** Acute kidney injury (AKI) is a common feature of Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2. Kidney Injury Molecule-1 (KIM-1) has been reported to be a receptor for Hepatitis A virus. KIM-1 is a scavenger receptor in kidney epithelial cells, and it has been hypothesized that KIM-1 is a receptor for SARS-CoV-2 and may play an important role in COVID-19-associated AKI.

**Methods:** Liposomal nanoparticles displaying the SARS-CoV-2 spike protein trimmer (S1 and S2) on their surface (virosomes) were generated. We evaluated spike protein and virome uptake by human KIM-1 expressing kidney epithelial cells and human kidney tubuloids, 3D structures of kidney epithelial cells. KIM-1-mediated uptake was compared to uptake by ACE2, a well-known receptor for SARS-CoV-2. Our recently developed specific KIM-1 spike inhibitor, JB-1 was used to further block virome uptake by KIM-1 expressing cells. KIM-1 expression was augmented in the tubuloids by infection with adenovirus vector carrying human KIM-1 cDNA to examine if the virome uptake was enhanced. Protein-protein interaction characteristics between purified SARS-CoV-2 spike protein and S1 binding domain and purified KIM-1 were determined using microscale thermophoresis.

**Results:** KIM-1 expression on kidney epithelial cells markedly enhanced virome uptake, despite no change in ACE2 expression. This KIM-1 specific uptake was inhibited by JB-1. Human kidney tubuloids also endocytosed virosomes, and tubuloids with enhanced KIM-1 expression secondary to infection of KIM-1/adeno virus had increased uptake of virosomes. Using microscale thermophoresis the Kd for interaction between KIM-1 and SARS-CoV-2 spike protein and the receptor binding domain were 56.2+/-28.8 nM and 0.95+/-3.10 nM respectively.

**Conclusions:** KIM-1 is a receptor for SARS-CoV-2. KIM-1 specific uptake of the SARS-CoV-2 virosome suggests that KIM-1 confers efficient SARS-CoV-2 binding in kidney epithelial cells where these cells are expressing KIM-1. The KIM-1 dependent virome uptake by 3D tubuloids indicates this can be a valuable human cell model for studying SARS-CoV-2 interactions and testing for inhibitors. KIM-1 inhibitors, such as JB-1, can be potential therapeutics for SARS-CoV-2 for COVID-19. Kidney tubular intraluminal and systemic circulating levels of KIM-1 ectodomain may be protective by acting as decoy receptor for the virus.

**Funding:** NIDDK Support

**Poster**

**Table 2. Summary of histopathologic findings**

**PO0831**

**Serum Induces Major Transcriptional and Epigenetic Changes at COVID-19-Associated Gene Loci in Primary Renal Epithelial Cells**

Kevin Lidberg, Selvaraj Muthusamy, Mohamed Adil, Jonathan Reichel, Jonathan Himmelfarb, Edward J. Kelly, Shreeram Akileshe. University of Washington, Seattle, WA.

**Background:** Tubular epithelial cells express high levels of COVID-19 entry receptors ACE2 and the accessory protease TMPRSS2. High systemic levels of IL-6 and IL-8 may contribute to the “cytokine storm” associated with poor outcome with COVID-19 infection. We sought to understand the regulation of these key genes in a 3D microphysiological system (MPS) containing primary human tubular epithelial cells cultured with human, a surrogate for a disease-state ultratranslate.

**Methods:** Primary human tubular epithelial cells cultured in the 3D MPS were exposed to 0.5 and 2% serum for 48 hours and their transcriptional responses were evaluated by RNA-seq. Observed changes in transcription of secreted proteins were validated by ELISA on MPS effluents. We also orthogonally validated our MPS findings against gene expression and chromatin accessibility (ATAc-seq) data generated from human renal cortex and primary tubular epithelial cells cultured in 2D in the presence of 10% serum.

**Results:** Serum exposure of tubular MPS elicited 535 up and 285 downregulated genes with upregulation of pro-inflammatory and chemotactic cytokines IL6 and IL8 consistently seen across multiple donors. This was associated with increased IL6 and HAVCR1 (KIM-1) protein secretion in MPS effluents. Tubular epithelial cells cultured in 2D with 10% serum expressed higher levels of HAVCR1 (up 4.5x), LCN2 (NAGL, up 6x), IL6 (up 11.2x) and CICL8 (IL8, up 7.6x) compared to renal cortex. In contrast, ACE2 (down 8.6x) and TMPRSS2 (down 4.4x) were significantly downregulated. Analysis of open chromatin regions revealed a stress response signature at these gene loci, indicating active regulation in response to injury.

**Conclusions:** Proteinuria is common in COVID-19 infected patients and we studied serum-exposure, as a model of glomerular dysfunction and subsequent proximal tubule responses in our kidney MPS. Serum induces the expression and secretion of IL6 and IL8, suggesting a localized, pro-inflammatory tubule response. Our epigenetic analysis revealed that COVID-19 associated genes have a stress response signature with implications for inter-individual variability in expression. Our kidney MPS model and data represent a powerful system for studying the complex effects that COVID-19 infection exerts on the kidney.

**Funding:** Other NIH Support - NCATS

**PO0832**

**Kidney Injury Molecule 1 is a Receptor for SARS-CoV-2**

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**Background:** Kidney injury molecule-1 (KIM-1), a type-I transmembrane glycoprotein, has been well studied as an specific injury marker for proximal tubules (PT). KIM-1 functions as a receptor for apoptotic fragments through a phagocytic process. KIM-1 (also called TIM-1) serves as a receptor for hepatitis A virus and Ebola virus, and possibly for severe respiratory syndrome-coronavirus (SARS-CoV-1). During the pandemic spread of coronavirus disease 2019 (COVID-19), many patients have suffered from acute kidney injury (AKI) as well as lung damage, Viral uptake has been attributed to interactions with ACE2, a receptor for the virus. The goal of this study was to understand whether there is kidney histological data that KIM-1 may also serve as a receptor for SARS-CoV-2 to infect the PT.

**Methods:** Two patients (one adult and one child) who died of COVID19 and 10 patients with AKI but no COVID19 (control group) were included in the study. All kidney tissue sections were stained for KIM-1 (monoclonal AKGT antibody) and scored from 0 to 3+. Electron microscopy was conducted using kidney tissue of the COVID19+ patients.

**Results:** Both COVID19+ patients had normal pre-mortem levels of serum creatinine (sCr) (adult 0.63 and child 0.17 mg/dl), whereas the control cases all had elevated sCr (1.9-10.7 mg/dl). Control renal biopsies revealed positive KIM-1 staining ranging from 1+ to 3+ along the surface of PT in a patchy pattern involving 20 to 80% of the cortex; no cytoplasmic granular materials were identified. By contrast, the KIM-1 staining in COVID19+ kidneys revealed spotty granular staining in the cytoplasm and diffuse staining in the PT. The staining intensity of 3+ in the COVID19+ kidneys compared to uptake by ACE2, a well-known receptor for SARS-CoV-2. Our recently published kidney tubuloids, 3D structures of kidney epithelial cells. KIM-1-mediated uptake was compared to uptake by ACE2, a well-known receptor for SARS-CoV-2. Our recently developed specific KIM-1 spike inhibitor, JB-1 was used to further block virome uptake by KIM-1 expressing cells. KIM-1 expression was augmented in the tubuloids by infection with adenovirus vector carrying human KIM-1 cDNA to examine if the virome uptake was enhanced. Protein-protein interaction characteristics between purified SARS-CoV-2 spike protein and S1 binding domain and purified KIM-1 were determined using microscale thermophoresis.

**Results:** KIM-1 expression on kidney epithelial cells markedly enhanced virome uptake, despite no change in ACE2 expression. This KIM-1 specific uptake was inhibited by JB-1. Human kidney tubuloids also endocytosed virosomes, and tubuloids with enhanced KIM-1 expression secondary to infection of KIM-1/adeno virus had increased uptake of virosomes. Using microscale thermophoresis the Kd for interaction between KIM-1 and SARS-CoV-2 spike protein and the receptor binding domain were 56.2+/-28.8 nM and 0.95+/-3.10 nM respectively.

**Conclusions:** KIM-1 is a receptor for SARS-CoV-2. KIM-1 specific uptake of the SARS-CoV-2 virosome suggests that KIM-1 confers efficient SARS-CoV-2 binding in kidney epithelial cells where these cells are expressing KIM-1. The KIM-1 dependent virome uptake by 3D tubuloids indicates this can be a valuable human cell model for studying SARS-CoV-2 interactions and testing for inhibitors. KIM-1 inhibitors, such as JB-1, can be potential therapeutics for SARS-CoV-2 for COVID-19. Kidney tubular intraluminal and systemic circulating levels of KIM-1 ectodomain may be protective by acting as decoy receptor for the virus.

**Funding:** NIDDK Support

**Poster**

**Table 2. Summary of histopathologic findings**

**PO0834**

**Kidney and Lung ACE2 Expression After an ACE Inhibitor or an Angiotensin II Receptor Blocker: Implications for COVID-19**

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**Background:** There have been concerns that ACE inhibitors and Ang II receptor blockers may cause an increase in full length (FL) membrane bound ACE2, the main receptor for SARS-CoV-2, that could enhance the risk and worsen the clinical course of COVID-19. Information on the impact of ACE deficiency and AT1 blockade on ACE2 expression at target sites is required to understand this issue.

**Methods:** Kidneys from two genetic models of ACE ablation and mice treated with captopril or telmisartan were used to examine ACE2 in isolated kidney and lung membranes.

**Results:** In global ACE KO mice, ACE2 protein abundance in kidney membranes was increased by 82% of wild type. In ACE2/ACE KO mice that over-express cardiac ACE protein but has no kidney ACE expression, ACE2 protein in kidney membranes was reduced to 42 % of wild type, p < 0.05. In ACE 8/8 mice that over-express cardiac ACE protein, ACE2 expression was reduced to 27 % of wild type, p < 0.05. ACE2 protein levels in ACE8/8 mice treated with captopril or telmisartan were reduced by 85% and 90%, respectively.

**Conclusions:** Our initial evidence suggests there is an atypical staining pattern of ACE2 in the PT of COVID19+ patients, raising a possibility that KIM-1 may also serve as a receptor for SARS-CoV-2 in the PT.
also decreased (38% of the WT, p<0.01). In kidney membranes from mice that received captopril or telmisartan for 2 weeks there was a reduction in ACE2 protein to the level of 37%, p<0.01 and 76%, p<0.05 of that of vehicle control mice, respectively. In lung membranes the expression of ACE2 was very low and not detected by western blotting but no significant differences in terms of ACE2 activity could be detected in mice treated with captopril (118% of control) or telmisartan (93% of control).

**Conclusions:** Genetic kidney ACE deficiency, suppressed ACE enzyme activity by Captopril or blockade of the AT1 receptor with telmisartan are all associated with a decrease in ACE2 expression in kidney membranes. These findings altogether suggest that ACE2 protein abundance at two potential target sites for SARS-CoV-2 infection is decreased or unaffected by RAS blockers. Since these medications do not increase ACE2 expression in lung or kidney epithelia, we conclude that they likely would not pose a risk for increased susceptibility to COVID-19.

**Funding:** NIDDK Support

**PO0835**

Noninvasive Mapping of the Cellular Response to COVID-19 via Urine Single-Cell RNA Sequencing (scRNAseq)

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**Background:** COVID-19 is associated with a high incidence of AKI. Mapping the transcriptional profiles of kidney and urinary tract derived single cell populations can establish a framework to assess renal molecular response to COVID-19 and emerging treatment strategies.

**Methods:** Patients throughout the COVID-19 disease course were recruited to the study. A modification of the protocol (Anzul et al. Nat Immunol) allowed for immediate isolation of urinary cell pellets followed by 10X Genomics Chromium based scRNAseq. **Results:** Urine scRNAseq data sets were generated from 13 COVID patients: age 50/17; 7 males; 7 African Americans; urine sampling 11 days post SARS-CoV-2 diagnosis (IQR 5-29) with 8 in AKI at time of sampling. 25,954 single cell profiles passed QC with a median of 433 cells per sample [IQR 271 to 718].

**Conclusions:** Genetic kidney ACE deficiency, suppressed ACE enzyme activity by captopril (118% of control) or telmisartan (93% of control).

**Funding:** NIDDK Support

**PO0836**

Stimulus and Cell-Specific Responses to Volume Depletion, Ischemia, and COVID-19

Katherine Xu, Tian Shen, Jacob Stauber, Krzysztof Kiryluk, Vivette D. D’Agati, Jonathan M. Barasch, Columbia University Irving Medical Center, New York, NY.

**Background:** A stimulus-response map of the injured kidney might reflect a common transcriptional profile of kidney and urinary track derived single cell populations can establish a framework to assess renal molecular response to COVID-19 and emerging treatment strategies.

**Methods:** Patients throughout the COVID-19 disease course were recruited to the study. A modification of the protocol (Anzul et al. Nat Immunol) allowed for immediate isolation of urinary cell pellets followed by 10X Genomics Chromium based scRNAseq. **Results:** Urine scRNAseq data sets were generated from 13 COVID patients: age 50/17; 7 males; 7 African Americans; urine sampling 11 days post SARS-CoV-2 diagnosis (IQR 5-29) with 8 in AKI at time of sampling. 25,954 single cell profiles passed QC with a median of 433 cells per sample [IQR 271 to 718].

**Conclusions:** Genetic kidney ACE deficiency, suppressed ACE enzyme activity by captopril (118% of control) or telmisartan (93% of control).

**Funding:** NIDDK Support

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
AKI necessitating renal replacement therapy. On kidney biopsy, all patients had varying degrees of ATN, with one patient having associated widespread myoglobin casts. In addition, two patients had findings of thrombotic microangiopathy (TMA), one patient had pauci-immune crescentic glomerulonephritis and another patient had global as well as segmental glomerulosclerosis with features of healed collapsing glomerulopathy. Interestingly, all autopsies had negative immunohistochemistry staining for SARS-CoV-2 on their kidney biopsy material.

**Conclusions:** This biopsy series reveals ATN as the most common kidney biopsy finding with AKI in COVID-19 infection with no evidence of significant viral presence in the kidney tissue.

PO0839
Kidney Pathology Findings in Patients Dying with COVID-19
Meghan E. Kaplan, Jose E. Najul, Michael H. Hines, Brian P. Strollo, Jonathan L. Babin, Paiste Paueskson, Mark Lusco, Agnes B. Fogo, Juan Carlos Q. Velez, Vanderbilt University Medical Center, Nashville, TN; Ochsner Health System, New Orleans, LA.

**Background:** The global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leading to coronavirus disease 2019 (COVID-19) has predominantly resulted in a profound hypoxic respiratory disease with a significant subset of patients manifesting nephrotic range proteinuria or syndrome. Acute kidney injury (AKI) in these patients is an independent risk factor for mortality; however, the mechanism for injury is unknown and our understanding of the pathologic findings is limited.

**Methods:** Kidney tissue from nine patients who died with COVID-19 was obtained at autopsy and evaluated by light, immunofluorescence, and electron microscopy. RNAscope technology was used to perform RNA in situ hybridization (RNA ISH) with probes to the SARS-CoV-2 virus (sense) and for human gene ACE2.

**Results:** The cohort was comprised of 6 men and 3 women, 78% black, median age of 65 years (37 - 78) and median body mass index 29 (26 – 48) kg/m 2. The global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leading to coronavirus disease 2019 (COVID-19) in New York City.

**Conclusions:** This was a retrospective case series of autopsy cases with confirmed SARSCoV-2 infection performed at the Mount Sinai Hospital in patients who died between 3/21/2020 to 4/23/2020. Patients who had a kidney transplant, were on dialysis, if severe autolysis was present, or had no clinical data were excluded. To identify SARS-CoV-2, sections were examined by Transmission Electron Microscopy (TEM) and stained by In Situ Hybridization (RNAscope) in kidney sections.

**Results:** 32 patients had autopsies done, of which 17 patients fulfilled our inclusion criteria. The median age was 64 (interquartile range (IQR) 50, 79), 70% were male, 18% were black, 42% had diabetes and 59% had hypertension. Of the 17 patients, clinical evidence of AKI was present in 12 (71%) patients; 4/12 (33%) had Stage 1 AKI, 6/12 (50%) had Stage 2 AKI, and 2/12 (17%) had stage 3 AKI. Median peak creatinine was 0.86 mg/dL, IQR 0.92-1.23 in those without AKI and 2.98 mg/dL. IQR 2.11 – 5.99 in those with AKI. 3 patients had urine studies performed, only one of them had AKI and had hematuria, proteinuria, and leukocyturia. On histopathology, 9/17(53%) had acute tubular injury (ATI) only (Fig 1A & B) and 1/17 (5%) had TMA and ATI (Fig 1C). ATI was present in 4/5 (80%) of patients without AKI. There was no TMA found in patients without AKI. Glomerular pathology included nodular sclerosis in diabetic nephropathy (Fig 1D) and glomerulosclerosis secondary to ischemic hypertension. Virus was found in 4 samples (Fig 1E & F).

**Conclusions:** There is direct involvement of kidney by SARS-CoV-2 supported by identification of viral particles by TEM, and by ISH RNAscope. The most common histopathologic finding in patients that died with COVID-19 was ATI, which was also present in patients who did not have AKI by serum creatinine criteria.

PO0840
Renal Histopathological Post-Mortem Findings of 17 Patients with COVID-19 in New York City
Nitzy N. Munoz Casablanca, Mohamed Rizwan Haroon Al Rasheed, Judy Hindi, Lili Chan, Steven G. Coca, Fadi Salem, John C. He. Icahn School of Medicine at Mount Sinai, New York, NY.

**Background:** While acute kidney injury (AKI) is a common and serious complication of patients with COVID-19, the mechanisms are unclear. Histopathologic reports of kidney tissue in COVID-19 are limited.

**Methods:** This was a retrospective case series of autopsy cases with confirmed SARS-CoV-2 infection performed at the Mount Sinai Hospital in patients who died between 3/21/2020 to 4/23/2020. Patients who had a kidney transplant, were on dialysis, if severe autolysis was present, or had no clinical data were excluded. To identify SARS-CoV-2, sections were examined by Transmission Electron Microscopy (TEM) and stained by In Situ Hybridization (RNAscope) in kidney sections.

**Results:** 32 patients had autopsies done, of which 17 patients fulfilled our inclusion criteria. The median age was 64 (interquartile range (IQR) 50, 79), 70% were male, 18% were black, 42% had diabetes and 59% had hypertension. Of the 17 patients, clinical evidence of AKI was present in 12 (71%) patients; 4/12 (33%) had Stage 1 AKI, 6/12 (50%) had Stage 2 AKI, and 2/12 (17%) had stage 3 AKI. Median peak creatinine was 0.86 mg/dL, IQR 0.92-1.23 in those without AKI and 2.98 mg/dL. IQR 2.11 – 5.99 in those with AKI. 3 patients had urine studies performed, only one of them had AKI and had hematuria, proteinuria, and leukocyturia. On histopathology, 9/17(53%) had acute tubular injury (ATI) only (Fig 1A & B) and 1/17 (5%) had TMA and ATI (Fig 1C). ATI was present in 4/5 (80%) of patients without AKI. There was no TMA found in patients without AKI. Glomerular pathology included nodular sclerosis in diabetic nephropathy (Fig 1D) and glomerulosclerosis secondary to ischemic hypertension. Virus was found in 4 samples (Fig 1E & F).

**Conclusions:** There is direct involvement of kidney by SARS-CoV-2 supported by identification of viral particles by TEM, and by ISH RNAscope. The most common histopathologic finding in patients that died with COVID-19 was ATI, which was also present in patients who did not have AKI by serum creatinine criteria.

PO0841
COVID-19-Associated Nephropathy (COVAN): An Emerging Entity of Severe Viral Podocyte Injury and Collapsing Glomerulopathy in Kidney Biopsies
Surva V. Seshan, Steven Salvatore, Billie S. Fye-Kirschner, Ronald Miick, Aqeel A. Siddiqui, Mohamed Kahlifa, Ramya Ramakrishnan, Richard E. Freundlich, Anthony D. Nicastri, Weill Cornell Medicine, New York, NY; Rutgers The State University of New Jersey, New Brunswick, NJ; Albert Einstein Healthcare Network, Philadelphia, PA; SUNY Downstate Health Sciences University, Brooklyn, NY; New York-Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY; Newark Beth Israel Medical Center, Newark, NJ; Lankenau Medical Center, Wynnewood, PA.

**Background:** COVID19 caused by novel Coronavirus SARS-CoV-2 initially presenting primarily as a respiratory illness, is now known to affect several organ systems as part of multorgan failure including acute kidney injury (AKI), some cases also manifesting nephrotic range proteinuria or syndrome.

**Methods:** 10 renal biopsies from 6 institutions (1 transplant) performed in April-May 2020 were processed for light microscopy, immunostaining (IS) and electron microscopy (EM) for clinic-pathologic analysis.

**Results:** The 10 patients ranged from 25-73 years (Mean 43), male:female 5:5, 8 African American, 1 Hispanic, 1 Asian Indian, having pre-existing co-morbidities of hypertension (7), Diabetes mellitus (5), obesity (9), presenting with AKI (10), nephrotic syndrome (9), proteinuria ranging from 1.5-25g/24hrs, lung symptoms or pneumonia (7), fever (5). SARS-CoV-2 RT-PCR positive (7), IgG antibody positive (2), both negative (1). All kidney biopsies showed widespread acute tubular injury with focal necrosis, 9 with typical features of segmental/global collapsing glomerulopathy in 10-53% of glomeruli, global glomerulosclerosis (0-35%), focal tubular microcystic changes (8), patchy (1) diffuse (2) active tubulointerstitial inflammation and scarring (10-40%), fibrous capillary inflammation, moderate to severe mesangial expansion (10-50%)

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diabetic kidney disease in 2. No immune deposits were localized by IS. By EM, varied glomerular changes were found and collapse with segmental or global loss of capillary basement membrane (7), total foot process effacement (7), with hyperplastic and vacuolated epithelial cells having protein droplets are noted. The endothelial cells are variably swollen, with tubulo-arteriolar inclusions in 2. Viral particles are identified within cells of glomeruli and tubulointerstitium, scattered or in clusters in the cytoplasm and endoplasmic reticulum vesicles, confirmed by IS.

Conclusions: The constellation of typical glomerular collapsing features with tubulo-interstitial findings and localization of virus by EM, suggests a distinct viral associated nephropathy, reminiscent of MV associated nephropathy. A role for viral cytopathic effect, cytokines and underlying APOL1 gene variants could be considered.

PO0842
COVID-19 Renal Pathology Protocols and Pathology Practice in Latin America: Analysis from GlomCon Latin America Working Group (LGlonCon)
Blanca Martinez-Chapolla,1 Denise Arellano-Mendez,2 Diana Aguirre,4 Desiree Garcia Antón,7 Julio A. Gutiérrez-Prieto,3 Sonia Rodriguez Ramirez,7 Javier Soto-Vargas,4 Franco H. Cabeza Rivera,4 Carmen Avila-Casado.3 GlomCon Latin America Working Group 1Pathology Department, University Health Network, Toronto, ON, Canada; 2Hospital General de Morelia Miguel Morelia, Mexico; 3Unidad Medica de Atencion Ambulatoria 254, IMSS, Morelia, Mexico; 4Hospital General de Mexico, Mexico City, Mexico; 5Hospital General de la Ciudad de Mexico, Mexico City, Mexico; 6Hospital General de Chihuahua, Chihuahua, Mexico; 7Multi-Organ Transplant Program, University Health Network, Toronto, ON, Canada; 8Hospital General Regional 46 IMSS, Guadalajara, Mexico; 9University of Mississippi Medical Center, Jackson, MS.

Background: A significant fraction of patients with COVID-19 display renal involvement (60%); however, the histological findings and pathology practice in Latin America (LA) have not been reported. The aim is to know how COVID-19 pandemic has affected the protocols for renal pathology and the main pathology findings in the kidney.

Methods: An online survey with 7 sections in 6 directions, directed to pathologists, nephrologists and other specialists from 16 Spanish speaking LA countries treating COVID patients with kidney involvement. We are analyzing the impact of COVID-19 in renal pathology and pathology practice in LA.

Results: From 430 responses, 360 (84%) were considered for analysis. Only 13 participants from 16 countries were renal pathologists but the rest of responders also collaborated with the pathology section involved. Only 10% were conducting renal biopsies in COVID-19 patients. Acute kidney injury (AKI) (85%) was the most frequent indication for RBx, hematuria-proteinuria (42%), nephrotic syndrome (28%) and subnephrotic proteinuria (21%). Combination of AKI and other syndrome was seen. Handling fresh tissue for immunofluorescence (IF) is a regular practice in the centers that perform IF (66%). No ultrastructural examination in 90% due to the lack of EM equipment. Postmortem studies only in 3% of the centers. Autopsy and biopsies shrewed thrombotic microangiopathy (TMA), with acute tubular injury (ATI). Pathology redeployment to clinical areas, ICU and inpatient care is seen in 12%. Only 70% of those received guidance or updating clinical courses.

Conclusions: The survey has highlighted the deep shortage of renal pathologists and the lack of equipment (EM) compromising the best practice of renal pathology in LA. Provision of training for tissue handling for COVID have not been established in any center, adding a burden to the practice. Most frequent indication for renal biopsy is AKI while the presence of TMA and ATI is found in autopsy and renal samples. Collapsing glomerulopathy (CG) has a high prevalence in hispanics and has been described in COVID patients, however CG is not seen. Outbreaks had forced pathology redeployment to clinical care without proper preparation.

PO0843
Oxidative Stress, the Final Common Pathway in Lung-Kidney Pathophysiologic Cross-Talk in an Experimental Model of COVID-19:
Clinical Implications
Firoozeh Farahmand,1 Saint Louis University, Saint Louis, MO.

Background: AKI occurs frequently in patients with COVID-19 disease early in the course, in temporal association with respiratory failure and is associated with a poor prognosis. AKI is primarily seen in Covid-19 patients with respiratory failure, with 90% of patients on mechanical ventilation developing AKI compared to 22% of non-ventilated patients. To develop experimental models investigating pathophysiologic mechanisms of Lung-kidney interactions is an essential part of understanding the mechanisms of organs cross talk, i.e., the complex biological communication and feedback between distant organs mediated via cellular and molecular pathways.

Methods: In a novel experimental model similar to human COVID-19, ARDS followed by AKI developed by single injection of a Toxoid.(TOX). Two days post injection lungs and kidney were analyzed for antioxidant enzyme activities including superoxide dismutase, glutathione peroxidase, catalase and oxidative stress. Lungs wet/ dry weight ratios were measured to evaluate edema. After sacrificing the animals, kidney and the lung were removed for histology.

Results: At 2 days post-TOX injection there was acute lung injury with cytotoxic influx, lung edema, neutrophil infiltration, hypoxemia and pulmonary artery thrombosis. In the kidney there was acute tubular necrosis with inflammatory infiltration. Oxidative stress was increased in the lung and the kidney. Antioxidant enzymes activities of SOD and CAT in the kidney were decreased in the kidney.

Conclusions: In this experimental model mimicking COVID-19 organ failure, AKI and ARDS in rats correlates with a decrease in antioxidant and increase in oxidative stress in the lung & the kidney. This suggest the role of antioxidant as the potential adjunct therapeutic agents in COVID-19 related organ failure.

PO0845
Renal Pathology of 34 Consecutive COVID Autopsies: A Single-Institution Experience
Steven Salvatore, Alain C. Bortzuk, Surya V. Seshan. Weill Cornell Medicine, New York, NY.

Background: Patients infected with the novel coronavirus 2019 (COVID19) have a wide spectrum of symptoms ranging from asymptomatic carriers to multisystem organ failure and death. While 20-40% of critically ill patients develop acute kidney injury (AKI) during the course of the disease, only few are biopsied. The most severely affected patients, frequently with multiple co-morbidities, provide insight into renal disease at autopsy.

Methods: 30 of 34 autopsies performed on COVID patients had kidneys available for routine evaluation. Clinicopathologic features are presented.

Results: The 34 patients range in age from 30-100 years (mean 68.5), 24 males and 10 females, 13 Caucasian, 10 Hispanic, 5 African American, 3 Indian, 3 Asian. All cases were positive by RT PCR renal swab for SARS-CoV-2 except 3 (presumably false negative). All had on average 3.4 comorbidities (range: 0-7, hypertension (HTN), diabetes (DM), obesity, COPD, asthma, stroke, dementia, cancer), frequently HTN (20%) and obesity (25%). 18 required intubation. 18 patients had AKI (53%), 2 previously ESRD, and 5 required renal replacement therapy. Presenting Cr ranged from 0.7-9.6 mg/dl (mean 1.7). Renal pathology included diabetic nephropathy (14, 47%), with tubulointerstitial scarring ranging from <25% (60%), 25-50% (23%), >50% (17%), and >75% (4%) chronic vascular sclerosis. Other findings: obesity related renal disease (2), chronic interstitial fibrosis (1), bilateral infarction (ACE/ARB) and (2), and thrombotic microangiopathy (2). No collapsing glomerulopathy was seen. Tubular autolysis prevents complete assessment of ATN. Platelet thrombi were seen by CD61 staining in 43% of cases to involve ~20% of glomeruli and tubulopapillary capillaries. C5b-9 staining was strong, 2-3+ arteriolar in 67% and glomeruli in 20%, suggesting localized complement activation. By electron microscopy, viral particles were identified within cells of glomeruli and tubulo-interstitium.

Conclusions: Pathology in autopsy kidneys from 30 patients with COVID display glomerular disease (43%) with co-morbidities in 25% with AKI or ESRD (59%). Despite varied tissue autolysis and the absence of significant proteinuria, the majority of AKI is assumed to be acute tubular injury due to ischemia and other causes. The viral particles in the renal glomerular and tubular cells may play a role in renal cytopathic injury.

PO0846
RAAS Inhibition, Mortality, and Severity in COVID-19 Patients: A Systematic Review and Meta-Analysis
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Background: The effect of angiotensin-receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) on outcome and severity in COVID-19 patients has been postulated.

Methods: We performed a systematic review in different databases to identify studies and research work that assessed the association of ACEi/ARBs on the severity of illness and mortality in COVID-19 subjects. Inclusion criteria for our meta-analysis were all studies that included human subjects with COVID-19 infection, were randomized or had a control group, were completed, and mortality data were available. The data collected were mortality and severity (inpatient and outpatient). We used the random-effects model for the meta-analysis and the funnel plot analysis to assess potential publication bias.

Results: Out of 4,702 records reviewed in different databases, 11 papers were included in our meta-analysis. Altogether, 8,643 patients were included in the final analysis. Random-effects model (REM) for (1), bilateral infarction (ACE/ARB) and (2), and thrombotic microangiopathy (2). No collapsing glomerulopathy was seen. Tubular autolysis prevents complete assessment of ATN. Platelet thrombi were seen by CD61 staining in 43% of cases to involve ~20% of glomeruli and tubulopapillary capillaries. C5b-9 staining was strong, 2-3+ arteriolar in 67% and glomeruli in 20%, suggesting localized complement activation. By electron microscopy, viral particles were identified within cells of glomeruli and tubulo-interstitium. We used the random-effects model for the meta-analysis and the funnel plot analysis to assess potential publication bias.

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PO0846
The Use of ACE Inhibitors and ARBs in Patients Admitted for COVID-19

Background: Angiotensin converting enzyme (ACE) 2 receptor has been implicated as an entry point for severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) causing pandemic coronavirus disease 2019 (COVID-19). Experts have postulated the potential benefits of using ACE/ARB to reduce the severity of acute lung injury and as the treatment of hypertension in COVID-19. However, there is limited data in showing the renal outcomes after the use of angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) in COVID-19 patients.

Methods: This is a retrospective, single center study of 300 patients diagnosed with COVID-19 confirmed by real-time reverse transcription polymerase chain reaction. Four groups were divided based on ACE/ARB exposure. Group 1 (n=51 patients; 17%) were on ACEIs/ARBs at home and discontinued, group 3 (n=76 patients; 25%) were on ACEIs/ARBs at home and continued during hospitalization and group 4 (n=116 patients; 38%) were never treated with ACEIs/ARBs. The primary end points including the incidence of AKI using KDIGO definition, hyperkalemia, the necessity of dialysis and the secondary end points being the length of total hospital stays, the recovery rate, mortality rate were compared between group 1,2,3 with 4 using adjusted odd ratios (ORs).

Results: In group 1, the use of ACEi/ARB has 4 times higher risk of developing AKI than the control group 4 (P=0.001, 95% CI of 1.8-11.5), and is 4.6 times for stage 2 or above AKI (P=0.001; 95% CI of 1.8-11.5). OR for hyperkalemia is 5.7 (P=0.001, 95% CI of 2.09-15.5) and for hemodialysis is 3.7 (P=0.02, 95% CI of 1.2-11.2). Their mortality rate is increased 2.9 times (P=0.026, 95% CI of 1.2-7.44). In group 2, the incidence of AKI is 7.5 times higher (P=0.001, 95% CI of 3.3-17) and 3.5 times (P=0.001, 95% CI of 1.6-7.7) for stage 2 above AKI. OR for the initiation of hemodialysis and the mortality rate are not statistically significant after adjusted with variables. In group 3, no statistically significant data were found.

Conclusions: Our findings suggest that the initiation of ACEi/ARB in COVID 19 patients have increased risk of AKI, hyperkalemia, necessity of dialysis and mortality rate.

PO0847
Prospective Feasibility Study with the Use of Losartan in COVID-19
Jeanwoo Yoo, Olena Bolotova, Imran Chaudhri, Nisha Nataraj, Hasena Sahib, Farrukh M. Koraishy, Sahar Ahmad, Michelle E. Bloom, Sandeep K. Mallipattu. Stony Brook University Hospital, Stony Brook, NY.

Background: The risks of administering Angiotensin II Receptor Blockers for hypertension in hospitalized patients infected with SARS-COV-2 remains debated. To date, there are no prospective studies evaluating outcomes with the use of ARBs in patients with hypertension and COVID-19.

Methods: We conducted a single-center prospective feasibility study to ascertain the safety and efficacy of losartan in patients with COVID-19 and HTN. Inclusion criteria are patients with age ≥18yr, PCR confirmed SARS-CoV-2, BP>130/80, and required O2 > 92%. These patients were started and titrated on losartan 25mg daily to maintain SpO2 > 92%. These patients were started and titrated on losartan 25mg daily to reach BP goal of <130/80. The vital signs, FiO2 requirements, LFTs, inflammatory markers, serum creatinine and K+ were monitored until discharge, with weekly evaluation of symptoms post-discharge.

Results: 250 patients were screened from April 22 to May 18, 2020, and 16 patients enrolled. Average time to enrollment was 5.5 days, with varying degrees of acuity. 6 patients were removed from the study (see Table 1). Eight patients completed the minimum 7 days of losartan while in the hospital 6/8 patients demonstrated no deterioration of SatO2/FiO2 ratio, SatO2/FiO2 compared on day 1 (201±1 108.1) and day 7 (252.3 ± 148.4), and 2/8 patients improved to room air on day 7. Among all patients, inflammatory markers were not significantly changed from admission to peak values (Table 1).

Conclusions: This study has demonstrated that patients admitted with COVID 19 and hypertension who completed 7 days of Losartan showed no significant deterioration in oxygenation/worsening of inflammatory markers, thereby providing the rationale for a RCT with the use of losartan versus nonRAAS blockade in COVID-19.

Table 1. Clinical characteristics of patients (N16)

<table>
<thead>
<tr>
<th>Patient Outcomes</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (45.6%)</td>
</tr>
<tr>
<td>Days of Hypothesis while on losartan</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>Transaminases</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>CR/RD Admission</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Remains in hospital</td>
<td>3 (18.7%)</td>
</tr>
<tr>
<td>Discharged</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>Average Length of stay (days)</td>
<td>14 (7.7 ± 7.8)</td>
</tr>
<tr>
<td>Removed from Study</td>
<td>1 (6.3%)</td>
</tr>
</tbody>
</table>

Reason for Removal

- Hypothermia: 3 (50.0%)
- Elevated Creatinine: 2 (16.7%)
- Respiratory Failure Requiring Intubation: 1 (6.3%

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO0848
Renin-Angiotensin-Aldosterone System Blocking Drugs in Patients with SARS-CoV-2: Systematic Review and Meta-Analysis
Chang Chu,1,2 Shufei Zeng,1,3 Ahmed A. Hasan,2,3 Carl-Friedrich Hocher,1 Bernhard K. Krämer,1 Berthold Hocher,1 Charité – Universitätsmedizin Berlin, Berlin, Germany; 2Department of Nutritional Toxicology, Institute of Nutritional Science, University of Potsdam, Potsdam, Germany; 3Fifth Department of Medicine (Nephrology/Endocrinology/Rheumatology), University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany.

Background: COVID-19 patients requiring treatment with blockers of the renin-angiotensin-aldosterone system (RAAS) are at highest risk of developing pneumonia and dying. ACE2 is the functional receptor for SARS-CoV-2. Animal studies suggest that RAAS blockers might increase the expression of ACE2 and hence potentially increase the risk of SARS-CoV-2 infection.

Methods: We conducted a systematic review and meta-analysis of published studies on the association of RAAS blockers with lung disease related outcomes.

Results: The effect of ACE inhibitor treatment on the incidence of pneumonia in non-COVID-19 patients was analyzed in 25 studies (330,780 patients). ACE inhibitor use was associated with a 27% reduction of pneumonia risk (OR: 0.73, p<0.001). Pneumonia related death cases in ACE inhibitor treated non-COVID-19 patients were reduced by 27% (OR: 0.73, p=0.004). ARB treatment was analyzed in 10 studies (275,621 non-COVID-19 patients). The risk of pneumonia was not different between patients who did or did not use ARBs. Poolled result from 13 studies (27,704 COVID-19 patients) showed that COVID-19 related severe adverse clinical outcomes were not different between patients who did or did not use RAAS blocking agents (OR: 0.87, p=0.28). All-cause mortality risk in COVID-19 patients was reduced by 27% (p=0.04).

Conclusions: Given the weak evidence coming from animal studies and the clear beneficial data of ACE inhibition in non-COVID-19 patients and the limited but promising data in COVID-19 patients, the use of RAAS blocking agents in patients with SARS-CoV-2 infection is justified. Further clinical studies analysing ARBs and ACE inhibitors separately in COVID-19 patients are needed.
PO0849
Association of Prehospital RAAS Inhibitor Use with AKI and Death in a Cohort of Hospitalized COVID-19-Infected Patients
Ryan Mocerino, Emad Alahiri, Matthew K. Abramowitz, Ladan Golestaneh. Montefiore Medical Center, Bronx, NY.

Background: The relationship of RAAS inhibitors (RAASi) and their purported role in increasing COVID-19 viral attachment and worse outcomes is controversial. In this study we examined the association of RAASi use with Acute Kidney Injury (AKI) and in-hospital death.

Methods: We assembled a cohort of all patients admitted to the main Montefiore hospitals and diagnosed with COVID-19. RAASi use was defined by a prescription within 365 days prior to hospitalization. The association of RAASi use with COVID associated AKI incidence and mortality was evaluated using logistic regression models. Propensity score matching was then used to derive the odds ratio (OR) of AKI and death in those using RAASi compared with controls.

Results: Of 3345 hospitalized patients, 9.3% were prescribed a RAASi prior to hospitalization. Those prescribed RAASi were older (71.9 vs 65.6 years, p=0.001), more commonly Black or Hispanic (RAASi users 41.3% Black and 41.0% Hispanic vs non-RAASi 35.4% Black and 36.9% Hispanic) and had higher Charlson co-morbidity scores (median 4 (IQR 3-7) for RAASi users vs 2(1-3) for non-RAASi users). In unadjusted analysis, RAASi use was associated with a higher OR for AKI (OR 1.32(95% CI 1.04-1.68)) and a higher OR for death (OR 1.53 (95% CI 1.18-1.98). Multivariate adjustment for age, demographics, and clinical co morbidity attenuated associations of AKI and death towards the null (AKI: OR 1.00 (95% CI 0.76-1.31); Death: OR 0.92 (95% CI 0.66-1.24)). Similarly, in propensity score analysis there was no association between RAASi use and either AKI (OR 0.96 (95% CI 0.88-1.04) or death (OR 0.96 (95% CI 0.89-1.05).

Conclusions: RAASi use prior to hospitalization was not associated with AKI or in-hospital mortality in a cohort of patients hospitalized with COVID-19.

PO0850
Outcomes Associated with the Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers in Hospitalized Patients with SARS-CoV-2 Infection
Imran Chaudhri,1 Farrukh M. Kornis,1y Olena Bolotova,1 Jeanwoo Yoo,1 Sandeep K. Mallipatii,1* Stony Brook University Hospital, Stony Brook, NY; 2Northport VA Medical Center, Northport, NY.

Background: SARS-CoV-2 uses the angiotensin converting enzyme (ACE) receptor for cell entry leading to COVID-19. The use of ACE Inhibitors (ACEIs) and Angiotensin II Receptor Blockers (ARBs) in hypertensive COVID-19 patients remains unclear. Since hypertension is a major comorbidity in COVID19, evaluating the efficacy versus adverse outcomes with the use of ACEI or ARB in patients with COVID-19 is essential.

Methods: In this retrospective single-center study, we analyzed electronic medical record data on 300 patients admitted with COVID-19 disease. Data collection included comorbidities, medications, vital signs, and laboratory values (on admission and during hospitalization). Outcomes included inflammatory burden (calculated using composite scores for multiple markers of inflammation), AKI, admission to the intensive care unit (ICU), need for mechanical ventilation, and mortality. For multivariate analyses, generalized linear model (continuous outcomes) and logistic regression (dichotomous outcomes) were used.

Results: Of the 300 patients, 80 patients (26.7%) had history of ACEI or ARB use prior to admission, with 61.3% (49/80) of these patients continuing the medications during hospitalization. Outpatient users of ACEI or ARB had a higher burden of comorbid disease and increased rates of admission and in-hospital AKI in the descriptive analysis, but on multivariate analysis (after adjusting for multiple covariates). Continuation of ACEI or ARB in an inpatient was associated with lower peak C-reactive protein (CRP) levels, peak inflammation score, ICU admission and mortality in the univariate analysis. On multivariate analysis, continuation of these agents during hospitalization predicted lower ICU admissions (OR=0.25, 0.08-0.81, p=0.02), peak CRP (4.9 ± 3.1 ng/dl, p=0.03) and peak inflammatory score (-2.3 ± 1.1, p=0.04) as compared to their discontinuation.

Conclusions: In hospitalized patients with COVID-19, the use of ACEI or ARBs as an outpatient was not associated with adverse outcomes despite greater comorbid illness in users. The continued use of these medications during hospitalization was also not associated with adverse events, rather it predicted fewer ICU admissions and decreased inflammatory burden.

Funding: NIDDK Support, Veterans Affairs Support

PO0851
Glomerular Diseases and Immunosuppression Practices in Latin America During the COVID-19 Pandemic: Analysis from GlomCon Latin America Working Group (LGlomCon)
Julio A. Gutierrez-Prieto,1 Franco H. Cabeza Rivera,2 Sonia Rodriguez Ramirez,2 Javier Soto-Vargas,2 Denise Arellano-Mendez,3 Desiree Garcia Antanas-Diego Aguirre,4 Blanca Martinez-Chagolla,4 Carmen Avila-Casado,6 GlomCon Latin America Working Group 1Hospital Central del Estado de Chihuahua, Chihuahua, Mexico; 2Hospital General Regional 46, IMSS, Guadalajara, Mexico; 3Unidad Medica de Atencion Ambulatoria 254, IMSS, Morelia, Mexico; 4Hospital General de Morelia “Dr. Miguel Silva”, Morelia, Mexico; 5Hospital General de Mexicali, Mexicali, Mexico; 6University of Medicine and Biomedical Sciences, Jacksonville, MS; 7Medel-Organ Transplant Program, University Health Network, Toronto, ON, Canada; 8Pathology Department, University Health Network, Toronto, ON, Canada.

Background: As COVID-19 spreads across the world, nephrologists are facing difficult decisions regarding the management of active glomerular diseases (GD). We aimed to report how COVID-19 pandemic may have changed the use of immunotherapies among nephrologists In Latin America (LA) for the treatment of glomerulopathies.

Methods: Descriptive analysis extracted from an online survey carried out among nephrologists, renal pathologists and other health workers treating kidney diseases between May 20-27, 2020 from sixteen Spanish speaking LA countries divided into 6 categories. We present the results for the GD and immunosuppression category.

Results: 430 responses were obtained of which 360 (84%) were considered for analysis. The participants were mainly nephrologists 276 (66%), renal pathologists 13 (4%) and physicians in training 213 (59%) of the respondents treat patients with GD. For patients at risk but without COVID-19 infection, the induction immunosuppression for GD treatment was not changed by 54.1% of the respondents while 24% gave only a fraction of it and 21.7% deferred the induction treatment. For maintenance immunosuppression, the same regimen was maintained by 74.2% of the respondents, 24.3% decreased it and 1.5% suspended it completely. In case of relapse or flare, 53.6% used standard increase of immunosuppression, 39.7% increased it but at lower levels than usual and 6.7% continued the maintenance regimen. For patients already on immunosuppression diagnosed with COVID-19 infection, 42% would decrease immunosuppressive regimens for mild disease, 62.3% in case of moderate disease and 78.8% would consider completely discontinuing immunosuppression in case of severe disease.

Conclusions: Over 40% of the respondents in LA are already prescribing lower than recommended doses of immunosuppression for induction, relapses or flares as a preventive strategy in the context of COVID-19 pandemic. How this change in practice would affect the renal outcomes remains to be seen. The experiences in the treatment of GD in patients with concurrent COVID-19 infection remains limited.
PO0852
Ramipril Decreases Lung and Kidney Angiotensin Converting Enzyme 2 (ACE2) in Diabetic Mice: Lessons for COVID-19 Infection
Ander Vergara,1,2 Conxita Jacobs Cachá,3 Pamela Domínguez Báez,4 Mineia Mofina Van den Bosch,5 Anna Giralt-López,2 Clara García-Carro,1,2 Daniel Serón,1,2 Maria Jose Soler,1,2 Nephrology Research Group Hospital Vall d’Hebron, Barcelona, Spain;2 Vall d’Hebron Institut de Recerca, Barcelona, Spain.

Background: ACE2 is a component of the renin-angiotensin system (RAS) that mainly degrades angiotensin II to angiotensin(1-7). It is expressed in renal tubular cells. Lung type 2 alveolar cells also express ACE2 where it acts as a receptor for SARS-CoV-2, which is responsible for the current coronavirus disease 2019 (COVID-19) pandemic. A controversy raised regarding the use of RAS blockers in COVID-19 patients despite its demonstrated efficacy in cardiovascular disease. We studied the effect of ramipril on ACE2 expression in experimental diabetes.

Methods: 12 weeks old diabetic db/db mice were given ramipril (8 mg/Kg/day) or vehicle during 8 weeks. db/m mice were used as controls. ACE2 expression and enzymatic activity were studied in kidney, heart and lung.

Results: In non-treated db/db, ACE2 mRNA expression was increased in kidney (p=0.0001) and ramipril treatment reversed this effect. In heart, ACE2 expression decreased in db/db compared to db/m (p=0.028) and ramipril had no effect. We found no differences in lung. ACE2 enzymatic activity was increased 23% in kidney and 22% in lung of db/db mice when compared to db/m. Ramipril treatment decreased ACE2 activity 25% in the lung and 13% in the kidney when compared to untreated db/db. In the heart, ACE2 activity tended to decrease in db/db mice when compared to db/m, and increased with ramipril, but did not exceed the cardiac ACE2 activity of the db/m.

Conclusions: ACE2 is increased in the kidney and in the lung, and decreased in the heart of diabetic mice. Ramipril treatment restores ACE2. Our results suggest that diabetes and hypertension may per se be risk factors for COVID-19 and not the treatment with ACE inhibitors, which may exert a protective effect on COVID-19 infection.

Funding: Government Support - Non-U.S.

PO0853
Caring for Patients with Kidney Disease in the COVID-19 Era: The Kaiser Permanente Northern California Experience
Siute Zhong,1 Ali Poyan-Mehr,2 Leonid Pravoverov,3 Sharina Belani,4 ‘The Permanente Medical Groups, Oakland, CA;5 Kaiser Permanente, Oakland, CA.

Background: The COVID-19 pandemic has presented health care system in the United States with unprecedented challenges. Kaiser Permanente Northern California is an integrated health care system with 4.5 million members, who are cared for by The Permanente Medical Group (TPMG), a multiple specialty medical group of 10,000 physicians. Utilizing coordinated care, sophisticated Electric Medical Record system, KPNC Nephrology service line has developed several strategies to mitigate the effect of COVID-19, including rapidly increased video visit appointments for members with CKD.

Methods: After the “Shelter in place” order in March 2020, KP nephrologists started weekly virtual townhall meetings to coordinate care among 85 nephrologists in 19 hospitals covering patients with chronic kidney disease, receiving dialysis, and post kidney transplant. TPMG nephrologists have developed guidelines on: 1. Tied testing for Person Under Investigation (PUI) members; 2. Management of patients with Glomerulonephritis; 3. Post-kidney transplant care; 4. Expand advance care planning; 5. Converting direct patient visits to video visits; 6. Coordinating care with contracted dialysis providers for members on outpatient dialysis.

Results: The video visits have increased 780% from March to April and 1968% from March to May of 2020 (Figure). The top three diagnosis for video visits were: CKD3, CKD4, and post kidney transplant. Since April 1st, 2020, average 0.038% of dialysis patients were tested positive for COVID-19 and average 0.0001% are PUI.

Conclusions: As an integrated health care system, KPNC has developed a systematic, collaborative and rapid crisis management of patients with CKD in COVID era. Further studies are needed to evaluate the long-term outcomes of these approaches.

PO0854
Benefits of Telephonic Case Management: Increased Home Dialysis and Decreased Hospitalizations
Rahul Dhawan, Wade M. Bannister, Cindy Gong, Jiang Tao, Kevin Plosser. KRS Team Optum Inc, Eden Prairie, MN.

Background: Home dialysis has been noted to improve quality of life in patients receiving dialysis. Patients at risk for COVID-19 include those on dialysis. The pandemic has resulted in additional focus on social distancing and home dialysis offers this distinct advantage compared to in-center hemodialysis. The ASN also similarly has supported advancing education around home dialysis, and COVID is being noted as a true catalyst to home dialysis care. Our study on a commercial population analyzed cost of care with regards to home versus in-center dialysis.

Methods: The KRS Case Management program identified and educated commercial patients with this case management benefit regarding the options for home versus in-center hemodialysis. Patients were enrolled in the program and educated on the benefits of home dialysis, the benefits of permanent access, and the benefits of transplantation. Cost of care analysis was conducted using claims paid until February 2020, and variables studied included in-patient cost, skilled nursing facility cost, professional cost for dialysis service, facility cost for dialysis service, non-dialysis outpatient cost and professional cost for physician visits. Patients were educated telephonically of the benefits of home dialysis and permanent access placement, and demographics including age and gender were also calculated.

Results: A total of 6692 members were analyzed. Of these patients 1793 members were attributed to home based dialysis. It was noted that when adjusting for per diem member per month, there was a 62% decrease in cost of care for in-patient hospitalizations in the home dialysis group. In addition, there was a striking reduction of 247% in skilled nursing facility costs for the home dialysis group as well. After adjusting for all variables, there was a 5% cost savings in the home dialysis group as compared to in-center.

Conclusions: There are cost of care benefits to home dialysis. Further studies are needed to help identify barriers to home dialysis, and given the advent of COVID-19, it is important to consider home dialysis for all patients more now than ever before.

PO0855
Bridging Office-Based Care with the Virtual Practice Care Model: Evolving Care for CKD Patients in the COVID-19 Pandemic—and Beyond
Jinbing Zhao,1 Lei Zhang,1 Peili Ji,1 Jianfeng Lin,1 Jianfang Han,1 Jiaying Li,1 Zijuan Zhou,1 Haiyun Wang,1 Xia Hong,2 Winfred W. Williams,3 Limeng Chen,4 Department of Nephrology, Peking Union Medical College, Beijing, China; 2Department of Psychological Medicine, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China; 3Department of Nephrology, Massachusetts General Hospital, Boston, MA; 4Department of Nephrology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China.

Background: Since the outbreak of the coronavirus epidemic, the “virtual” telemedicine has become a critical substitute for patient-provider interactions. However, virtual encounters often face challenges in care for high-risk patients such as chronic kidney disease (CKD) patients. In this study, we explore the patient’s satisfaction and practical effects of a newly established telemedicine program in CKD patients’ care during the pandemic.

Methods: We established an online CKD patient care program, including triage strategy, medical care delivery, and psychological support, based on a smartphone application. A total of 278 CKD patients were invited, at least 3 months before the pandemic or during the pandemic. A pilot survey interrogating medical and psychological Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
along with conference attendance, will likely never return to their pre-pandemic levels. And typical in-office activities, such as meeting with pharmaceutical representatives, will be similar to pre-COVID levels. Additionally, as practices try to rebuild from significant lost revenues, staffing structures may remain significantly different moving forward.

**Methods:** Survey data was collected weekly or bi-weekly between March 20th and May 10th to provide rapid responses on the quickly evolving COVID-19 outbreak. Approximately 50 nephrologists participated in each wave, along with 200 neurologists, dermatologists, rheumatologists, and gastroenterologists.

**Results:** The impact of the COVID-19 outbreak on nephrologists was swift and monumental. As of early May, nephrologists remained one of the hardest hit groups and continued to report 85% fewer patients compared to a typical, pre-COVID week. Nephrology was the most affected specialty. By the final week of May, nephrology reported a “substantial” impact on the financial health of their practice by early May. Nephrology was the most affected specialty. The COVID-19 pandemic and resulting social distancing and stay-at-home orders significantly impacted physician practices across the board. The objective of this study was to evaluate the COVID-19 impacts and responses across different specialists as they unfolded and to understand how the model of patient care delivery will change moving forward.

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**Background:** The COVID-19 pandemic has necessitated increased use of telemedicine for outpatient care. Accessing effective telemedicine is important to optimize care delivery during the pandemic.

**Methods:** We examined trends in telemedicine use during the COVID-19 pandemic using data from Geisinger, a large, integrated, predominantly rural health system in central and northeastern Pennsylvania. We also examined the association between patient characteristics (age, sex, patient portal status, Charlson Comorbidity Index [CCI]) and use of telemedicine nephrology visits.

**Results:** As of early May, nephrology was the top adult specialty using telemedicine at Geisinger in terms of proportion of office visits using telemedicine (televised or telephone) with 1911 (94% of all outpatient visits). The proportion of nephrology visits using telemedicine increased rapidly from <1% pre-COVID-19 crisis to 21% (week of 3/15/20) to consistently around 95% each week from 3/22/20 to 5/29/20. Visit completion rate during this time was 84% with 8% same-day cancellations and 8% no-shows/late prior to being seen. The majority of nephrology clinic patients were 65 years old (63%), had severe CCI score 5+ (70%), and had active patient portal status (65%). The proportion of nephrology visits using televised was 42% overall with large differences by CCI score, and patient portal status (Figure). For example, the proportion of nephrology visits using televised was as low as 10% (65+ year old patients, CCI 5+, non-user of patient portal) and as high as 86% (<50 year old patients, CCI score 0-4, active patient portal users).

**Conclusions:** Telemedicine may serve an important role in providing nephrology care to elderly patients with multiple comorbidities who are particularly susceptible to ill effects from COVID-19. Patient portal users were much more likely to use televidoe for telemedicine visits. Further investigation into the digital divide (e.g. broadband internet access) is needed to optimize care delivery during the COVID-19 crisis.

**Resource Utilization and Provision of In-Hospital Dialysis in an Academic Hospital in New Orleans During the COVID-19 Pandemic**

Jason R. Leduc, Kenneth Chauvin, Vernelle T. Mitchell, Juan Carlos Q. Velez.
Ochsner Nephrology Department of Nephrology, Ochsner Health System, New Orleans, LA.

**Background:** COVID-19 has caused an ominous healthcare toll in the United States. New Orleans rates among the top affected cities. Acute kidney injury (AKI) requiring renal replacement therapy (RRT) affected 10% of COVID-19-related hospitalizations, resulting in an exponential upsurge in resource utilization related to RRT. We report our single center experience providing metrics of overall utilization and workforce expansion.

**Methods:** We conducted a prospective collection of data from daily census of hospitalized patients with COVID-19 and AKI or ESKD for 7 weeks (3/8-4/30, 2020) quantifying usage of RRT personnel. Two independent electronic health record databases were simultaneously used to track the data.

**Results:** Within 1 month, in-hospital COVID-19 census peaked at 377 patients, with 97 (26%) of them receiving RRT at peak day. Starting from a mean of 65 patients on RRT per day in pre-COVID-19 era, the estimated RRT growth peaked at 496%. For management, 6 newly purchased Fresenius K2 SLED machines (FKs) were utilized by week 5 after delivery, assembly and negative culture. Starting from an average 80% usage of baseline capacity (31 of 38 FKs), usage of 42 FKs at peak revealed 35% growth. Four new reverse osmosis units were recruited, increasing the number of providers from 9 to 13 (44% growth).

**Conclusions:** The pandemic of COVID-19 resulted in substantial increase in in-hospital RRT demand and resource utilization. Our experience may provide other centers a guide to optimize preparedness in the event of facing a “second wave” of COVID-19 in the near future. Delay in implementation has to be accounted for during strategic planning.

**PO0858**

**Telemedicine for Nephrology Outpatient Care in a Large Integrated Health System During the COVID-19 Pandemic**

Waled Zalar, Prince Mohan, Evan Norfolk, Jamie A. Green, Alex R. Chang. Geisinger Health, Danville, PA.

**Background:** The COVID-19 pandemic has necessitated increased use of telemedicine for outpatient care. Accessing effective telemedicine is important to optimize care delivery during the pandemic.

**Methods:** We examined trends in telemedicine use during the COVID-19 pandemic using data from Geisinger, a large, integrated, predominantly rural health system in central and northeastern Pennsylvania. We also examined the association between patient characteristics (age, sex, patient portal status, Charlson Comorbidity Index [CCI]) and use of telemedicine nephrology visits.

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**Conclusions:** Telemedicine may serve an important role in providing nephrology care to elderly patients with multiple comorbidities who are particularly susceptible to ill effects from COVID-19. Patient portal users were much more likely to use televidoe for telemedicine visits. Further investigation into the digital divide (e.g. broadband internet access) is needed to optimize care delivery during the COVID-19 crisis.
# PO0860

**Urgent Training with the Tablo Hemodialysis System in Response to COVID-19**

Michael A. Aragon, Michelle L. Gilliland, Marc Maynard, *Outset Medical, Inc., San Jose, CA.*

**Background:** During the COVID-19 pandemic, many facilities experienced dialysis resource shortages of specialized dialysis staff, sterile dialysate, dialysis systems, and treatment locations. The Tablo® Hemodialysis System was deployed in numerous hospitals to help meet the increased need for dialysis delivery. Tablo is an all-in-one, easy-to-learn system indicated for clinic, hospital and home settings. Features include integrated water purification, on-demand dialysate production, simplified user interface and two-way wireless connectivity. Tablo’s clinical versatility and simplicity allow for broad prescribing and treatment location options. The objective is to report on Tablo training effectiveness during urgent deployment to facilities amidst the COVID-19 pandemic.

**Methods:** Standard training with Tablo (< 4 hours) was performed during the peak COVID months of March through May at 51 facilities. Information regarding nursing experience and current role was recorded. Nursing staff trained on Tablo in May completed an electronic survey post-training. Based on a Likert scale ranging from Strongly Agree to Strongly Disagree, respondents rated their satisfaction with training, system ease of use, and confidence performing dialysis independently post training.

**Results:** Of 926 clinicians trained, 854 were registered nurses (RNs). 136 RNs completed the survey and were representative of the entire group (49% vs 47% ICU, 35% vs 34% HD, 11% vs 16% Non ICU/Non HD). Responses of Strongly Agree or Agree are presented in Table 1 by experience and current role.

**Conclusions:** Nurses of varied experience and areas of focus trained on Tablo during the pandemic reported: high levels of satisfaction with training, the device was easy to use, and confidence in providing treatment to patients. The Tablo Hemodialysis System can allow training of existing staff to efficiently expand a facility’s renal replacement capabilities.

**Funding:** Commercial Support - Outset Medical, Inc.

**Table 1 - Tablo Training Survey Responses**

<table>
<thead>
<tr>
<th>RN Experience</th>
<th>HD Experience</th>
<th>ICU Experience</th>
<th>Has Training</th>
<th>Easy to Learn and Use</th>
<th>Less Confident Training Tablo Independently</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP</td>
<td>EXP</td>
<td>EXP</td>
<td>Yes</td>
<td>100% (130/130)</td>
<td>95% (127/130)</td>
</tr>
<tr>
<td>EXP</td>
<td>EXP</td>
<td>EXP</td>
<td>Yes</td>
<td>100% (130/130)</td>
<td>95% (127/130)</td>
</tr>
<tr>
<td>EXP</td>
<td>EXP</td>
<td>EXP</td>
<td>Yes</td>
<td>100% (130/130)</td>
<td>95% (127/130)</td>
</tr>
</tbody>
</table>

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Underline represents presenting author.

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# PO0861

**Use of Tablo Hemodialysis Systems to Extend Dialytic Capabilities for the COVID-19-Associated Surge of AKI**

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**Background:** The COVID-19 pandemic was associated with a greater incidence of AKI than expected. At the NY Harbor VA we faced an overwhelming number of AKI patients who were critically ill with multi-organ failure. We needed to invoke new mechanisms of providing kidney replacement therapy (KRT).

**Methods:** We obtained 3 Tablo systems in late March, 2019. The machines have self-contained reverse osmosis capabilities and do not require other equipment to operate. They can make dialysate from concentrate and tap water and so do not require special plumbing adaptation. Their self-contained step-by-step procedures are relatively simple to follow and allow rapid training of previously unskilled personnel. Tablo generates 300 ml dialysate per minute, and blood flow was increased up to 400 ml/min as tolerated.

**Results:** Training was completed by 2 nephrologists and 2 RNs without previous dialysis experience. We used the Tablo Hemodialysis System to provide KRT to critically ill patients. In the first week we demonstrated that water cultures and endotoxin testing were negative, and that AAMI water tests were acceptable. We used the machines to provide KRT for ICU patients with double-lumen dialysis catheters. In addition we used the machines on hospital wards where KRT had not been provided before because of a lack of the plumbing needs of conventional HD machines. We provided multiple treatments 3-6 times per week for 15 AKI patients, mean age 65 years. The mean of the best serum creatinine ratio achieved in the first 1-4 treatments, if available, was 41% (often limited by hypotension and fulfillment of ultrafiltration, UF, needs). Most treatments were successful and were slowed for hypotension or tachycardia. Some were aborted because of water pressure alarms if sediment filters needed replacement, or lines clotted due to hypercoagulability associated with COVID-19. Personnel availability dictated that most treatments were 3-4 hours (and up to 8h), and generally achieved UF goals. Later HD nurses cannulated arteriovenous fistulas in ESKD patients and left treatment to non-HD nurses to complete.

**Conclusions:** By incorporating a user-friendly platform and an accelerated training program including nephrologists and RNs without previous dialysis experience, we were able to nearly double our capacity to deliver KRT during the surge.

**Funding:** Veterans Affairs Support

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# PO0862

**The Introduction of Quanta SC+ to Critical Care for Haemodialysis During the COVID-19 Pandemic**

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**Background:** Of 800 patients treated annually in 19 ICU beds (catchment 500,000) 120 require renal replacement therapy (RRT) delivered by Baxter Prismaflex® (continuous veno-veno haemodiafiltration (CVVHDF)). With the onset of the COVID19 pandemic significant increased incidence of acute kidney injury (AKI) requiring RRT & existing intermittent haemodialysis (IHD) patients contracting COVID19 requiring ICU support raised concerns regarding RRT ICU capacity. Additionally a worrying national shortage of CVVHDF consumables & new machines to deliver this requirement; all critical doctors to seek local solutions for RRT provision beyond usual capacity.

**Methods:** A kidney unit neighbour described their successful experience trialing SC+ in IHD patients. Transitions of SC+ from home use to safe IHD treatment in ICU was quickly apparent alongside ease of supporting technical infrastructure set up & minimal training requirements. Immediate availability & fiscal acceptability of purchasing 4 Quanta SC+ & supporting RO machines were critical determinants in making this a realistic & sustainable solution to desperate RRT shortages. Provision of expert technical support and clinical nurse specialist facilitation expedited training of ICU workforce & enabled swift implementation

**Results:** 27 ICU nurses were trained in 3 weeks (23 in 14 days). Between 22/4/20 & 17/5/20 8 patients (range 37-63 yrs, median 53.5; 7/8 known IHD, 1/8 AKI; 7/8 COVID19 positive) received 20 treatments (1-5/patient) using SC+ in ICU. An agreed ICU IHD protocol was co-designed gaining consensus in an unfamiliar territory of provision of IHD in ICU & differing clinical perspectives in IHD prescription in a critical care setting.

**Conclusions:** As a time of unprecedented national shortage of dialysis machines & increased RRT need associated with COVID19, Quanta provided an effective solution for safe provision of IHD in ICU. Ease of use with training delivered in <6 hours enabled ICU nurses to effectively treat patients independent of dialysis nurses allowing continuity of the chronic HD programme. Learnings identified the importance of training, enabling rapid growth of a critical mass of expertise & confidence. Critical elements included mastering unfamiliar technique, establishing infrastructure, procurement & team communication enabled by online & face-to-face troubleshooting support.

**Funding:** Commercial Support - Quanta Dialysis Technologies
Design of PREVENT: A Phase 2 Study of the Effect of RBT-9 on Progression of COVID-19 Infection in High-Risk Individuals, Including Those with Advanced CKD

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Background: Coronavirus 2019 (COVID-19) has infected millions of people worldwide, with the US reporting the most deaths. Many individuals are at high risk of disease progression, which may result in multi-organ failure and death. Risk factors include advanced age, cardiovascular disease (CVD), and chronic kidney disease (CKD). In addition, more than 40% of hospitalized patients develop acute kidney injury (AKI), with 20% of those requiring dialysis. Several therapeutic agents are in development, but patients with advanced CKD or those requiring immunosuppressive therapy are frequently excluded from participation in clinical trials. RBT-9, a proprietary formulation of stannous protoporphyrin, has organ protective effects, as demonstrated in animal models of kidney, liver, and lung injury. RBT-9 also has antiviral effects, as demonstrated in several enveloped viruses, including influenza, HCV, dengue, and yellow fever. A Phase 2, randomized, placebo-controlled study was designed to evaluate the effect of RBT-9 on progression of COVID-19 infection in high-risk individuals.

Methods: This study will enroll up to 252 subjects with documented SARS-CoV-2 infection who are at risk of progression based on age (≥70 years) or comorbidities, including CKD (all stages, not on dialysis), CVD, chronic lung disease, diabetes mellitus, obesity, and mild hypoxemia. Subjects will be randomized 2:1 to receive a single dose of RBT-9 or placebo and will be followed for 56 days.

Results: Study Objectives The primary objective is to evaluate the effect of RBT-9 versus placebo on clinical status measured using the 8-point World Health Organization (WHO) Ordinal Clinical Scale at Day 28. Secondary objectives include time to first occurrence of death from any cause or new/worsened organ dysfunction, survival, AKI incidence, new or worsening heart failure, hospitalization status and duration, ICU status, days on ventilator, vasopressor utilization or ventilator arrhythmias.

Conclusions: The organ protective and antiviral effects of RBT-9 warrant conduct of this clinical study, which is aimed at preventing progression to severe COVID-19 and organ failure. The primary objective is expected to be enrolled in June 2020.

Funding: Commercial Support - Renibus Therapeutics

The COVID-19 Infodemic

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Background: In Situation Report #13 by the World Health Organization and 39 days before declaring COVID-19 a pandemic, the WHO declared a “COVID-19 infodemic”, a rapid volume of coronavirus tweets was far too great for one to find accurate or reliable information. Healthcare workers were flooded with “noise” which drowned the “signal” of valuable COVID-19 information. To combat the infodemic, physicians created healthcare-specific micro-communities to share scientific information with other providers.

Methods: We analyzed the content of six physician-created communities and categorized each message in one of five domains (Symptoms, Diagnostics, Therapeutics, Prevention, and Pathophysiology). We programmed 1) an application programming interface to download tweets and their metadata in JavaScript Object Notation beginning November 1st and 2) a reading algorithm using visual basic application in Excel to categorize the content. We superimposed the publication date of each tweet into a timeline of pandemic events. Finally, TD created a free repository of the dataset in the #NephTwitter Archives (https://bit.ly/2MHHGQ2) to help healthcare workers find quality information when treating patients.

Results: From 11 March to 27 April, 45% of the 19270 tweets in the dataset were categorized (signal). Tweets about Therapeutics spiked six times; the first coming 4 days after the WHO declared COVID-19 a pandemic. The largest spike came on day 8: 5 days after the US President suggested hydroxychloroquine as a potential treatment. Tweets about antimalarial therapy comprised 15% of tweets in this category. Tweets about Prevention spiked five times; the largest coming 21 days after the pandemic declaration by 1 million global cases were reported. Protective equipment comprised 13% of tweets in this category. There were 2210 searches performed of the signal tweets in the #NephTwitter Archives. Evidence-based tweets comprised 1 in every 8 tweets in the categorized corpus. The tweets covered both antimalarials and vaccines (2:3), the same for protective equipment, and worse for mechanical ventilation (1 in 31).

Conclusions: Algorithmic coding can 1) mitigate the COVID-19 infodemic and 2) identify & elevate illuminating evidence-based tweets. Both outcomes help healthcare workers find higher-quality information to combat the pandemic.

The Impact of the COVID-19 Pandemic on the Mental Health of Health Workers Treating Patients with Kidney Diseases in Latin America (LA): Analysis from GlomCon Latin America Working Group (LGlomCon)

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Background: The rapid spread of the COVID-19 pandemic into LA countries where health systems were already facing major limitations might further challenge their physician’s emotional and mental wellbeing. We aimed to describe the perception of health workers managing kidney diseases in the context of the COVID-19 pandemic.

Methods: Descriptive analysis extracted from an online survey carried out among nephrologists, renal pathologists, and other health workers treating kidney diseases between May 20-27, 2020 from sixteen Spanish speaking Latin American countries divided into 6 categories. We present the results for the mental health category.

Results: 430 responses were obtained of which 360 (84%) were considered for analysis. Participants were mainly nephrologists 276 (86%), renal pathologists 13 (4%), and physicians in training 11 (3%). Ages ranged between 30-49 years old in 271 (75%), mostly working on tertiary centers 258 (71%). 329 (90%) participated in inpatient care. 277 (86%) considered that the COVID-19 pandemic has impacted their mental health.

Conclusions: This study will enroll up to 252 subjects with documented SARS-CoV-2 infection who are at risk of progression based on age (≥70 years) or comorbidities, including CKD (all stages, not on dialysis), CVD, chronic lung disease, diabetes mellitus, obesity, and mild hypoxemia. Subjects will be randomized 2:1 to receive a single dose of RBT-9 or placebo and will be followed for 56 days.

Funding: Commercial Support - Renibus Therapeutics

PO0864

PO0865

PO0866

Developing a COVID-19 Screening Program for an Emergency-Only Dialysis Cohort Within a Large Public Safety-Net Hospital

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Background: As the prevalence of coronavirus disease 2019 (COVID-19) worsens, one patient population that warrants further inquiry are those receiving emergency-only hemodialysis (EoHD). This cohort specifically at Grady Health System (GHS) in Atlanta, consisting largely of undocumented immigrants, receives 1-3 times weekly hemodialysis (HD) via emergency departments due to legislative restrictions on Medicaid funding. GHS has one of the largest populations of EoHD patients in the nation. The cohort of 91 patients is 89% Hispanic with a mean age of 51. The majority of patients, 69%, reside in Fulton or DeKalb counties, the intended service region for GHS. The remaining patients reside in more distant counties, potentially increasing risk of transmission to a larger area. Prior to our screening program, 6 patients in the cohort had positive diagnostic tests and 4 of these patients required hospitalization (67%). Notably, 3 out of those 4 patients were admitted due to hypertensive emergency with pulmonary edema, so symptomatic COVID disease is debatable. Due to the frequency of hospital visits and requirement of in-person treatments if COVID+, a screening of the cohort was conducted. Our aim was to establish a baseline prevalence rate to direct an ongoing screening program in this vulnerable population.

Methods: Over 5 days, we conducted 84 COVID PCR screening tests via nasopharyngeal swab. One patient was excluded due to missed sessions. Patients were asked about symptoms prior to swabs. Swabs were obtained by a single operator in a consistent fashion. Data was collected and stratified by patient demographics.

Results: A total of 84 patients were screened for COVID. Notably, 3 asymptomatic patients had positive results, a rate of 3.6%, and 6 patients had positive diagnostic tests prior to screening, resulting in a rate of 9.9% positive COVID tests. 6 patients were DeKalb/Fulton residents (67%).

Conclusions: The risk of COVID-19 in EoHD patients is an issue that will require a coordinated effort to prevent the spread of disease. A collaboration between nephrology and infectious diseases has led to the implementation of a bimonthly screening program. Future directions include antibody screens and contact-tracing to understand more fully the spread of disease as well as elucidating the asymptomatic positive rate vs. actual disease prevalence.
Background: During the initial phase of the SARS-CoV-2 pandemic our institution had high rates of acute kidney injury (AKI) requiring renal replacement therapy (RRT). Nephrocheck (NC), a renal biomarker, indicating renal stress was the basis of a continuous quality improvement (CQI) program to identify patients at risk for AKI & RRT.

Methods: Patients admitted from 4/17-5/15/2020 were all tested for SARS-CoV-2. All positive patients ≥ 18 years old & with a creatinine ≤2.0 mg were tested with NC. Values ≤ 0.7 led to nephrology consultation & utilization of a renal-protective strategy including monitoring volume status, scrutinizing nephrotoxic medications & urines. A “Plan-Do-Study-Act” approach was used to increase utilization of NC and the resulting protocol for positive results. Intervention was biphasic with a follow up maintenance phase, each lasting 10 days. Phase 1 was adding NC to the SARS-CoV-2 admission order set & Phase 2 was educating hospitalist providers about using and interpreting NC to increase appropriate nephrology consults. Education was reinforced with protocol cards & reminders via encrypted text services. Additionally, intervention team members reviewed charts daily & reminded providers in real time.

Results: In Phase 1, Phase 2 included the SARS-CoV-2 positive patients had a NC but only 48% of NC positive patients had a renal consult. In Phase 2, 79% of SARS-CoV-2 positive patients had a NC with 80% of positive patients getting a renal consult. In the maintenance phase, 67% of SARS-CoV-2 positive patients had NC with 59% of NC positive patients giving a renal consult.

Conclusions: During our CQI project, efforts to mitigate severe AKI by using a biomarker-based alert for nephrology consultation saw the number of SARS-CoV-2 positive patients screened with NC & the number of positive NC patients seen by nephrologists rise significantly. Barriers to implementation included the weekly turn-over of house staff & a reliable alert system to ensure adequate screening. The multidisciplinary team reviewing charts and reminding hospitalists of the protocol also helped significantly but was difficult to sustain.

Background: The COVID-19 surge for the NY area severely stretched hospital resources as critical care areas expanded 2-3 fold. In addition to well chronicled ventilator management of respiratory failure, 37% sustained some degree of AKI with many requiring continuous renal replacement therapy (CRRT). The challenge of providing optimal care to critical care areas (as described in the previous paragraph) was met with a defined project plan which required close integration of physician, nursing, pharmacy and materials management resources over multiple hospital sites.

Methods: The Renal Critical Care Project Management Team (T) initially met on 3/11 and reviewed the unprecedented CRRT demand with a defined project plan which required close integration of physician, nursing, pharmacy and materials management resources over multiple hospital sites.

Results: The T met daily from 3/11 to 5/15. Of 4579 patients, 51.8% were male. Median age was 65 years, IQR (52-76).

Conclusions: During the COVID-19 pandemic, CRRT management was managed by a multidisciplinary team. The ability to shift resources among multiple units using a CQI program to identify patients at risk for AKI & RRT has allowed for future pandemic surges.

Figure 1. Prevalence of Electrolyte Abnormalities in Patients with and without COVID-19
PO0871

Clinical Relevance of AKI Trial Data for Severe COVID-19 Patients
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Background: Coronavirus disease 19 (COVID-19), caused by SARS-CoV-2 was declared a pandemic in March 2020 and remains without any approved treatments. After entering the cells, the virus begins to replicate and viral antigen is presented to antigen presenting cells (APCs), the cells that stimulate the body’s normal anti-viral immune response. In severe cases however, this immune reaction becomes dysregulated as evidence by high levels of certain cytokines and chemokines in the blood, a reaction known as cytokine storm. This results in a systemically uncontrollable inflammatory state that triggers a violent attack by the immune system to the body, causes acute respiratory distress syndrome (ARDS) and multiple organ failure, leading to death.

Methods: Mesenchymal stromal cells (MSCs) are a unique source of secreted factors that modulate an inflammatory response and enhance the repair of injured tissue. MSCs have been extensively studied in ARDS and other acute organ injuries. Sentien has created a novel delivery approach to enable sustained exposure to MSCs and their secreted factors, overcoming limits of cell transplantation/infusion while preserving their broad acting and dynamically responsive properties. Our lead product, SBI-101 contains allogeneic human MSCs inoculated into a hollow-fiber hemofilter, which enables communication with patient blood via the semi-permeable membrane, while maintaining MSC viability. Through this interplay, SBI-101 aims to restore balance to the immune system by reprogramming the molecular and cellular components of blood in patients with severe inflammation and organ injury.

Results: Sentien’s Phase I/II clinical study of SBI-101 in critically ill patients with Dialysis-Requires Acute Kidney Injury (AKI-D) has produced data to support the therapeutic hypothesis of SBI-101. Consistent with MSC biology, inflammatory markers, such TNFa and IFNg, were shown to be modulated, suggestive of a shift from a pro- to an anti-inflammatory state in treated patients.

Conclusions: Data obtained in our AKI-D trial showed modulation of many biological molecules and immune populations that may be correlated with severe COVID-19 immunopathology. Here we make the case, using our existing AKI-D trial data, that SBI-101 may be of therapeutic benefit to severe cases of COVID-19.

PO0872

Point-of-Care Ultrasound Findings in Patients with COVID-19 and AKI

Background: More than one third of patients presenting with COVID-19 in the United States develop acute kidney injury (AKI) and many require dialysis. AKI portends a poor prognosis particularly if dialysis is required. Point-of-care ultrasound (POCUS) is a valuable tool for the evaluation of AKI particularly for assessment of volume status. Here we describe clinical and ultrasonographic characteristics of COVID-19 patients with AKI.

Methods: This cohort includes prospectively enrolled adult patients with confirmed COVID-19 who developed AKI as part of their hospital encounter in April and May of 2020. Ultrasounds were performed using a published 12-point lung and limited assessments included an average of 10 of the 12 specified zones, favoring the anterior flat IVC. 5 had pericardial effusion. 2 had right-ventricular dysfunction. The lung US findings. Most had normal ejection fractions but there was wide variation in IVC distension. More studies are needed to determine if ultrasound can guide fluid management or identify reversible causes of AKI.

Conclusions: Our data describes cardiac and lung US findings in patients who experience AKI during their COVID-19 course. Most patients had multifocal b-line findings. Most had normal ejection fractions but there was wide variation in IVC distension. More studies are needed to determine if ultrasound can guide fluid management or identify reversible causes of AKI.

PO0873

Constitutive Activation of Hedgehog Signaling Disrupts Nephrogenic and Stromal Differentiation
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Background: Nephron progenitors (NP)s and stromal cells differentiate from a common Osr1+ progenitor. While maldifferentiation of nephrogenic and stromal tissue is a signature of renal dysplasia, signaling mechanisms regulating the genesis of stroma relative to NPs are largely undefined. We have shown that increased Hedgehog (Hh) signaling in murine Osr1+ cells in vivo causes urinary tract obstruction through abnormal stromal cell localization (Sheybani-Delouie et al., 2018). Here, we investigated mechanisms that lead downstream of Hh to control NP and stromal cell differentiation using human induced pluripotent stem cell (hiPSC) kidney organoids and genetic mouse models.

Methods: Agonists of the Hh receptor, SMO, were added to hiPSCs differentiated into kidney organoids at the stage of cell aggregation. Mature organoids were analyzed by histology, light sheet fluorescence microscopy, and RNA microarray. Processes downstream of Hh signaling were investigated in mouse kidneys with deficiency of Ptc1 specific to FOXD1+ stromal cells (FoxD1Cre;Ptc1−/−) using histology, RNAseq, and scRNAseq.

Results: Stimulation of Hh activity in kidney organoids with SAG (120 nM) or Purmorphamine (10 μM) resulted in a 26% increase in surface area compared to controls. Volumetric analysis using light sheet fluorescent imaging of WT1+ nephrogenic structures and CDH1+ tubular structures in SAG-treated organoids demonstrated an 88% (n=3, p<0.01) and 67% (n=3, p<0.05) reduction, respectively. In contrast, the mass of non-epithelial cells was increased by 79% (n=2, p<0.05). RNA microarray analysis of SAG-treated organoids (n=5) revealed elevated expression of medullary stromal markers Tr6 (2.60 fold change [FC], p<0.01) and Pdgfrb (1.60 FC, p<0.01), and decreased expression of nephron markers Nphsl (0.23 FC, p<0.01), Slc1a1 (0.32 FC, p<0.01), and Slc2a1 (0.08 FC, p<0.001). Mice with constitutive Hh activity in FOXD1+ stromal cells showed a 41% reduction in nephrons at E18.5 (n=4, p<0.05) and a 19.5% decrease in nephron intermediate structures at E15.5 (n=4, p<0.01). In contrast, RNAseq of E13.5 mutant kidney tissue demonstrated increased expression of medullary stroma genes Trc and Pdgfrb.

Conclusions: Increased Hh signaling in human and mouse increases differentiation of stroma compared to NPs, providing new insights into mechanisms that may underlie kidney dysplasia.

Funding: Government Support - Non-U.S.

PO0874

Caspase Inhibition in a Mouse Model of Prenatal Ureteropelvic Obstruction Rescues Normal Urerter Development
Ross Villiger, Malia H. Harrison-Chau, Michael Ortega, Ben Fogelgren. University of Hawaii at Manoa, Honolulu, HI.

Background: The most common cause of congenital obstructive nephropathy is ureteropelvic junction obstruction (UPJO). We previously described a unique mouse model of in utero UPJOs through urethral knockout of Exocs5, a central subunit of the exocyst trafficking complex. In this neonatal lethal model, UPJO formation is preceded by urethral cell death in the ureter between E16.5 and E17.5. Here, we investigated if normal ureteral development could be restored in this mouse model by blocking cell death pathways, and conversely, if we could induce UPJOs by simply activating urethral cell death during ureter development.

Methods: We utilized the Cre-lox system to achieve either targeted gene knockout or activation during mouse embryonic development. For inhibition of cell death pathways in Exocs5−/−Ksp-Cre uterers, we performed IP injections of caspase inhibitors into pregnant mice at gestational day 16.5. Also, diphtheria toxin A (DTA) mice crossed with Ksp-CreOsr1+ mice were used to investigate the effect of inducing urethral cell death with tamoxifen administration at E16.5.

Results: Morphologically, dying Exocs5-KO urethral cells appeared more necrotic than apoptotic, and they were negative for cleared PARP and active caspase-3. However, a single IP injection of pan-caspase inhibitor z-VAD-FMK at E16.5 rescued ureter development in all Exocs5−/−Ksp-Cre mice analyzed. At E18.5, all z-VAD-FMK treated embryos displayed patent ureters with no hydrourephrosis (n=9 from multiple litters). If followed past birth, z-VAD-FMK treated Exocs5−/−Ksp-Cre mice survived to adulthood. Remarkably, caspase-1 inhibitor Ac-3P-trans-thio-Val-Ala-Asp-FMK was added as a downstream target to ureter development when injected at E16.5, supporting the hypothesis that a non-apoptotic pathway is responsible for urethral cell death in this mouse model. Conversely, DTA-induced urethral cell death in E16.5 uterers showed evidence of UPJO formation by E18.5.

Conclusions: Based on these findings, we have shown that urethral cell death is a critical event leading to UPJO pathogenesis and lethality in our mouse model. The data suggest inflammansome-associated caspase-1 may play a role in activating cell death in urethral cells with disrupted exocyst trafficking.

Funding: NIDDK Support

Key - TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
**PO0875**

Exocyt Inactivation in Urothelial Cells Disrupts Autophagy and Upregulates the Fibroblast Growth Factor-Inducible 14 (Fn14) Receptor

Michael Ortega, Ross Villiger, Malia H. Harrison-Chau, Suzanna K. Lieu, Kadeci-Kalia Tamashiro, Amanda J. Lee, Geetika Y. Patwardhan, Ben Fogelgren. University of Hawai'i at Manoa John A Burns School of Medicine, Honolulu, HI.

**Background:** Despite their prevalence, the etiology of congenital uterter obstructions in infants is poorly understood, with little evidence identifying genetic or environmental causes. We previously reported a unique mouse model of *in utero* ureteropelvic junction obstruction (UPJO) in which uterter cells with deleted Exoc5 gene failed to differentiate into a stratified epithelium and underwent cell death. This resulted in bilateral UPJOs, hydrourephrosis, and neonatal lethality. Here, we investigated the uterter cells prior to cell death to identify the disrupted cell processes necessary for uterteral differentiation and uterteral development.

**Methods:** Gene expression profiling was performed on E16.5 uterter of Exoc5<sup>-/-</sup>; Ksp-Cre mice and control littermates, with validation using real time qPCR and immunohistochemistry. Follow up investigations utilized an *ex vivo* uterter explant organ culture model, where mouse embryonic utereters were isolated at E15.5 and maintained in culture for 72 hours. Additionally, we used primary human urothelial cells (pHUCs) and immortalized SV-HUC1 cells for advanced studies on exocyst regulation of autophagy, which was measured through immunoblotting and immunostaining of p62, LC3I/II, and Fn14 (>30-fold), a member of the TFN receptor subfamily that binds the ligand TWEAK. Fn14 is upregulated in damaged tissues and can activate non-canonical NF-kB signaling and cell death via multiple pathways. Using uterter explants and cell line models, we found exocyt is critical for uterteral autophagy, which when disrupted, led to a high Fn14 increase and cell death.

**Conclusions:** From our data, we propose that autophagy is necessary for uterteral differentiation during uterter development, and irregular autophagy may trigger uterter cell death through Fn14 signaling. This disruption of autophagy during a critical stage in uterter development may contribute to UPJOs in humans.

**Funding:** NIDDK Support

**PO0876**

Transcription Factor 21 Regulates Nephron Progenitor Cells Self- Renewal/Induction and Podocyte Development

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**Background:** Most forms of C A K U T arise from mutations in genes of kidney development, and the mechanisms underlying these mutations are not fully understood. We previously showed that Transcription Factor 21 (Tcf21) regulates branching morphogenesis by downregulating GDNF. We now aim to study Tcf21 in nephron progenitor cells (NPC). During nephrogenesis, WNT9b signals to NPC through the canonical Wnt/beta-catenin pathway, which promotes both self-renewal at a state of low beta-catenin level and differentiation at a state of high beta-catenin. Following induction of beta-catenin level, protein partners to promote MET and persistently elevated beta-catenin is essential for NPC differentiation to podocytes. Hence, discrete levels of beta-catenin promote disparate cell fates. It remains unclear however what drives this change and direct NPC to exit/maintain self-renewal.

**Results:** Using gene expression profiling from E16.5 Exoc5<sup>-/-</sup>;Ksp-Cre utereters revealed that metabolic pathways were significantly downregulated and NF-kB signaling was significantly upregulated, implicating cell stress. The highest upregulated gene was Fn14 (30-fold), a member of the TFN receptor subfamily that binds the ligand TWEAK. Fn14 is upregulated in damaged tissues and can activate non-canonical NF-kB signaling and cell death via multiple pathways. Using uterter explants and cell line models, we found exocyt is critical for uterteral autophagy, which when disrupted, led to a high Fn14 increase and cell death.

**Conclusions:** From our data, we propose that autophagy is necessary for uterteral differentiation during uterter development, and irregular autophagy may trigger uterter cell death through Fn14 signaling. This disruption of autophagy during a critical stage in uterter development may contribute to UPJOs in humans.

**Funding:** NIDDK Support

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**PO0877**

A Novel ADPKD Model Using Kidney Organoids Derived from Disease-Specific Human Induced Pluripotent Stem Cells

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**Background:** Autosomal dominant polycystic kidney disease (ADPKD) is one of the most prevalent hereditary diseases, accounting for up to 10% of end-stage kidney disease worldwide. Although many disease models have been proposed for ADPKD, the pre-symptomatic pathology of the human disease remains unknown and no definitive therapies are currently available. To elucidate the mechanisms of early cystogenesis, robust and genetically relevant human models are needed.

**Methods:** Using a stepwise differentiation protocol that we have recently reported (Tsujimoto H. et al., 2020), we generated kidney organoids from two kinds of disease-specific human induced pluripotent stem cells (hiPSCs), PKD1<sup>-/-</sup> gene-edited hiPSCs and ADPKD patient-derived hiPSCs. We applied chemical treatment to reproduce cystic phenotypes within kidney organoids, quantitatively analyzed macroscopic cystic lesions, and performed immunofluorescence analyses. ADPKD patient-derived kidney organoids were further utilized to examine the effects of known inhibitors of cystogenesis.

**Results:** Although wild-type organoids developed cystic lesions under forskolin, PKD1-mutant organoids exhibited significantly larger cystic areas depending on the PKD1 genotype. Importantly, ADPKD patient-derived kidney organoids as well as gene-edited heterozygous PKD1-mutant ones also recapitulated cystogenesis in *vitro*. Immunofluorescence analyses confirmed that the cyst epithelia predominantly originate from LTL-positive cells. Furthermore, inhibitor experiments suggested the predictive validity of patient-derived kidney organoids as a disease model.

**Conclusions:** We established a novel model for ADPKD using kidney organoids differentiated from gene-edited PKD1-mutant and ADPKD patient-derived hiPSCs. Further, we demonstrated the possibility of ADPKD kidney organoids serving as drug screening platforms. This newly developed model will contribute to identifying novel therapeutic targets, extending the field of ADPKD research.

**Funding:** Government Support - Non-U.S.

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**PO0878**

Kidney Organoids Represent a Novel Platform to Study Adaptive and Innate Immunity

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**Background:** Human kidney organoids have been utilized as a model to study genetic kidney diseases and kidney development. Innate or adaptive immune responses in organoids are currently poorly defined. Kidney transplant rejection and activation of complement pathways are two common renal immune phenomena. SARS-CoV-2 virus, the pathogen of the recent pandemic, leads to complement pathway activation in human kidneys and can infect kidney organoids. Here, we investigated (i) the ability of kidney organoids in a humanized mice model, and (ii) the responses to exogenous complement C5a and spike protein (S1) of SARS-CoV-2 in kidney organoids.

**Results:** Kidney organoids were generated from human embryonic stem cells using protocols developed in our laboratory, and transplanted under the kidney capsule in non-humanized (BLT) mice. Immunophenotype, mixed lymphocyte reaction, and intracellular cytokine staining were analyzed from grafts and mouse spleenocytes collected after 30 days of transplantation. In other experiments organoids were treated with S1 protein to induce human C5a. In kidney organoids, transplanted organoids after direct activation of C5aR by exogenous C5a. We confirmed ACE2 expression on proximal tubules and parietal epithelium of glomeruli, consistent with recent findings. Reflecting innate responses, robust interstitial fibrosis was found in non-transplanted organoids after direct activation of C5aR by exogenous C5a. We confirmed that the cyst epithelia predominantly originate from LTL-positive cells. Furthermore, inhibitor experiments suggested the predictive validity of patient-derived kidney organoids as a disease model.

**Conclusions:** Using patient-derived kidney organoids differentiated from gene-edited PKD1-mutant and ADPKD patient-derived hiPSCs, we demonstrated the possibility of ADPKD kidney organoids serving as drug screening platforms. This newly developed model will contribute to identifying novel therapeutic targets, extending the field of ADPKD research.

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Kidney Organoids Derived from a Pediatric Patient with Type 1 Diabetes and Steroid-Derived Nephrotic Syndrome Shows Losses of Podocyte Podocalyxin and Increased Proximal Tubule Injury

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Background: Whole exome sequencing of a pediatric patient, who at age 3 developed Type 1 diabetes mellitus and steroid-dependent nephrotic syndrome, revealed a de novo heterozygous mutation of the GREM1 gene. Gremlin is a BMP antagonist crucial for kidney development and also implicated later in life in diabetic kidney disease. Specifically, gremlin has been associated with kidney inflammation, Notch activation and fibrosis, and proposed to be a mediator of diabetic nephropathy and other progressive kidney diseases. 3D kidney organoids differentiated from induced pluripotent stem cells (hiPSCs) provide a platform technology to explore the effects of genetic changes on pathobiology of human tissue.

Methods: An induced pluripotent stem cell (iPSC) line was created from the patient. Organoids were generated from iPSCs by modifications of our laboratory’s prior published techniques without use of undefined matrices. Structures of kidney organoids were imaged by immunostaining for LTL, CD11, GATA3, PODXL, NPHS1, NPHS2, and CD31. Organoids were also stained for gremlin, SGLT2, and KIM-1 to investigate phenotypes.

Results: A de novo heterozygous mutation of the GREM1 gene was identified. The GREM1 mutation specifically eliminates one of the three known GREM1 splicing isoforms while leaving the other two intact. When compared to organoids generated from embryonic stem cells or BJFF iPSCs the patient-derived organoids had several kidney disease phenotypes including decreased expression of podocalyxin, aberrant expression of SGLT2, and pronounced expression of KIM-1, an indicator of proximal tubule injury. The phenotypes could be rescued by treatment of the kidney organoids with recombinant GREM1 protein, altering the balance of long and short forms of gremlin.

Conclusions: Organoids derived from a patient with a GREM1 heterozygous mutation demonstrated decreased podocalyxin, aberrant SGLT2 staining, and increased proximal tubule injury. Better understanding of the relative roles for GREM1 isoforms could lead to better understanding of diabetic progressive kidney disease and organoids can be used to find potential therapies.

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PO0880

CD133+ Progenitor Cells in Proximal Tubules Are Most Likely the First Responding Cells to Acute Tubular Injury in Human Kidneys

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Background: Proximal tubules (PT) are mainly used for the reabsorption of electrolytes and fluid. Recent studies reveal CD133+ progenitor cells scattered along the PT, and CD133+ tubules were isolated from healthy WT kidney, whereas clusters differentially expressing Kap and pericytes prevents chemically-induced kidney fibrosis in interstitium. Here, we present our findings from single cell RNAseq analyses of PDGFRβ+ pericytes with or without fibrosis.

Methods: Single-cell RNAseq. 2-3 samples from kidneys isolated from healthy WT kidney, whereas clusters differentially expressing Kap and Cd74 became dominant in WT kidney treated with AA. This shift was abrogated in cells isolated from fibrotic SARA+ kidney. RNA velocity analyses to reveal specific clusters

Results: Single-Cell RNA Sequencing Reveals Subpopulation of PDGFRβ+ Pericytes as Fibroblast Precursor in Interstitial Kidney Fibrosis, and Smad Anchor for Receptor Activation Overexpression Modifies Their Fates

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Background: In last several ASN meetings, we showed that SARA plays a critical role for fibroblast precursor activation, and that overexpressing SARA in PDGFRβ+ pericytes prevents chemically-induced kidney fibrosis in interstitium. Here, we present our findings from single cell RNAseq analyses of PDGFRβ+ pericytes with or without fibrosis.

Methods: PDGFRβ-Cre; Z/EGR; SARA+ or WT mice that express GFP and SARA (in SARA+ line) only in PDGFRβ+ cells were given aristolochic acid (AA, 10 mg/kg, i.p., 3x week for 3 weeks). After 3 more weeks, kidneys were harvested and digested with Liberase/DNase I. GFP+ cells were flow sorted and subjected to scRNAseq.

Results: Unsupervised analyses with Surat identified 30 clusters. Clusters characterized with differential expression of Apoe1 and C14a were dominant in cells isolated from healthy WT kidney, whereas clusters differentially expressing Kap and Cd74 became dominant in WT kidney treated with AA. This shift was abrogated in cells isolated from fibrotic SARA+ kidney. RNA velocity analyses reveal specific clusters that transition to fibroblasts are being analyzed.

Conclusions: These results implicate a sub-population of PDGFRβ+ pericytes as progenitors for fibroblasts in fibrosing kidney and genes identified that are differentially expressed could have therapeutic implication in treating kidney fibrosis.

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PO0883

Successful Introduction of Renovascular Units into the Mammalian Kidney
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Background: Various cell-based therapies, aimed at replenishing renal parenchyma, have been proposed as means to treat chronic kidney disease (CKD). However, a key limitation to the applicability of these strategies is the failure of in-vivo administered cell types to develop donor-derived vessels, resulting in poor graft survival. Similarly, such strategies do not address renal hypoxia, a key factor in CKD progression. We hypothesized that administering self-organizing human renal tubule-forming cells (RTFCs) derived from adult and fetal kidneys, previously shown to exert a functional effect in CKD mice, alongside mesenchymal stromal cells (MSCs) and endothelial colony-forming cells (ECFCs), would result in generation of both vessels and tubules with potential interaction.

Methods: NOD-SCID mice were injected with either RTFCs or a mix of RTFCs, MSCs and ECFCs in Matrigel into the sub-cutis (SC), under the renal capsule or into the renal parenchyma. The resulting grafts were analyzed after 2 weeks.

Results: While RTFC-derived grafts harbored few host-derived vessels, injection of MSC, ECFCs and RTFCs into the SC, sub-renal capsular space, or renal parenchyma, resulted in robust formation of donor-derived renal-vascular units. These consisted of both well-developed renal tubules and epithelial tubes of different nephron segments, and human vascular networks, which connect to host vasculature. The latter demonstrated the presence of both CD31+ endothelium and oSMA+ pericytes, originating from administered ECFCs and MSCs, respectively. Notably, MSC/ECFC-derived vessels augmented in-vivo tubulogenesis by RTFCs while in vitro co-culture experiments showed MSC/ECFCs to induce self-renewal and mesenchymal-epithelial transition-associated genes in RTFCs, disclosing paracrine effects.

Conclusions: Combined cell therapy of vessel-forming cells and RTFCs aimed at enhancing tubulogenesis and potentially alleviating renal hypoxia may serve as the basis for new renal regenerative therapies.

PO0884

Elastin-Microfibril Axis Proteins Form Transient 3D Structures During Murine Nephrogenesis
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Background: Dynamic changes in the composition and structure of the extracellular matrix (ECM) are understood but critical during renal development. Our recent proteomic study indicated proteins in the elastin-microfibril axis protein (EMILIN1), FREM2, and proteoglycans (WGA), imaged using confocal microscopy, and rendered in 3D using Fiji. For comparison, E18.5 cryosections were stained for additional members of the elastin-microfibril axis (COL26A1, FBNI).

Results: At perinatal timepoints, elastin-microfibril axis proteins were organized in the interstitium surrounding developing tubular and glomerular elements, including vertical fibers connecting to the capsule and medullary ray sheath fibers. Patterning was lost in the adult (Fig. 1). Different elastin-microfibril axis proteins displayed similar staining patterns perinatally (Fig. 2).

Conclusions: The 3D corticomедullary junction structures for elastin-microfibril axis proteins at the perinatal timepoint were consistent with the proteomic trends. We hypothesize the structures are important for nephrogenesis through mechanical support and growth factor modulation

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Figure 1 (top): 3D visualization of EMILIN1 showed medullary ray sheath fibers transiently formed at E18.5. EMILIN1 was localized to the corticomedullary junction (green, white arrow) fibers surrounding tubules at E14.5 that grouped into medullary ray sheath fibers (*) at E18.5 but regressed in the adult murine kidney. Insets are visualization of the EMILIN1 channel. scale bar=500 μm

Figure 2 (bottom): Elastin-microfibril axis proteins displayed similar staining patterns at E18.5. Elastin-microfibril axis proteins (green) were co-stained for ECM (red). medullary ray sheath fibers (*), scale bar=500 μm

PO0885

Development of Noninvasive Clinically Applicable In Vivo Tracking of Extracellular Vesicles Using Magnetic Resonance Imaging (MRI)
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Background: Extracellular vesicles (EVs) derived from amniotic fluid stem cells (AFSC) hold great potential for the treatment of chronic kidney diseases (CKD). We have already shown that AFSC-EVs are renoprotective in a mouse model of CKD, Alport syndrome. However, there is an important unmet need for real-time in vivo monitoring of these therapeutic EVs after they are injected into a subject to understand their safety, targeting, and effectiveness. While current optical imaging solutions like bioluminescence and fluorescence are useful for EV tracking studies in animal models, there is limited utility in clinical applications. Here we present a novel in vivo tracking solution for our therapeutic EVs in Alport mice, utilizing clinically applicable MRI technology.

Methods: To generate trackable EVs, AFSC were labeled with a novel magnetic agent (VSCM). EVs secreted by the labeled AFSC were isolated by ultrafiltration. The viability and morphology of labeled-cells were evaluated, and the in vitro MR properties of EVs were analyzed by magnetometer. Purity, potency and identity of labeled EV was compared to non-labeled EVs. In vivo biodistribution of labeled EVs was evaluated in WT and Alport mice by MRI at 10 min and 3 hr post injection, and retro-orbital and intra-cardiac routes of delivery were compared.

Results: The magnetic label did not affect the physiological characteristics of the cells and did not change identity, purity and potency (therapeutic effect in vivo) of EVs. MRI phantom studies showed the in vitro in vivo detectability of labeled-EVs. Importantly, as expected MRI studies showed that EV homing to the kidney injected intra-cardiacally into Alport mice was more efficient vs the retro-orbital route, and Prussian blue staining of sections confirmed EV homing to the kidney.

Conclusions: We have developed a clinically applicable novel magnetic nanoparticle agent that can be used to label and track the biodistribution of EVs in the kidney and other organs using non-invasive, safe, and effective MRI technology that’s widely available. This technology is highly adaptable and can be deployed in both preclinical and clinical settings.

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PO0886

Obesity Blunts the Reparative Function of Human Adipose Tissue-Derived Mesenchymal Stem Cells in Ischemic Murine Kidneys
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Background: Obesity is a health burden that can affect cellular processes. Mesenchymal stromal/stem cells (MSC) ameliorate renal injury in several diseases. Obesity impairs MSC function in vitro, but its effect on in vivo reparative function of human MSC remains unknown.

Methods: MSC were harvested from non-obese (‘lean’) (body mass index [BMI] <30 kg/m²) and obese (BMI≥30) human subjects during kidney donation or bariatric surgery, respectively. To test their function in vivo, MSC (5x10⁵/200 µL) or vehicle were injected into 129S1 mice 2 weeks after renal artery stenosis (RAS) or sham surgery (n=6-8/group). Two weeks later, mice underwent magnetic resonance imaging to assess renal perfusion and oxygenation, and kidneys then harvested.

Results: A similar number of lean and obese human MSC engrafted in stenotic mouse kidneys. Vehicle-treated RAS mice had reduced cortical and medullary perfusion. Lean (but not obese) MSC normalized cortical perfusion (p=0.2 vs sham+vehicle) (Figure A&B), whereas both effectively mitigated renal hypoxia. Serum creatinine and blood pressure were elevated in all RAS mice, and lowered only by lean MSC (p=0.4 vs sham+vehicle). Both alleviated renal fibrosis in RAS, but lean more effectively than obese MSC (p=0.02). Tubular and glomerular injury was improved similarly by both.

Conclusions: Lean MSC are superior to obese MSC in repairing ischemic kidney injury and blood pressure in murine RAS, implying dysfunction of the endogenous MSC repair system in obese patients. This should also be considered during autologous cell-based approaches.

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PO0887

Single-Cell Transcriptional and Chromatin Accessibility Profiling Redefines Cellular Heterogeneity in the Adult Human Proximal Tubules
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Background: Single nucleus RNA sequencing (snRNA-seq) has improved our understanding of cell-specific genes and pathways, however, relatively less is known about how chromatin accessibility contributes to cell identity. We hypothesized that an integrated analysis by snRNA and ATAC sequencing (snATAC-seq) would enhance our ability to detect unique cell types and states in the kidney, uncovering previously unrecognized cellular heterogeneity.

Methods: We performed snRNA-seq and snATAC-seq on 5 healthy adult kidney samples (3M and 2F, mean age = 55.8y, mean snChr = 1.07 mg/dl). Nuclear preparations were processed using 10x Genomics 5’ v2 (snRNA) and Single Cell ATAC (snATAC) Chromium kits, sequenced and counted with Cell Ranger. Seurat was used to integrate snRNA and snATAC datasets with label transfer. Chromatin interactions were predicted with Cicero and pseudotemporal ordering was performed with Monocle.

Results: We analyzed a total of 52,097 nuclei by snRNA-seq (n=19,985) and snATAC-seq (n=32,112), identifying 214,890 accessible chromatin regions that confer kidney cell identity. This multi-modal analysis highlighted a unique subpopulation of proximal tubule (PT) cells characterized by increased chromatin accessibility in VCA1 and a pro-inflammatory gene expression signature. Immunoﬂuorescence studies showed that these cells are present in a scattered distribution in the kidney cortex. Transcription factor motif analysis implicates ZFHX1B signaling in the transition between healthy PT and VCA1-positive subpopulation. We identiﬁed candidate regulatory regions that are predicted to interact with the VCA1 promoter via cis-co-accessibility networks. Inter-species snRNA-seq data integration suggests this subpopulation exists in the post-IRI repair phase and bulk RNA-seq deconvolution implicates a potential role in CKD and kidney aging.

Conclusions: Our multi-omics approach improves the ability to detect unique cell states within the kidney and reveals a previously unrecognized subpopulation of proximal tubule cells with a pro-inﬂammatory signature.

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PO0888

Vegfr3 Is Expressed in Fenestrated Microvascular Beds of the Kidney and Is Required for Glomerular Development
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Background: Chronic Kidney Disease is associated with pathological changes to the kidney vasculature which contribute to disease progression. Despite the recognized importance of vascular dysfunction in kidney disease, the mechanisms by which these changes occur are poorly understood, limiting therapeutic design. Disruption of Vascular Endothelial Growth Factor Receptor 3 (VEGFR3), known for its role in lymphangiogenesis, is causally linked to the development of kidney diseases, including renal fibrosis and cystogenesis. How VEGFR3 signaling influences kidney disease progression and the specific vascular beds involved remains unclear.

Methods: We performed a detailed expression analysis of Vegfr3 in the kidney using a Vegfr3-TFP reporter mouse line. We generated a new transgenic mouse model to investigate the role of Vegfr3 in the kidney vasculature (Vegfr3M). Conditional and cell-specific excision of the floxed allele was performed using the Rosa-rTA-TetOCre, Cdh1-Cre, and Pdpn-GFPPCre driver strains to evaluate global, pan-endothelial, and lymphatic endothelial cell deletion of Vegfr3 respectively. Mice underwent a detailed phenotypic evaluation and kidney sections were processed for histology.

Results: Vegfr3 undergoes dynamic expression through development in several fenestrated microvascular beds of the kidney including the peritubular capillaries, the ascending vasa recta, and the glomerular capillaries. Constitutive deletion of Vegfr3 results in early embryonic lethality while induced deletion at later embryonic stages results in lymphatic pathologies including chylous ascites, blood-filled lymphatic vessels, and reduced viability. Both global and endothelial-cell-specific deletion of Vegfr3 at embryonic day 11.5 resulted in marked disruption of glomerular development with cavernous capillary malformations. Immunoﬂuorescence and electron microscopy revealed endothelial cell lined structures surrounded by immature podocytes with disrupted basement membrane development.

Conclusions: VEGFR3, while typically associated with lymphatic vessels, is expressed in fenestrated microvascular beds of the kidney and is required for glomerular development. These findings have important implications for the development of therapeutics targeting this pathway for the treatment of kidney disease.

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PO0889

Malnutrition During Pregnancy Impairs Nephrogenesis by Interrupting Methionine Metabolism
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Background: Poor nutritional status during pregnancy has long term effects on kidney health by impairing nephron endowment in an unknown mechanism. Nephron progenitor cells are dependent on constant nutrient supply for maintaining high metabolic activity. We aimed to study the effect of malnutrition during pregnancy on the metabolic profile of nephron progenitor cells.

Methods: Six2 Cre<sup>+</sup> males were mated with wild type females. Pregnant mice were fed with 70% of the daily chaw intake in individual cages. Six2 NPC’s cells were FACs sorted and the metabolites were extracted and measured using mass spectrometry. For kidney organ cultures, kidneys were dissected and immediately incubated in well plates containing media either with or without L-methionine. Nuclear preparations were processed using 10x Genomics 5’ v2 (snRNA) and Single Cell ATAC (snATAC) Chromium kits, sequenced and counted with Cell Ranger. Seurat was used to integrate snRNA and snATAC datasets with label transfer. Chromatin interactions were predicted with Cicero and pseudotemporal ordering was performed with Monocle.

Results: We analyzed a total of 52,097 nuclei by snRNA-seq (n=19,985) and snATAC-seq (n=32,112), identifying 214,890 accessible chromatin regions that confer kidney cell identity. This multi-modal analysis highlighted a unique subpopulation of proximal tubule (PT) cells characterized by increased chromatin accessibility in VCA1 and a pro-inflammatory gene expression signature. Immunoﬂuorescence studies showed that these cells are present in a scattered distribution in the kidney cortex. Transcription factor motif analysis implicates ZFHX1B signaling in the transition between healthy PT and VCA1-positive subpopulation. We identiﬁed candidate regulatory regions that are predicted to interact with the VCA1 promoter via cis-co-accessibility networks. Inter-species snRNA-seq data integration suggests this subpopulation exists in the post-IRI repair phase and bulk RNA-seq deconvolution implicates a potential role in CKD and kidney aging.

Conclusions: Our multi-omics approach improves the ability to detect unique cell states within the kidney and reveals a previously unrecognized subpopulation of proximal tubule cells with a pro-inflammation signature.

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PO0890

Generation of Branching Ureteric Bud Organoids from Human Pluripotent Stem Cells

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Background: Directed differentiation of human pluripotent stem cells (hPSCs) to kidney organoids has been well established; however, the generation of hPSC-derived ureteric bud (UB) which undergoes branching morphogenesis to generate collecting duct (CD) epithelia, has remained a significant challenge. Here we describe a highly efficient method for deriving UB/CD organoids from hPSCs, which form unprecendented branching structures. This method provides a new platform for studying human CD development, physiology, and disease modeling. Moreover, this will provide the opportunity to markedly enhance existing kidney organoids by providing a collecting system and importantly, introducing an iterative branching component that is essential to driving metanephric kidney development.

Methods: First, we modified existing methods to efficiently direct hPSCs into anterior intermediate mesoderm in monolayer format. From that point, we optimized a process of 3-D development that included forced aggregation followed by spontaneous budding and then branching of the UB epithelia.

Results: We generated GATA3/PAX2 AIM with >80% efficiency within 5 days of induction, which was then aggregated into 3-D spheres. Over the subsequent days, the cells underwent a spontaneous process of organization and maturation that parallels normal development of the embryonic nephric duct (ND). Nearly synchronously, each aggregate gave rise to a mesenchymal epithelial outgrowth that exhibited expression of UB markers PATX2, GATA3, RET, SOX9 and CALB1. Next, we embedded the UB-like buds into a hydrogel matrix, and they underwent a complex branching morphogenetic program driven by growth factor signals. At later stages, we identified culture conditions to stimulate differentiation of the ureteric episthesia into CD principal cells, identified by expression of AQP2 and SCA11A/B. Additionally, GATA3+ UB progenitor cells were maintained and expanded over several passages in our 3-D culture system.

Conclusions: We have developed a novel strategy to generate branching UB tissues from multiple cell lines which are also competent to differentiate into CD epithelia. Efforts are ongoing to investigate the functional and physiologic properties of these tissues, as well as to model genetic diseases that impact morphological development of the collecting system.

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PO0891

Modeling Damage-Associated Molecular Pattern Injury and Fibrosis Using Human Kidney Organoids

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Background: Recent developments in generating human kidney organoids in vitro, have provided an invaluable tool to study human renal diseases, injury, and screening new therapeutics. In order to study acute kidney injury (AKI) we have developed a human kidney organoid model of injury with the damage associated molecular pattern molecule (DAMP), hemin, which is released during hemolysis, often occurring after ischemia/reperfusion and rhabdomyolysis. To spatially and temporally characterize tubule injury in the hemin AKI model, we generated transgenic iPSC lines that carry an early apoptosis biosensor, CytochromeC-GFP. Healthy cells within organoids will localize CytochromeC to the mitochondria but, upon injury, will diffuse into the cytoplasm before activating the apoptotic pathway. This approach provides a real-time readout of injury progression in the kidney organoids.

Methods: Kidney organoids at day 14 of culture were treated for 48 hours with varying concentrations of hemin to determine the optimal dose for measurable injury at day 26. CytochromeC-GFP iPSC lines were generated using AAVS1 Safe Harbor targeting approach. CytochromeC-GFP response in the organoid was validated using menadione (mitochondrial toxin) and tested with hemin to determine the extent of injury. To test efficacy of new therapeutic compounds, hemin injured organoids were treated with varying concentrations of 4-(phenylthio)butanoic acid (PTBA) analogs for 10 days and analyzed to determine changes in fibrotic, and oxidative stress markers.

Results: We show injury in the organoids with optimal hemin dosage leading to a reproducible increase in fibrotic, and oxidative stress response. CytochromeC-GFP biosensor iPS lines allowed us to monitor organoids under hemin insult. Organoids treated with nephrotoxin or hemin exhibit cytoplasmic GFP signal in the injured cells and morphological changes of the mitochondria. Hemin injured organoids treated with PTBA analogs showed a reduction in fibrotic markers at day 26 suggesting a reduction in fibrotic scar tissue development.

Conclusions: We have developed a reliable injury model using hemin, and together with CytochromeC-GFP as a biosensor, these tools can be exploited to test nephrotoxicity, study acute kidney injury, and new therapeutic compounds in a human based in vitro model.

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PO0892

Delaying Nephrogenesis In Vitro Results in Enhanced Proximal Tubule Alignment and Maturity in Kidney Organoids

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Background: Stem cell-derived organoids represent a promising model for complex organs such as the kidney, with studies of disease, physiology and drug interactions relying mostly on simplistic cell cultures or animals that do not completely recapitulate the complex human environment. However, kidney organoids are still less mature than the in vivo organ, a limitation arguably most apparent in the proximal tubule (PT) compartment. The critical role of the PT in performing the bulk of solute reabsorption makes it a key requirement for drug screening and bioengineering. By inhibiting promiscuous epithelialisation, we report the development of PT-enhanced kidney organoids with improved PT alignment, maturity, functionality and suitability for therapeutic applications.

Methods: Standard and fluorescent reporter iPSC lines were subjected to prolonged monolayer differentiations, with 4 - 5 day initial CHIR exposure durations (modified from: Howden et al, EMBO Rep, 2019; Vanslambrouck et al. JASN, 2019) and precisely timed modifications to signalling pathways such as canonical WNT, BMP and NOTCH. Organoids were generated as previously published (Takasato et al, Nat Protoc, 2016) and analysed using confocal immunofluorescence, live imaging of fluorescent reporters, transcriptional profiling (single cell RNAseq) and functional transport assays.

Results: PT-enriched organoid could be generated in a highly reproducible manner from multiple cell lines. Proximal tubules showed mature protein and gene expression, as well as transport capacity in multiple assays. Nephron spatial arrangement/directrality, as well as shifts in proximo-distal nephron patterning, were influenced by these modified conditions.

Conclusions: Here, we describe PT-enhanced kidney organoids with improved PT maturity and functionality, with this approach providing a more stringent control over the spatial arrangement of nephrons. Such findings have significant implications for downstream applications including drug screening, toxicology assays and bioengineering of functional replacement cells or tissues.

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PO0893

Glomerular Endothelial Glycocalyx Damage Occurs in Human Diabetic Nephropathy and Could Be Prevented by Early Mineralocorticoid Receptor Inhibition

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Background: The glomerular endothelial glycocalyx (GenGlx) forms the first part of the filtration barrier. In rodent models, damage to the GlGenGlx occurs early in the development of diabetic nephropathy (DN). Until now, no techniques have been available to quantify GenGlx damage in human disease. Mineralocorticoid receptor (MR) antagonists slow disease progression, but side effects limit their clinical use. We aimed to develop a method to study GlGenGlx changes in human disease and investigate whether MR inhibition could preserve the GlGenGlx in a rat DN model.

Methods: Human renal biopsies from patients with DN and thin basement membrane disease (TBMD) were analysed using our novel peak-to-peak confocal imaging method (UEA-1 lectin) to assess GlGenGlx depth. Male Wistar rats injected with streptozotocin (50mg/kg IP) were used to study if spironolactone (50mg/kg daily S.C.), an MR inhibitor, could preserve the GlGenGlx and limit the development of DN. Our glomerular permeability assay was used to directly measure the albumin permeability (Ps/albumin), in isolation from haemodynamic changes. Peak-to-peak (WGA lectin) was validated against electron microscopy GenGlx depth measurements. MMP2 activity was quantified using a specific activity assay and ELISAs were used to measure urine albumin levels.

Results: In human DN, GlGenGlx depth was reduced compared to patients with TBMD (p=0.013). Diabetic rats developed albuminuria and the Ps/albumin increased 1.6-fold (p<0.001). Again, GlGenGlx depth was reduced in DN compared to controls (p<0.001). Plasma and urinary active MMP2 were increased (p=0.017 and p=0.001). MR blockade preserved the GlGenGlx, restored Ps/album to control values and prevented albuminuria progression. Reduced urinary active MMP2 (p=0.012) and glomerular Shmp2 mRNA expression (p=0.002) were seen following MR blockade in DN. GlGenGlx enzymatic degradation, with hyaluronidase, reversed the effect of MR blockade in DN confirming the importance of GlGenGlx preservation in this model.

Conclusions: MR blockade in DN preserves the GlGenGlx, reduces Ps/album and retards the development of albuminuria. The alternate approach to block MR inhibition in GlGenGlx damage represent a novel potential therapeutic strategy, to reproduce the benefit of MR antagonists without adverse side effects.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Targeting αvβ3 Integrin Improves Renal Function Through Local Inhibition of TGFβ-Activation

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Background: TGFβ signaling plays a central role in the development and progression of renal interstitial fibrosis in chronic kidney disease (CKD), which predicts time to dialysis. Systemic blockade of TGFβ has shown severe adverse effects (progression of premalignant lesions) and limited efficacy at doses that were safe for patients, highlighting the need for a targeted inhibition of TGFβ in the kidney. αvβ3 integrins have a unique ability to activate latent TGFβ1 using its LAP-domain to release active TGFβ and therefore can modulate fibrotic processes. Consequently, they have emerged as promising therapeutic targets.

Methods: We generated MED8367, an antibody that specifically binds human integrin β3 and works allosterically reducing its affinity for the LAP domain, hence preventing β3-mediated TGFβ activation but not its cell adhesion function. We confirmed its neutralising activity using a reporter cell in vitro assay that detects TGFβ bioactivity.

Results: To assess its therapeutic effect ITGB8 humanized mice were subjected to unilateral ureteral obstruction to induce fibrosis. Obstructed kidneys showed strong up-regulation of integrin β3 in the tubular compartment and MED8367 significantly improved fibrosis without affecting integrin β3 expression. This was accompanied by inhibition of TGFβ activation, which mimicked the effect of a pan-TGFβ neutralizing antibody. MED8367 reduced renal fibrosis by blocking local TGFβ activation. We next tested the effect of targeting integrin β3 in a mouse model of diabetic nephropathy, the db/db-uninephrectomy model. Mice underwent uni-nephrectomy at 8 weeks of age and were randomized to receive either an anti integrin β6/8 or an anti integrin β6 antibody at 12 weeks of age for 3 weeks. Blocking integrin β6 did not affect albuminuria in these mice while blocking integrins β6/8 stopped the progression of albuminuria in all the mice tested (n=9). These data suggest that it is the blockade of integrin β3 that has a beneficial effect on albuminuria.

Conclusions: We conclude that targeting integrin β3 in CKD ameliorates kidney dysfunction and reduces fibrosis, an effect that is mediated by inhibition of local TGFβ activation.

Integrated Single Nucleus RNA and ATAC-Seq Implicate Cis-Regulatory Chromatin Interactions That Promote Gluconeogenesis in the Human Diabetic Proximal Tubule

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Background: Type 2 diabetes is characterized by impaired glucose metabolism, but relatively little is known about cell-specific changes in the kidney. We hypothesized that single cell ATAC (ATAC-seq) and RNA (snRNA) sequencing of kidney tissue from patients with early diabetes would reveal cis-regulatory chromatin interactions that promote expression of genes that lead to glucose intolerance.

Methods: We analyzed five kidney samples from patients with early diabetes and five healthy controls. Diabetic patients had elevated A1c and two of five had proteinuria. Serum creatinine (mean = 1.01 mg/dl) was not different between groups. Nuclear preparations were processed with 10x Genomics 5’ v2 or Single Cell ATAC kits, sequenced and counted with Cell Ranger. Analysis was performed with Seurat. snATAC peaks were called with MACS2 using SnapATAC. Chromatin interactions were predicted with BISON.

Results: A total of 80,576 nuclei were analyzed by snATAC (n=46,564) or snRNA (n=34,012) sequencing and included all cell types. In the diabetic proximal tubule, we observed increased expression of gluconeogenic genes PKLR, ALDOB, FBP1, and GLP2 and the sodium bicarbonate exchanger, SLC44 (Figure 1; green-upregulated, red-downregulated). Increased expression of GLS and GLUD1 implies glutaminolysis as a gluconeogenic substrate. Transcriptional changes were accompanied by cell-specific differential chromatin accessibility in regulatory regions that were linked to their respective promoters via predicted chromatin interactions. Differentially accessible regions in the proximal tubule were enriched for NFκB binding motifs, suggesting it may regulate chromatin accessibility in diabetes.

Conclusions: This is the first single cell multi-omic analysis of early human diabetic kidney injury. Our analysis reveals that early diabetes induces changes in chromatin accessibility that promote gluconeogenesis and ammoniagenesis in the proximal tubule, and suggests utility for single cell multi-omic analyses.

Mapping the Response of Murine Diabetic Nephropathy to Therapy at Single-Cell Resolution

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Background: Diabetic Kidney Disease (DKD) is the major cause of kidney failure in the USA. Angiotensin blockers (ACEi/ARBs) and SGLT2 inhibitors (Canagliflozin) are only approved therapies demonstrated to slow the progression of DKD. Methods: We treated 40 diabetic db/db hypertensive (reninAAV) mice either with ACE inhibitor (lisinopril), an SGLT2 inhibitor (JNJ-39933673), a PPAR agonist (Rosiglitazone), or vehicle control (n=10/group). Each group received either 2 days or 2 weeks of treatment. We measured BP, glucose and UACR and collected kidneys for snRNA-seq.

Results: Drug treatment at 2d and 2 wks significantly reduced BP (lisinopril), glucose (Rosi and JNJ3673), and Uacr (lisinopril, Rosi and JNJ3673) from baseline demonstrating that either BP or glucose control independently impact Uacr in this model. We generated 1,324,051 single nucleus transcriptomes, detecting 2,028 unique genes/cell on average. Unbiased clustering identified 19 cell clusters representing all major cell types, including rare ones such as the JGA (3,614 cells), podocytes (8,851 cells) and macula densa (MD, 4,239 cells). Drug treatment at 2 days significantly reduced JGA renin expression which was strongly downregulated by exogenous renin in ReninAAV db/db mice compared to WT. SGLT2 expression was restricted to the S1 segment of the PT, and SGLT2 inhibition acutely downregulated S1 glucose transporter Slc5a2 (Glut5) perhaps reflecting compensation. SGLt1 expression was strongly downregulated in db/db reninAAV MD, and Sglt2 inhibition partially restored this expression. MD Sgl1 has been shown to act as a glucose sensor and, inhibit tubuloglomerular feedback, so increased expression would increase GFR.

Conclusions: This is the first comprehensive single cell transcriptional atlas of the effects of diabetic nephropathy treatments in a mouse model. Drug specific and overlapping gene expression patterns were identified and should help elucidate cell-specific mechanisms of therapeutic intervention.

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The β2-Adrenergic Receptor Agonist Formoterol Restores Mitochondrial Dynamics and Energy Production in the Diabetic Renal Proximal Tubule

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Background: While diabetic kidney disease (DKD) is the leading cause of end stage renal disease, the early pathophysiology of this disease remains poorly understood. In type 2 diabetes mitochondrial dysfunction and changes in energy metabolism occurs in proximal tubules. We examined the effects of formoterol, a β2-adrenergic receptor agonist (R) previously demonstrated to induce mitochondrial biogenesis and promote recovery from acute kidney injury, on renal mitochondrial homeostasis and energy production in diabetic db/db mice and in renal proximal tubule cells (RPTC) treated with high glucose.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Podocyte Injury in Diabetes

UCP2 Activates Autophagy to Protect Against Albuminuria and Podocyte Injury in Diabetes

Results: RPTC treated with glucose for 96 hr exhibited a decrease in ATP, uncoupled OCR and the mitochondrial fusion protein Mfn1. In contrast, the fission protein pDrp1 and the fusion (FIP) complexes I-V increased. Treatment with formoterol (30nM) restored ATP, Mfn1, pDrp1 and ETC complexes to control levels. Similarly, vehicle treated db/db mice exhibited increases in ETC protein complexes I, II, III and V, and pDrp1 in renal cortex. Diabetic mice showed a decrease in Mfn1 in renal cortex. The mice treated with formoterol complexes I, II, III and V, pDrp1 and Mfn1 to control levels in db/db mice. ATP was decreased in db/db mice and was restored to control levels with formoterol treatment.

Conclusions: Together, these in vivo and in vitro results suggest that increased glucose alters mitochondria dynamics (increase fission/ decrease fusion) and decreases ATP-poor gene expression of ETC proteins. Formoterol reverses these glucose-induced effects and may be used as a potential therapy to prevent early disease progression of DKD.

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Diabetic Kidney Disease: Basic Mechanisms

PO0989
UCP2 Activates Autophagy to Protect Against Albuminuria and Podocyte Injury in Diabetes
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Background: Podocyte injury and albuminuria are leading features of glomerular damage in diabetic kidney disease. Autophagy plays an important role in maintaining podocyte homeostasis. However, the underlying mechanism remains unknown. In this study, we reported a critical role of mitochondrial uncoupling protein 2 (UCP2) in maintaining autophagic activity and protecting podocyte from hyperglycemia-induced injury.

Methods: First, to elucidate the role of UCP2 in podocyte homeostasis and injury in vivo, we generated conditional knockout mice in which UCP2 is specifically ablated in podocytes by using Cre–LoxP recombination system. Second, autophagosome was detected by transmission electron microscopy. Dual-fluorescence lentiviral mRFP-GFP-LC3 was transfected into podocyte to detect the autophagic flux. Autophagy marker, LCH2, p62 and Beclin1, were tested by quantitative real-time PCR and western blot. At last, AMPK activator and mTORC1 inhibitor were used to identify the signaling pathway. UCP2-mediated to regulate autophagy.

Results: UCP2 was upregulated synchronously with autophagy marker during glomerulosclerosis development. Loss of UCP2 in podocytes led to a decrease of autophagic activity and an increase of podocyte injury. Podocyte-specific knockout of UCP2 aggravated age-related proteinuria and increased podocyte susceptibility to hyperglycemia in streptozotocin (STZ)-induced DKD mice. UCP2 promotes podocyte autophagy through activation of AMPK/mTOR signaling pathway.

Conclusions: Our findings demonstrates a critical protective role of UCP2 in podocyte survival via maintaining autophagic activity through AMPK/mTOR signaling pathway.

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PO0989
Darunavir Protects Mice with Type 1 Diabetes Against Kidney Injury
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Background: Despite the success of antiretroviral therapy (ART) in improving morbidity and mortality of HIV-positive patients still have increased risk of death and kidney disease and diabetes mellitus are important contributors to this excess mortality. Data from our laboratory demonstrate that the HIV protease inhibitor darunavir (DRV) prevents kidney disease in HIV-transgenic mice via mechanisms independent of HIV protease. Since diabetic kidney disease (DKD) is the most common cause of chronic kidney disease (CKD), diabetes mellitus and HIV are of particular interest, as more than 80% of patients with diabetes type 2 will develop CKD, which is one of the most common causes of ESRD. To delineate the role of HIV pathogenesis and progression of DKD, we studied the efficacy of DRV in the non-HIV model of DKD.

Methods: 8-week-old C57BL/6 mice underwent induction of diabetes by administration of 5 daily 50mg/kg doses of streptozotocin (STZ) injection. Blood glucose was measured before and after DRV treatment. 14 weeks after STZ induction, mice were treated with either DRV (100mg/kg) or control by daily oral gavage for 4 weeks. Mouse blood pressure (BP) was measured before and after DRV treatment. 14 weeks after STZ induction, mice were treated with either DRV (100mg/kg) or control by daily oral gavage for 4 weeks. Mouse blood pressure (BP) was measured before and after DRV treatment.

Results: Darunavir decreased systolic blood pressure in diabetic mice. However, DRV did not change renal VEGF expression in diabetic eNOS-/- mice. Surprisingly, DRV treatment reduced mean BP to levels similar to non-diabetic mice. DRV also increased endothelial CD31 and VEGFR2 expression in glomeruli, but did not change renal VEGF expression in diabetic eNOS-/- mice. Similarly, DRV treatment reduced mean BP to levels similar to non-diabetic mice.

Conclusions: These data demonstrate that DRV protects mice against type 1 diabetic renal injury. Further studies are needed to determine whether changes to renal gene expression are due to direct effects of DRV or secondary to reduced renal injury, resulting in normalization of gene expression suppression and BP.

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PO0990
Proteasome Mediated NF-E2 Degradation Occurs Upstream of JNK Activation-Mediated CTGF Expression in Renal Tubules and Diabetic Kidneys
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Background: TGF-β is a critical mediator of diabetes-induced renal fibrosis. We recently demonstrated that TGF-β and diabetes (Type 1 and type 2) decreased NF-E2 expression and promoted pro-fibrotic signaling in renal cells and kidneys. P38 MAPK and ERK MAPK pathways contributed to proteasome activation and NF-E2 degradation. As JNK pathway is known to induce CTGF expression, current studies examined the contribution of JNK pathway in mediating NF-E2 degradation in TGF-β treated renal tubule cells.

Methods: HK-11 cells were pre-treated with/without JNK inhibitor SP600125, p38 inhibitor SB203580, or p38 and MEK/ERK inhibitor PD98059, or proteasome inhibitor MG132, for an hour prior to treatment with TGF-β for 24 hours. Cell lysates were immunoblotted with appropriate antibodies. Kidney homogenates from FVB and OVE26 diabetic mice treated with 10 µg/kg MG132 daily for 3 mo starting at 3 mo of age were used for protein expression analysis and were immunoblotted with appropriate antibodies. MG132 were included intraperitoneally at a dose of 10 µg/kg daily for 3 mo starting at 3 mo of age when OVE26 mice already displayed significant albuminuria.

Results: Inhibition of p38 MAPK partially preserved NF-E2 expression but induced CTGF expression, as p38 blockade induced ERK phosphorylation. Blockade of both p38/ERK, prevented NF-E2 degradation and inhibited CTGF expression. Blockade of JNK pathway, inhibited CTGF expression without preserving NF-E2 expression. Interestingly, proteasome inhibition in renal cells and OVE26 mice preserved NF-E2 expression and inhibited JNK activation and CTGF expression suggesting JNK activation occurs downstream of proteasome activation.

Conclusions: Our studies have demonstrated that p38 and ERK MAPK pathways promote proteasome activation and NF-E2 degradation while proteasome activation promotes JNK activation and CTGF expression in renal cells and diabetic kidneys. We have recently demonstrated that NF-E2 over-expression inhibited CTGF expression however; future studies will examine effects of NF-E2 over-expression on TGF-β-induced and diabetes-induced JNK activation in renal cells.

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PO0991
Single-Cell Immune Landscape of Mouse Diabetic Kidney Disease
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Background: Diabetic kidney disease (DKD) is historically been considered as a non-inflammatory glomerular disease that is induced by metabolic and haemodynamic derangement. Increasing evidence suggests that renal inflammation contributes to the pathogenesis and progression of DKD. However, specific characteristics of dysregulated immune cells under diabetic conditions are poorly understood. We hypothesized that single cell RNA-seq could provide insight into the cellular mechanisms of diabetic nephropathy.

Methods: We collected kidney samples from control(n=9) and OVE26 (n=9) mice at 16 weeks. CD45 + innate immune cells were harvested by flow cytometry cell sorting and processed using 10x Genomics Chromium platform.

Results: 18000 immune cells (avg=1400 unique genes detected/cell) from control and diabetic mice were included in the integrated analysis. 17 immune cell clusters were identified and included all major immune cell types, with differential expression of hundreds of genes across all clusters. Increased expression of inflammatory cytokines and chemokines in diabetic kidney suggested a metabolic inflammation in specific cell types, with macrophage showing the highest enrichment suggesting multiple unique functionalities may contribute to dysfunctional kidney physiology in diabetes.

Conclusions: This is the first comprehensive single cell landscape of a mouse model of DKD. We demonstrated that (1) activated macrophage subtype recruitment, (2) spectrum of macrophage activation, (3) detailed diabetic immune cell intercellular communication, (3) Macrophage-specific expression of KIR5 that associated with progression of ESRD in T1DM and T2DM patients.

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Rab27b Repression by Foxo1 Leads to Decreased Exosome Production in Diabetic Kidney Disease
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Background: Diabetic kidney disease (DKD) is associated with changes in exosomes. However, it is unclear whether the production or secretion of exosomes is affected in DKD. This study aims to investigate whether and how the secretion of exosomes is affected in DKD using in vivo and in vitro diabetic models.

Methods: In vivo, exosomes were isolated from kidney cortical tissues of Akita and streptozotocin-induced diabetic mice for analysis. In vitro, mouse kidney proximal tubular BUMPT cells were incubated with high glucose (30mM, HG) or mannitol (control) for 8 days to collect exosomes in culture medium. Exosomes were examined by electron microscopy, nanoparticle tracking analysis (NTA), and Western blotting. Knockdown and overexpression were used to study the roles of Rab27b and Foxo1 on exosome secretion.

Results: In vivo, diabetic mice had a reduced number of exosomes in renal cortical tissues compared with non-diabetic mice. In vitro, HG treatment led to a significant decrease in exosome secretion in BUMPT cells, which was associated with the specific downregulation of Rab27b, a key GTPase for exosome secretion. Overexpression of Rab27b restored exosome secretion in HG-treated cells, suggesting a role of Rab27b downregulation in decreased exosome secretion in DKD. For the mechanism of Rab27b downregulation, bioinformatic analysis predicted Foxo1-binding sites at Rab27b gene promoter. We demonstrated the phosphorylation of Foxo1 in HG-treated cells, accompanied by less Foxo1 accumulation in the nucleus. Overexpression of Foxo1 increased Rab27b expression, whereas Knockdown of Foxo1 had opposite effects. Moreover, expression of non-phosphorylatable (constitutively active) Foxo1 led to the upregulation of Rab27b and increases in exosome secretion in HG treated cells.

Conclusions: In diabetic kidney cells and tissues, Foxo1 is phosphorylated and inactivated, leading to decreases in Rab27b expression and consequential secretion of exosomes.

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Disruption of Long Non-Coding RNA MIAT Induces Mitotic Catastrophe of Podocyte in Diabetic Nephropathy
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Background: Diabetic nephropathy (DN) is becoming the principal inducement of end-stage renal disease (ESRD) worldwide. Importantly, mitotic catastrophe (MC) is considered as an important mitosis-linked cell death, which plays an essential role in expediting podocyte loss and detaching from glomerular basement (GBM). The concrete mechanism of MC in podocyte injury and proteinuria, however, remains inadequately elucidated. In the current study, we demonstrated the biological function and underlying mechanism of a long non-coding RNA myocardial infarction-associated transcript (Lnc MIAT) in podocytes.

Methods: The role of MIAT was investigated by resorting to cultured podocytes, CRISPR/Cas9 MIAT knockout mice and human samples. Immunofluorescence, western blot, transwell assay, TEM and histology staining including PAS and Masson staining were performed to assess the lesion of podocytes. RNA-FISH, RIP and luciferase reporter assays were utilized for mechanistic study of the interaction between MIAT, miR-130b and Sox4 further. Moreover, apoptosis and cell cycle of podocytes were determined by flow cytometry and the expression of G2/M transition-related proteins (p21 cip1/waf1, cyclin B and cdc2).

Results: MIAT is noticeably upregulated in HG-stimulated podocytes, STZ-induced mice and serum of DN patients, accompanied by higher creatinine production and significantly lower eGFRs values in clinical and MIA contributes to the proliferation, apoptosis, migration and G2/M arrest of podocytes, while depletion of MIAT significantly mitigates podocytes injury and albuminuria by reducing slit diaphragms (SD) integrity, attenuating foot processes effacement (PFE) and suppressing cyclin B/cdc2-mediated G2/M arrest. Mechanistic investigation reveals that MIAT not only elevates Sox4 protein expression and subsequently manipulates the ubiquitination and acetylation of p53, thereby stifling downstream factors cyclin B/cdc2 via enhancing p21[ser10] activity, but also participates in crosstalk with Sox4 mRNA through competition for miR-130b binding sites.

Conclusions: Our findings provide plausible insight into the interplay between LncRNA MIAT, miR-130b and Sox4 which consequently lead to podocyte mitotic dysfunction involved in the progression of DN, indicating MIAT may act as a promising biomarker and therapeutic target for DN patients.

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The Decrease in Renal Cystathionine β-Synthase/Hydrogen Sulfide Was Involved in the Pathogenesis of Diabetic Nephropathy
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Background: Hydrogen sulfide (H2S) and its producing enzymes are associated with human diseases including coronary heart disease, Alzheimer’s disease, diabetic retinopathy and obstructive kidney disease, etc.

Methods: In order to determine their roles in pathogenesis of diabetic nephropathy, we examined plasma H2S levels in diabetic nephropathy patients and mice, renal H2S production & H2S producing enzymes in the mouse model, and the effects of glucose on H2S producing enzymes, mainly Cystathionine β-synthase(CBS), in cultured mouse proximal convoluted tubule cells (mPTC).

Results: Plasma H2S levels were decreased in patients (17.8±0.5 vs 24.8±0.8 umol/l, p<0.05, n=18/group) and mice(18.7±1.6 vs 40.7±1.8 umol/l, p=0.05, n=6/group). The renal H2S production in mice was decreased (vs 52.1±2.9 vs 81.5±5.8 umol/l, p=0.01) along with the reduction of renal protein expression of CBS (52.1±13.4% of control). A similar protein decrease of CBS(52.5±12.2, p=0.01) was found in cultured mPTC stimulating by high glucose (25mmol/D-glucose), but not CSE or MST. CBS protein expression was correlated negatively with glucose concentration (0.5,10,15,20,25,5M) (p<0.01). The significant decrease of CBS by glucose occurred at 1, 2, 4 and 8 hrs. Up-regulation of CBS was increased remarkably (58.7±14, p<0.05) in high glucose stimulation. CBS immunostaining became less strong with high glucose at the time points of 1hr & 2hr while the co-staining of CBS and LAMPA, a lysosome marker, reached the maximum at 30 min. The decrease of CBS mRNA expression was also found at podocyte and 12hr High glucose in H9c2 (170.7±22.9, p<0.05) in mPTC, which was restored by GYY4137, a slow-releasing H2S donor. The expression of NT was not increased by inhibition of CBS protein with its siRNA but was reversed by GYY4137 in normal glucose medium. Furthermore, in diabetic nephropathy mice, the up-altered 58.6±6.6 vs 86.5±6.6 g/dl, p<0.01)mesangial matrix proliferation and glomerular basement membrane thickening were ameliorated by exogenous supplement GYY4137 at 20mg/kg for 8 weeks.

Conclusions: These findings suggest that high glucose may decrease renal CBS protein by increasing its ubiquitination / degradation and inhibiting its mRNA, eventually induce proximal tubular cell injury due to loss of protective mechanism of H2S.

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Lysophospholipids Predict Fast Decliners with Diabetic Kidney Disease Kentaro Yoshikai,1,2 Yusuke Hirakawa,1 Kensuke Kojima,1 Masao Nangaku,1 Reiko Inagi,1,2 Kyowa Kirin Kabushiki Kaisha Kenkyu Kaikatsu, Chiyoda-ku, Japan; 2University of Tokyo School of Medicine, Bunkyo-ku, Japan, 1University of Tokyo Graduate School of Medicine School of Medicine, Bunkyo-ku, Japan.

Background: In type 2 diabetes, lipid metabolism disorder is frequently complicated due to insufficient insulin secretion and cytokes by visceral fat and regarded as one of the most important risk factors for diabetic dyslipidemia. However, specific lipid metabolites that have critical effects on renal dysfunction are not fully understood.

Methods: We performed the metabolomic analysis for patients with diabetic kidney disease (DKD) to identify novel metabolites related to renal prognosis. Plasma and urine biosamples in stage G3 DKD patients (n=135) are collected, and the whole metabolites of them were quantified by capillary electrophoresis mass spectrometry (CE-MS). Significantly fluctuating metabolites in patients with rapidly impaired renal function within 3 years (called “fast decliners”; about 10% in total) were statistically extracted. We also validated the metabolomic candidates with animal DKD model of SDT-fatty rats, or in vitro study using renal proximal tubular cells (HK-2).

Results: In the clinical metabolomic analysis of the biosamples, over 250 metabolites, including lipids, glycates, and amino acids were identified by CE-MS. Among them, specific urinary lysophospholipids (named as LPLsX) in the fast decliners of DKD were significantly increased. The LPLsX were moderately correlated with eGFR decline after 3 years (r=0.42, p<0.01). In animal experiments, the level of LPLsX was also increased in both the urine and the kidney in the subnephrectomized SDT-fatty rats, while we did not see these damages in normal SD rats. In vitro experiments: the exposure of LPLsX to HK-2 cells induced apoptosis and cytotesis within 24 h and upregulated pro-apoptotic gene expressions. More physiological changes were investigated in reference to transcriptomic analysis, and we could find that LPLsX also deranged the lipid metabolism, estimated by intracellular lipid droplet accumulation, and increased the level of mitochondrial reactive oxygen species. Conclusion: LPLsX predict “fast decliners” in DKD patients or DKD rats and may have crucial roles in renal tubular damage and dyslipidemia. Our findings provide new insights into the pathophysiological understanding of the relationship between lipid metabolism disorder and DKD progression.

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PO0906
Podocyte-Specific Induction of KLF6 Attenuates Diabetic Kidney Disease in Mice
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Background: Krüppel-Like Factor 6 (KLF6), a zinc finger transcription factor, is a key regulator of cytochrome c oxidase assembly in the podocytes. Podocyte-specific Klf6 knockout increases the susceptibility to streptozotocin (STZ) induced-diabetic kidney disease (DKD). However, salutary effects of podocyte-specific KLF6 induction in DKD remain to be explored.

Methods: Podocyte-specific inducible human KLF6 (hKLF6) was generated in mice using the "Tet-on" system, by breeding NPHS2-rtTA mice with newly generated TRE-Δ-KLF6 to generate KLF6Flox/fox mice. TRED-KLF6 transgene were generated using the (TetO7/CMV) regulatory element driving the full-length human KLF6 coding sequence (CGDS 7600.1). Transgene was purified from plasmid vector sequences and microinjected into the pronucleus of FVB/N single-celled embryos. Founder mice were selected based on the level of KLF6 induction after doxycycline (DOX) treatment. STZ-Unilateral nephrectomy (STZ-UNIX) was utilized to induce DKD in mice. First, DOX diet was administered at 8 weeks of age in all mice. UNIX or Sham was performed at 10 weeks of age followed by low-dose STZ or vehicle (VEH) treatment respectively, at 12 weeks for 5 consecutive days. DOX-STZ-UNIX treated NPHS2-rTaT and DOX-VEH-Sham treated NPHS2-rTaT and KLF6Flox/fox mice served as controls. All mice were euthanized at 20 weeks of age and assessed for functional and histological changes in the kidney.

Results: DOX-STZ-UNIX treated KLF6Flox/fox mice exhibited significantly lower albuminuria, focal and global glomerulosclerosis, mesangial expansion, and improved mice survival as compared to age and gender-matched DOX-STZ-UNIX treated NPHS2-rTaT mice. DOX-STZ-UNIX treated KLF6Flox/fox mice also exhibited less tubulointerstitial fibrosis and inflammation (pathology scoring) as compared to age- and gender-matched DOX-STZ-UNIX treated NPHS2-rTaT mice.

Conclusions: These data suggest that podocyte-specific induction of human KLF6 attenuates podocyte injury and DKD, and improves overall survival in mice.

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PO0907
nPOD-Kidney, a New Tool for Investigating Diabetic Kidney Disease
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Background: Diabetic kidney disease (DKD) is a common complication of diabetes, yet it remains poorly understood. The network for Pancreatic Organ donors with Diabetes - Kidney (nPOD-K) project was initiated to assess the feasibility of evaluating human kidneys from organ donors with long-standing diabetes (~8 years), with the long-term goal of improving our understanding of DKD pathogenesis.

Methods: Formalin-fixed paraffin-embedded sections from nPOD-K were stained for specific renal cell and disease markers by multiplex immunofluorescence, followed by periodic acid-Schiff (PAS) staining. Whole sections were imaged using an Axiocam 51 zernal (20X objective) and quantitative image analyses were performed using Visiopharm software.

Results: Tissue integrity and histological stage were independently assessed by two renal pathologists. The majority of cases presented a moderate or severe diagnosis, and 20% of the cohort displayed no overt sign of kidney disease despite long-standing diabetes.

Conclusions: In conclusion, kidneys obtained from organ donors are viable and display all expected features of human DKD at the level of light microscopy. This cohort provides a unique opportunity to better understand DKD pathophysiology through analysis of large, CKD stage-specific regions. Similar to the results from the nPOD pancreas cohort, all historical stages of disease can be detected in affected kidneys, providing a pseudo-timeframe of the evolution of DKD and supporting the potential to identify novel therapeutic targets.

Funding: Commercial Support - Novo Nordisk, Inc.

PO0909
Integrin aVb8/TGF-b Activation in Kidney Is Associated with Renal Function Deterioration and Can Be Monitored in Urine

Background: Integrin aVb8/TGFb activation plays a central role in fibrosis. The specificity of TGFb activation is regulated by the expression of integrin isoforms in tissues. We set out to study molecular signatures associated with various aetiologies in CKD, the specific integrins that modulate TGFb activation and fibrotic initiation in the kidney and the potential for non-invasive monitoring of renal TGFb activation.

Methods: Kidney biopsies were obtained from CKD cohorts of diverse aetiologies and living donor (LD) controls. Gene profiling data (Microarray) were obtained from fibrosis and tubulointerstitial (TI) RNAseq aVb8/TGFb vector by using ViaFectTM Kit, the effect of siNGF was verified by western blot. knockdown of NGF decreased the expression of Sirt1 and Cleaved caspase.

Results: In the Gene Set Variation analysis (GSVA), fibrosis signatures including collagen signature increased with CKD severity compared to LD. This was more prominent in diabetic nephropathy (DN) in both glomeruli (N=12, p=1.09e-04) and tubulointerstitium (N=17, 2.31e-04). Further analysis showed that renal integrin b8 (ITGB8) was enriched and elevated at CKD stage 2, maintained at the similar level at high stage.

Conclusions: The objective of this article is to investigate the mechanism of NGF protecting podocyte apoptosis by regulating Sirt1 expression and to provide a new biological target for clinical treatment.

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: Mean estimated glomerular filtration rate and urinary protein-to-creatinine ratio were significantly increased in controls and DKD patients. The urine albumin-to-creatinine ratio was strongly increased in both groups compared to controls (p < 0.0001), respectively. Upon the analysis of public dataset, we identified 11 candidate microRNAs for DKD, whose expression in urinary exosomes were all significantly higher in patients with DKD compared to controls. In particular, urinary exosomal miR-30a-5p and miR-335-3p levels showed positive correlation with the degree of interstitial inflammation and arterial hyalinosis, respectively. There was no significant association between the remaining microRNAs and the degree of glomerular injury, tubulointerstitial fibrosis, or arteriosclerosis. Finally, we found significant correlation between urinary protein-to-creatinine ratio and the levels of urinary exosomal miR-98-5p.

Conclusions: Urinary exosomal microRNAs could reflect the degree of interrenal pathologic status in patients with diabetic kidney disease.
by the treatments of both insulin and hyaluronan, despite comparable levels of both high glucose and high pressure. Furthermore, urinary L-FABP may be a useful marker reflecting the therapeutic efficacy of liraglutide.

Conclusions: Liraglutide may exert a renoprotective effect via prevention of glomerular endothelial dysfunction and acceleration of autophagy in the early phase of DKD, independently of both blood glucose and blood pressure levels. Furthermore, urinary L-FABP may be a useful marker reflecting the therapeutic efficacy of liraglutide.

PO0914
PLVP as a Novel Marker for Endothelial Injury in Diabetic Nephropathy
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Background: Diabetic nephropathy (DN) is associated with endothelial cell dysfunction and progressive loss of kidney function. The plasmalemma vesicle-associated protein (PLVP) has been found to be necessary for the formation of endothelial diaphragms in fenestrae, caveolae, and transendothelial channels. In the adult kidney, glomerular endothelial cells lack diaphragms in the fenestrae. Previous studies reported glomerular expression of PLVP in transplant glomerulopathy, in mesangio proliferative glomerulonephritis, and in mice developing renal thrombocytopenia microangiopathy as a consequence of defective G protein-coupled receptor signaling in renal cells. Therefore, we investigated whether PLVP expression in glomerular capillaries is induced in different models of DN.

Methods: To induce a model of type 1 diabetes, one dose of streptozotocin (STZ, 180 mg/kg) was administered by intraperitoneal injection in 6-8 weeks old mice. 16-week-old black and tan brachyter (BTBR) ob/ob mice, with spontaneous mutation in the leptin gene were used as a model of type 2 diabetes. Immunohistochemical staining and analysis was performed to examine the expression of PLVP. We co-stained the Intercellular Adhesion Molecule 2 (ICAM2) as a marker for endothelial cells.

Results: Glomerular hypertrophy was found in STZ mice and BTBR ob/ob mice, which was interpreted as evidence for successful induction of DN (STZ: 275 ± 5 mm², control: 2527 ± 24 mm²; BTBR ob/ob: 4471 ± 23 mm², control: 2295 ± 4 mm²). Using immunohistochemical analysis, the BTBR ob/ob mice and the STZ mice revealed induced PLVP expression in their glomeruli, as compared with non-diabetic controls (p<0.05 respectively). ICAM2 expression in glomeruli of STZ mice tended to be lower than in control mice, but the difference was not statistically significant. In BTBR ob/ob mice, the expression of ICAM2 was significantly decreased compared to lower control mice (p<0.05).

Conclusions: Our results indicate that the expression of PLVP is induced in diabetic nephropathy. The protein PLVP represents a potential novel marker for endothelial injury in diabetic nephropathy.

Funding: Private Foundation Support, Government Support - Non-U.S.

PO0915
MTORC1/STAT1 Signaling Stimulates CFB Expression and Alternative Complement Pathway Activation to Induce Podocyte Dysfunction and Diabetic Kidney Disease
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Background: Alternative complement pathway activation has been reported in diabetic nephropathy, suggesting a role of alternative complement pathway activation in diabetes-related glomerulopathy. However, the underlying mechanisms for this activation are not yet understood.

Methods: To induce diabetic nephropathy, ten-week-old male CD1 mice or FVB/NJ mice were used.

Results: The analysis of GSE39528 data and the immunohistochemical staining results showed that mTORC1 signaling, STAT1, complement factor B (CFB) and complement alternative pathway were activated in podocytes from patients and animal models with DKD. Knockdown of CFB remarkably alleviated podocyte loss, glomerular basement membrane thickening, mesangial expansion, and proteinuria in DKD mice. In addition, ablation of Tsc1 in podocytes led to mTORC1 and STAT1 signaling activation, basement membrane thickening, mesangial expansion, and proteinuria in DKD mice. In STZ-induced DKD mice, db/db mice, and Podocyte-specific TSC1 deletion mice were used.

Conclusions: Our results indicate that the gluco toxic stress in diabetes-related glomerulopathy results in activation of the metabolic pathway for gluconeogenesis. The increase in reactive oxygen species and inflammation have been identified as major components in the progression of this microvascular complication. Transcription factor Nr2 (NF-E2-related factor), which plays essential roles in the protection against oxidative/toxemic stresses, is known to alleviate inflammation and oxidative tissue damage. We hypothesized that keeping Nr2 activated is beneficial for the treatment of DKD.

Methods: To clarify roles Nr2 plays in the pathogenesis of DKD, we generated Nr2 deficient Akita mice (Nr2−/− mice) by crossing Tsto/2 (Akita) mice (C57BL/6J) with Nr2 knockout (Nr2−/− mice) (C57BL/6J). Phenotypic parameters of male mice were measured, and samples were harvested from the mice at 4 months.

Results: We found that Akita:Nr2−/− mice displayed more pronounced hyperglycemia and hyperlipidemia compared to Akita mice did. While expression of Nr2-targeted genes Nqo1 and Ihhosc1 was induced in Akita mouse kidneys; the expression was significantly reduced in kidneys of Akita:Nr2−/− mice. Histologically, Akita mice showed modest mesangial expansion, but Akita:Nr2−/− mouse glomeruli showed marked distended capillary lumina with increased mesangial matrix and widening of mesangial capillary lumina. We observed more severe glomerular damage in Akita:Nr2−/− mice. In this model, mice exhibited glomerular basement membrane thickening, mesangial expansion, and proteinuria in DKD mice. In addition, ablation of Tsc1 in podocytes led to mTORC1 and STAT1 signaling activation, basement membrane thickening, mesangial expansion, and proteinuria in DKD mice. In Akita:Nr2−/− mouse kidneys, the expression of Nr2-targeted genes was induced, and the expression was significantly reduced in kidneys of Akita:Nr2−/− mice. Histologically, Akita mice showed modest mesangial expansion, but Akita:Nr2−/− mouse glomeruli showed marked distended capillary lumina with increased mesangial matrix and widening of mesangial capillary lumina. We observed more severe glomerular damage in Akita:Nr2−/− mice. In this model, mice exhibited glomerular basement membrane thickening, mesangial expansion, and proteinuria in DKD mice. In addition, ablation of Tsc1 in podocytes led to mTORC1 and STAT1 signaling activation, basement membrane thickening, mesangial expansion, and proteinuria in DKD mice.

Conclusions: These results demonstrate that Nr2-deficiency exacerbated inflammatory response, oxidative stress and interstitial fibrosis in the Akita mouse kidneys, indicating that Nr2 plays important roles in the protection of DKD kidneys.

Funding: Government Support - Non-U.S.

PO0917
The Novel Soluble Guanylyl Cyclase (sGC) Activator Runcaciguat Improves Cardiorenal Morbidity in a Diabetic Rat Model of CKD
Gustav Carus,1,3 Erfan Eidenschink,1 Florian Gembardt,1 Yexin Dai.1,2

Background: Patients with chronic kidney disease (CKD) and Type-2 Diabetes (T2D) have a high risk of kidney failure and cardiovascular events. CKD and T2D are associated with oxidative stress impairing NO/sGC signaling thus driving CKD progression. Runcaciguat is a novel potent and selective, sGC activator able to restore sGC signaling by activating the oxidized and heme-free sGC. Here we investigated the therapeutic potential of Runcaciguat in a rat model of T2D associated CKD.

Methods: Cardiorenal morbidity was studied in diabetic and proteinuric rats. Rats (ZDF/CFI-Lebr-fa/r, 22 weeks old male, n=20/group) were treated orally for up to 42 weeks with Runcaciguat (3 mg/kg) or placebo. Key outcome parameters included mortality, blood pressure, proteinuria, kidney histology, biomarkers of kidney and heart damages, and gene expression.

Results: Proteinuria steadily increased over time in the placebo arm (uPCR (g/mmol) 9.9±0.1 @ baseline, 1.8±0.1 @ 12 wk, 5.9±0.7 @ 42 wk) and was significantly reduced in the Runcaciguat arm (0.8±0.1 @ 12 wk, 3.0±0.5 @ 42 wk). Improved proteinuria was paralleled by significantly improved glomerular filtration rates @ 42 wk (55±5 ml/min vs. 36±9 in the placebo arm). Histological examination of kidney revealed that Runcaciguat significantly reduced tubular dilatation, glomerulopathy and accumulation of protein cylinders. Runcaciguat significantly improved left ventricular heart weight as well as several kidney and heart injury markers in urine and in plasma.

Conclusions: The novel sGC activator Runcaciguat improved kidney and heart function and ameliorates diabetic nephropathy rat model and may become an effective treatment option for diabetic and chronic kidney disease patients.

Funding: Private Foundation Support

PO0918
RNA-Binding Proteins Tristetraprolin and Human Antigen R Are Novel Modulators of Podocyte Injury in Diabetic Kidney Disease
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Background: Diabetic kidney disease (DKD) is one of the most common complications of diabetes and the most common cause of end-stage renal disease, with no definitive therapy yet available to halt its progression. As key RNA-binding proteins (RBP) that play a pivotal role in epigenetic regulation, Tristetraprolin (TTP) and human antigen R (HuR) competitively bind to mRNAs of myriad cytokines, exert opposite effects on RNA stability, and dictate overall inflammatory states. However, the roles of these RBP in diabetes-related glomerulopathy is poorly understood. Herein, we investigated whether and how TTP and HuR are involved in the posttranscriptional regulation of podocyte-specific molecules and inflammatory cytokines in DKD.

Methods: Kidney tissues were procured from diabetic patients and from db/db mice. Quantitative RT-PCR was performed to measure mRNA expression levels of IL-17 and capillary loops via reverse transcription and competition was employed to overexpress or silence target proteins. RNA immunoprecipitation (RIP) and co-immunoprecipitation assays were used to identify RNA-protein and protein-protein interactions.

Results: In DKD patients and db/db mice, TTP expression was significantly decreased and HuR expression was increased in glomerular podocytes, concurrent with podocyte desorption/ionization mass-spectrometry imaging (MALDISHMS) and lowered expression (IL-17 and claudin-1), which are targets of TTP and HuR, as evidenced by RNA

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immunoprecipitation. In cultured podocytes, exposure to high ambient glucose amplified HIF-1α transcription, while TTP expression was associated with diabetic microvascular complications. Other probes included cg13366628 (p=1.62E-5) in Platelet Derived Growth Factor Alpha (PDGFA) on chromosome 7, a known type 2 diabetes risk gene, as well as cg60392169 (p=3.14E-5) in Interferon Related Factor 4 (IRF4) on chromosome 6 and cg12577105 (p=4.11E-5) in Coronary Releasing Hormone Receptor 1 (CRHR1) on chromosome 17 involved in the HPA axis.

Conclusions: We identified cytosine methylation changes that correlated with early kidney function decline in Pima Indians with type 2 diabetes.

PO0921 Pathogenic Impact of Altered Leptin in Diabetes Induced by Genetic Deletion of theCanonical Transient Receptor Potential Channel 1 (TRPC1): Role of Insulin, Body Weights, Calcium-Sensing Receptor, and Intracellular Calcium

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Background: We recently reported diabetic phenotypes in TRPC1 mutaition. The role of the elevated serum leptin & reduced adiponectin is unclear. Like CaSR, TRPC1 participates in cell Ca homoeostasis & its deficiency impairs Ca entry & induces hyperparathyroidism (JCI Apr 2020). We tested if by raising serum Ca by 4-5 mg%, we would raise cell Ca in adipocytes to lower leptin & elevate adiponectin, based on published in vitro data.

Methods: In age- & sex-matched trp-1+/-, +/- & -/- mice, we did metabolic studies, IP glucose tolerance tests, & measured serum cytokines & PTH by ELISA. At 10 m, we injected leptin (IP) to cause hyperleptinemia (~15 mg%) to raise cell Ca enough to lower PTH, & by inference, similar rises in adiponectin & beta cells to alter leptin & insulin. At 16 m, we injected calcimimetic (Parabiv) IP x 2 wk to evaluate if glucose tolerance is improved by chronically raising cell Ca .

Results: Serum leptin increase in +/- mice was +/- by 17% at 4.5 m, 75% (p<0.05) at 6.5 m, & 130% (p<0.001) at 9.5 m. It is directly related to body weight (BW) & 4.5 m more regardless of genotypes or gender (N=80; p<0.05). The relationship holds true at 17 m (p<0.05 for +/- & p<0.05 for -/+). High fat diet x 3 stimulates leptin to 3 fold for all 3 genotypes, but linkage to BW holds. Serum leptin after fast (r=0.93) & 30 min post IP glucose (r=0.75) are highly correlated with simultaneous insulin. Leptin rise from 6.6 to 10.6 mg%/2 h after IP glucose (p<0.01). With induced hypercalcaemia, PTH, elevated in null (288 vs 119 pg/ml), fell 75% (vs. 48% in +/-), but the elevated leptin (15.1 vs. 6.6 mg%) in Ca-/- mice did not fall; insulin, serum Ca, or PTH fell; & glucose was more elevated in both genotypes. GTT did not improve in +/- or -/- mice after 2 wk of calcimetics.

Conclusions: 1. Leptin is upregulated by anabolism, high fat diet, weight gain, & correlated with body weight & insulin in normal & TRPC1 null mice. 2. It is however unpredictable in TRPC1 deficiency, uncurred by raising intracellular Ca by hypercalcaemia (sufficient to inhibit PTH by 50 to 75%). 3. Like insulin-resistant diabetes in mice with leptin receptor deficiency, we postulate the lack of TRPC1 impairs leptin signaling in neurons inhibiting hypophagia. The elevated leptin reflect negative compensation to combat obesity.

Funding: NIDDK Support, Veterans Affairs Support, Private Foundation Support, Clinical Revenue Support

PO0922 The Significance of Renal TSPAN9 Overexpression in Diabetic Nephropathy

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Background: Diabetic nephropathy (DN) is the leading cause of end-stage renal disease. We performed proteomic analysis in isolated human glomeruli (DN vs. normal control) and RNAseq in glomeruli from a murine model of DN (db/db/NOS−/− vs. nondiabetic controls (eNOS−/−)). We identified differentially expressed molecules with potential impact in DN, including tetraspanin 9 (TSPAN9), which mediates transduction signaling and regulates cell development, growth and motility. We investigated the potential distribution of TSPAN9 in DN.

Methods: Human kidney biopsies from DN (class II, III and IV, total n=30) were studied, and compared to control (non-cancer regions of human nephrectomy (Nx), n=10). TSPAN9 immunostaining was assessed and correlated with morphologic lesions and clinical data. Human mesangial cells (HMC) were cultured in normal glucose, mannitol or high glucose medium. TSPAN9 expression in HMC was determined by qPCR, western blot and immunofluorescence. HMC viability and migration were assessed by MTT assay and transwell experiments. Collagen IV protein in the cellular supernatant was detected by ELISA. Apoptosis regulating molecules Bax and BCL-2 were assessed by qPCR and western blot.

Results: TSPAN9 was expressed weakly in normal human kidney control, in glomerular mesangial areas and luminal side of tubules. Immunostaining intensity was strong and increased in class II, III and IV DN. TSPAN9 translocated from the luminal to apical side in tubular epithelial cells, and extended to more extracellular expression in mesangial areas. In DN samples, glomerular TSPAN9 expression correlated with extent of glomerulosclerosis, hyalinosis, mesangial expansion and proteinuria, while tubular
TSPAN-9 correlated with extent of interstitial fibrosis, proteinuria and serum creatinine. In vitro, TSPAN9 HMC was significantly upregulated in mamillar and high glucose, accompanied by decreased cell viability, migration and increased apoptosis. 

Conclusions: DN was associated with increased TSPAN9 overexpression and translocation in mesangial and tubular epithelial cells, respectively, and was associated with worse renal function and more severe structural injury. 

Funding: NIDDK Support

PO0923

Lox44 Deacetylates OPA1 to Regulate Mitochondrial Dynamics During Diabetic Kidney Disease

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Background: Mitochondrial morphology is regulated by the balance between two counteracting mitochondrial processes of fission and fusion. There is significant evidence suggesting a stringent association between morphology and bioenergetics of mitochondria. Morphological alterations in mitochondria are linked to several pathological disorders, including diabetic kidney disease. The consequences of high glucose- induced acetylation of mitochondrial proteins on the organelle morphology and function remain largely unexplored.

Methods: Here, we examined the kidneys of mice with streptozotocin-induced diabetes and primary tubular epithelial cells exposed to high glucose.

Results: Using high-resolution mass spectrometry, we identified 152 hyperacetylated and 19 hypoacetylated proteins in the mitochondria from kidney tubule of diabetic mice compared with control mice. OPA1, a mitochondrial fusion protein was hyperacetylated at lysines 792 and 847 residues under high glucose-induced pathological stress and this posttranslational modification increased mitochondrial fragmentation. Overexpression of a deacetylation-mimetic version of OPA1 recovered the mitochondrial functions of OPA1-null cells, thus demonstrating the functional significance of K228/792/847 acetylation in regulating OPA1 activity. The newly discovered deacetylase hyst oxidase like 4 (Lox44) interacts with OPA1 in mitochondria. Overexpression of Lox44 prevents high glucose-induced acetylation, preserved mitochondrial networking and protected the high glucose-induced decrease of oxygen consumption rate.

Conclusions: In summary, these data indicated that hyperacetylation of OPA1 regulates mitochondrial fusion and fission under diabetes conditions. Lox44 promotes mitochondrial function by regulating mitochondrial dynamics by targeting OPA1.

Funding: Government Support - Non-U.S.

PO0924

Discovery of a Small-Molecule Drug for Treating Diabetic Kidney Disease

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Background: Diabetic Kidney Disease (DKD) is the leading cause of chronic kidney disease and one of the fastest growing epidemics worldwide. Podocyte injury is a hallmark of DKD. As such, preventing podocyte injury is necessary for effectively treating DKD. Our prior studies demonstrated that the accumulation of lipid droplets (LDs) in podocytes is associated with increased susceptibility to apoptosis in the context of DKD. Conversely, reducing LD accumulation in podocytes prevented renal disease in a mouse model of DKD (BTRB ob/ob). Thus, compounds that reduce LD accumulation may protect podocytes from injury and prevent the progression of DKD.

Methods: Advances in high throughput synthetic chemistry have enabled the design of combinatorial libraries for efficient screening and identification of novel bioactive compounds. The approach is particularly powerful when combined with a phenotypic screening assay that recapitulates disease biology. We have developed a high content screening assay to quantify LD accumulation in human podocytes in response to stress stimuli, including sera from DKD patients. Further studies to deconvolute and validate those compounds, and test them in an animal model of DKD, are underway.

Funding: Government Support - Non-U.S.

PO0925

Altered Protein Translation in the Kidney Precedes the Development of Diabetic Kidney Disease

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Background: Diabetic kidney disease (DKD) is one of the most serious complications of diabetes. Diabetes is characterized by a variety of physiologic derangements and remodeling pathways that contribute to end organ damage. The Nidkseq was done in parallel to examine transcriptional pathways of translation and augment findings from the translome.

Results: Ribo-seq in 12 week-old db/db mice and age-matched, background C57BL/6j control mice (BC) demonstrated a marked (50%) global increase in translation in kidneys from db/db mice as compared to BC mice. This findings of increased translation was further supported by polyribosomal profiling and pathway analysis of RNA-seq done in parallel. Increase of global translation was also observed as the vintage of diabetes increased from 9 weeks to 12 weeks in db/db mice. Increased translation in the kidney of diabetic animals was associated with activation of signal transduction pathways centered in cell cycle (p21), fibrogenesis (fibronectin), inflammation (tumorostatin), glucose transport (SGLT2), and oxidative stress (NOX4). Although overall transcription and translation of p53 was not observed early in diabetes, translation of Anp53 (40p53), a stress-induced translationally-regulated isoform of p53 important for development of the diabetic phenotype was found to be increased by Ribo-seq. These findings underscore the importance of examining the translome in the kidney as a missing omics layer in DKD.

Conclusions: Generalized protein translation is increased in the kidney early in the course of DKD. Pharmacological manipulation of translation may represent a novel therapeutic approach to the development and progression of DKD.

Funding: NIDDK Support

PO0926

Esculin Restores Kidneys Mitochondrial Function in the Early Stage of Experimental Diabetic Nephropathy

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Background: Diabetes mellitus (DM) is a chronic disease which progresses with many complications such as diabetic nephropathy (DN). Mitochondria are the main producer of reactive oxygen species (ROS) in a hyperglycemic condition, consuming oxygen without providing ATP to the cell. In turn, ROS act as a trigger to activation of inflammatory processes. Coumarin derivatives, as esculin, reduced oxidative damage seen in intestinal inflammation, arthritis and cognitive impairment related to diabetes. The aim of this study was to evaluate the effect of esculin on mitochondrial function and on the kidneys cortex in the DN development in rats.

Methods: DM was induced in 7-week-old male Wistar rats, using a single dose of streptozotocin (60 mg/kg, i.v) and confirmed with blood glucose 200mg/dL. The animals received daily doses of esculin (50 mg/kg, p.o) or its vehicle, during 8 weeks. After this period they were euthanized under anesthesia and the kidneys cortex were collected for histology and mitochondria isolation, to be analyzed by high resolution respirometry. Statistical analysis was performed in GraphPad Prism 6. The results are described as mean ± SEM, significance defined for *p<0.05.

Results: Esculin reduced 24 hs proteinuria in DM rats. The histological analysis of kidneys cortex showed the presence of intense inflammatory lymphomononuclear infiltrate, mild fibrosis and interstitial atrophy characterized by collagen IV deposition in diabetic animals, that were not observed in any of those treated with esculin. In addition, esculin restored mitochondrial function in the kidneys cortex of diabetic rats as analyzed by glycolysis (3.08 ± 0.17 vs 2.39 ± 0.08, p < 0.05) and β-oxidation substrates (4.75 ± 0.08 vs 3.68 ± 0.20, p < 0.05).

Conclusions: Esculin restored mitochondrial function in DM rats and probably through ROS control, reduced the kidney lesions. We suggest the use of esculin as an adjuvant therapy to control the development of DN.

Funding: Government Support - Non-U.S.

PO0927

Selonsertib Reduces TNFα-Induced Markers of Injury and Inflammation in an Organ-on-a-Chip Model of Proximal Tubular Injury

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Background: Increased circulating levels of TNF Superfamily Receptors 1 and 2 (TNFRSF1A and TNFRSF1B) in patients are associated with rapid declines in eGFR and proposed as biomarkers of DKD progression. In a phase 2 DKD trial which evaluated
safety and efficacy of the ASK1 inhibitor Selonsertib (SEL), higher serum tSNFR1 levels associated with progression to End Stage Renal Disease (ESRD). In vitro, mono-culture studies have demonstrated that ASK1 signaling is required for TNFα induced apoptosis in kidney and other organ systems. Current studies with a microfluidic organ-on-a-chip system to investigate the effects of TNFα in a kidney co-culture system and determine effect on kidney proximal tubular injury.

Methods: After populating cells in a co-culture, microfluidic device (Emulate Bio) containing either Lonza RPTEC (top channel) or kidney microvascular endothelial cells (bottom channel), TNFα (2ng/ml) was added at Day 0 along with SEL (10μM) to inhibit flow of each channel. After 7 days, RNA was isolated from each channel and gene expression analyzed by qPCR. Outlet supernatant from each channel was analyzed for kidney injury and inflammation markers on Mesoscope Discovery device (MSD). Data shown as fold-of-change or mean ± standard error of the mean (s.e.m.)

Results: TNFα increased significantly expression of both TNFRSF1α and TNFRSF1β in the RPTEC channel (1.4 and 2.6-fold, respectively vs. control), and SEL decreased TNFRSF1α expression by 108% (p=0.0058) and lowered TNFRSF1β expression by 64% (p=0.1549). SEL decreased TNFα-induced expression of IP-10 (6.4 x vs. 16.5-fold, p<0.0083) and IL-1β expression (0.67-fold vs 1.6-fold, p<0.0001) in proximal tubules. Osteoactivin and Clusterin, biomarkers used to assess proximal tubular injury were significantly increased in RPTEC supernatant following TNFα stimulation treatment (2.1 and 3.7-fold, respectively, p<0.0001 for each). SEL significantly reduced levels of osteoactivin (39.5 x vs. 778.2 ± 44.24 pg/ml, p<0.0001) and clusterin (28.9 ± 18.8 vs. 108.5 x, p<0.0001).

Conclusions: In a microfluidic, RPTEC/RPTEC co-culture model, treatment with the ASK1 inhibitor Selonsertib reduced several markers of kidney injury. Efficacy to reduce inflammatory gene expression and biomarkers of proximal tubular damage indicate SEL treatment may have potential to impact DKD progression.

Funding: Commercial Support - Gilead Sciences

PO0928

The Usefulness of Antisense Oligonucleotide Modified with Serinol Nucleic Acid for Kidney Disease
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Background: The use of nucleic acid drugs such as antisense oligonucleotides (ASOs) and siRNA has received a lot of attention as next-generation drugs. However, the development of nucleic acid drugs has been limited due to the nucleases and cell uptake. Recently, we have newly developed the serinol nucleic acid (SNA) modified ASO which had strong nuclease resistance. In this study, we investigated the in vivo efficacy of SNA-modified ASO in mouse kidney.

Methods: Various types of PS-modified gapmer ASOs with or without SNA targeting both human and murine SGLT2 (sodium glucose cotransporter 2) were tested in the immortalized human proximal tubule epithelial cell (HK-2), and subcutaneously administered into mice. Urinary and blood glucose levels, renal function, liver function and renal SGLT2 expression were analyzed.

Results: First, we confirmed that SGLT2 ASO had enough inhibitory effects of SGLT2 expression in HK-2 cells. Next, we synthesized various types of SNA gapmer SGLT2-ASO(SGLT2-SNA-ASO). Subcutaneous administration of SGLT2-SNA-ASO significantly suppressed renal SGLT2 mRNA and protein expressions and increased urine glucose in dose dependent manner. Those inhibitory effects of SGLT2-SNA-ASO were high and long-lasting compared with ASOs without SNA (SGLT2-ASO). No apparent kidney disfunction was observed. Mild and similar liver damages were found in both SGLT2-SNA-ASO and SGLT2-ASO groups. After subcutaneous administration of Cy5-labeled SGLT2-SNA-ASO, we observed the SGLT2-SNA-ASO accumulation in kidney, especially in renal proximal tubules, by in vivo imaging system (IVIS) and fluorescent microscopy.

Conclusions: Systemic administration of SGLT2-ASO modified with novel artificial nucleic acid SNA well suppressed renal SGLT2 expression and induced urinary sugar excretion. These results indicated that ASOs modified with SNA might be applied to the development of neucleic acid drugs.

PO0929

Empagliflozin Inhibits Basal and IL-1β-Mediated CCL2 and Endothelin-1 Expression in Human Proximal Tubular Cells
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Background: SGLT2 inhibitors (SGLT2i) slow the progression of type II diabetic kidney disease, however, evidence for underlying molecular mechanisms is scarce. As renoprotection is observed promptly after starting SGLT2i, we aimed at investigating pathways involved in early disease pathogenesis.

Methods: SGLT2 expression in human proximal tubular cell (HTPC) culture (HK-2 and RPTEC), microarray hybridization - Department of Internal Medicine IV, ELSA.

Results: Microarray hybridization identified 1263 genes that presented a uniform expression pattern 24h after ligand stimulation: IL-1β-mediated up- and Empagliflozin (Empa) mediated down-regulation in two HPTC lines (n=2, each). Functional annotation of these genes using DAVID enrichment analysis identified 33 pathway clusters. Based on emerging evidence of the key role of SGLT2 in cellular autophagic degradation, we focused on early autophagic gene expression during SGLT2i administration compared to control.

Conclusions: SGLT2-ASO modified with novel artificial nucleic acid SNA well suppressed renal SGLT2 expression and induced urinary sugar excretion. These results indicated that ASOs modified with SNA might be applied to the development of neucleic acid drugs.

PO0930

Comparison of the Effect of Calorie-Matched High Saturated Fat and High Unsaturated Fat Diets on Lysosomal Renal Injury in Non-Obese, Streptozotocin-Infused CD-1 Mice
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Background: Type 2 diabetes mellitus often causes renal injury characterized by autophagic vacuoles. Although many studies with comparisons of high fat versus a normal balanced diet have been reported in diabetes models, there are few studies that equalized calorie intake and body weights. We reported that a high fat diet induced renal injury with impaired lysosome-mediated autophagic degradation in streptozotocin (STZ) injected mice (ASN Kidney Week 2019). However, the effect of fat type, saturated- or unsaturated-fat, was not determined. In the current study, an AIN93M diet (CONT group) was compared to energy-matched lard derived high saturated fat (LARD group) and soybean oil derived high unsaturated fat (SOY OIL group) diets to compare their effects on biochemical markers and renal morphology with lysosome-associated membrane protein 1 (LAMP1) expression.

Methods: Male CD1 mice were randomly divided into three pair-fed groups with 380 kilocalorie/100 energy from 7 to 20 weeks of age. CONT group: AIN93M diet with 62% (w/w) cornstarch, 10% sucrose, 4% soybean oil and 5% cellulose; LARD group: Diet with 31% cornstarch, no sucrose, 22% lard oil and 28% cellulose; SOY OIL group: Diet identical to the LARD diet, except that soybean oil replaced lard oil. At 17 and 18 weeks of age, STZ (100mg/kg body wt) was injected. At 20 weeks of age, blood was taken for measurements of insulin, triglyceride, total cholesterol, ALT, AST, creatinine and SUN. Kidneys were prepared for H&E staining and immunohistochomical staining to detect LAMP1.

Results: Final body weight, total intake of water, food and energy were not different between all groups. No statistical differences in all blood biochemical markers were detected as well. In kidneys, the number of LAMP1-positive renal tubular lipid vacuoles was higher in LARD compared with SOY OIL and CONT groups, whereas no difference was shown between SOY OIL and CONT groups.

Conclusions: The results suggest that high intake of saturated-fat may aggravate lysosomal renal injury in a non-obese, streptozotocin-induced diabetes mellitus model.

Funding: Government Support - Non-U.S.
were harvested after intraperitoneal injection with 2 mL of 4% thiglycolate solution into mice. Mice possessing MGF-overexpressing plasmid was electroporated into Raw 264.7 to evaluate cytokine release and migration ability. ACE 10/10 mice was deficient of ACE in the whole body but overexpressed only in monocytes/macrophages. We induced diabetes in ACE 10/10 and wild-type mice and analyzed albuminuria or pathological changes of kidney after six months of diabetes.

**Results:** ACE mRNA was increased in peripheral blood monocytes and peritoneal macrophages from diabetic mice. LPS-induced release of IL-6 and nitric oxide was increased in macrophages overexpressing ACE. The migration ability of macrophages overexpressing ACE was higher than that of control vector-expressing cells. In diabetic ACE 10/10 mice, glomerular hypertrophy and glomerular hyperfiltration were not evident as in diabetic wild-type mice. Although ACE 10/10 mice lacks ACE in vascular endothelial cells and tubular cells, mesangial expansion and interstitial fibrosis in the kidney, and albuminuria from diabetic ACE 10/10 mice were similar to those from diabetic wild-type mice.

**Conclusions:** In diabetes, the expression of ACE in macrophage is enhanced. As a result, dysregulation of macrophage function occurred, and it may be involved in the development of diabetic kidney disease.

**PO0932**

**Transgenic Mechano-Growth Factor Overexpression in Mice Induces Glomerular PKCα and Type I Collagen with Glomerulosclerosis**

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**Background:** Mechano-Growth Factor (MGF), a normally expressed component of several positive feedback loops in the renal glomerular mesangial cells (MC), was implicated by us in the control of glomerulosclerosis. Transgenic mice overexpressing MGF (LK440-mMGF) were produced to determine the role of MGF in glomerulosclerosis (GS).

**Methods:** Our previous studies demonstrated that MGF was induced in the glomeruli of diabetic mice with subsequent induction of several factors responsible for diabetic GS. In the current study, immunohistochemistry using specific antibodies was performed to compare the expression of select glomerular proteins involved in GS, in MGF-overexpressing transgenic mice (MGF Tg) vs. non-transgenic control mice (NT). DAB staining with 0-4+ scoring in glomeruli was performed, and p < 0.05 between groups was considered significant. PAS staining was performed to assess development of overall GS. The effects of transgenic MGF overexpression on mouse body weights and kidney weights was also assessed.

**Results:** A 2.5-fold higher expression of MGF was found in glomeruli of MGF Tg as compared to NT mice. This resulted in 2.1-fold increased expression of active PKC α, a potential mediator of the 2.2-fold increased GLUT1 expression observed. These changes appeared to drive the 2.2-fold increased Collagen Type 1 (Col-I) in glomeruli. All these proscleotic factors likely contributed to the resultant GS, evidenced by 2.2-fold increased PAS positive material in MGF Tg glomeruli. All the above results were found to be significant with a P value <0.0001. Adult body weight in MGF Tg tended to be 8% higher in both males and females (NS). Mean kidney weights were 14% larger in MGF Tg vs same gender NT mice (NS).

**Conclusions:** MGF Tg displayed increased glomerular PKCα activation, Coll-I protein, and PAS-positive extracellular matrix similar to diabetic GS with increased MGF.

**Funding:** Private Foundation Support

**PO0933**

**Severe Diabetic Glomerulosclerosis in Chronic Hypoxic Housing of db/db Mice: The Role of Mesangiolysis and Podocyte Injury**

Naoki Takahashi,1 Haruyoshi Yoshida,2 Hideki Kimura,3 Kazuko Kamiyama,1 Seiji Yokoi,1 Kenji Kasuno,1 Hiroyuki Kurosawa,2 Yoshiaki Hirayama,2 Masanori Hara,1 Masayuki Iwano.1 1Fukui Daigaku Igakubu, Yoshida-gun, Fukui, Japan; 2Hyogo College of Medicine, Hyogo, Japan; 3Fukui Prefectural University, Fukui, Japan.

**Background:** Chronic hypoxia may play a pivotal role in the development of diabetic nephropathy (DN). However, the precise mechanisms underlying progressive hypoxia-induced glomerular injury remain unclear.

**Methods:** We housed db/db mice in a hypoxia chamber (12% O2) for up to 16 weeks beginning at 8 weeks of age. Various urine, serum and kidney abnormalities and glomerular mRNA expression were compared with those in age-matched db/db mice housed under normoxia.

**Results:** Levels of urinary albumin and podocalyxin (PCX) were significantly higher in hypoxic mice early during hypoxia. Ultra centrifugation of urine samples revealed that podocytes in the hypoxic mice had PCX-positive microparticles into the urine. After 16 weeks of hypoxia, the mice also had higher hematocrits with lower serum glucose and various degrees of mesangioytic glomerulosclerosis with microaneurysms and the frequent occurrence of nodular lesions. Immunohistologically, hypoxic mice showed significantly decreased endothelial cell densities early during hypoxia and decreased podocyte densities later. In both hypoxic and normoxic mice, glomerular macropoly and transforming growth factor-β1 (TGF-β1) staining significantly increased with aging, without changes in vascular endothelial growth factor or endothelial nitric oxide synthase (eNOS). Glomerular mRNA expression of monocyte chemotactrant protein-1, eNOS, and TGF-β1 was significantly enhanced in the hypoxic mice.

**Conclusions:** These results indicate that chronic hypoxia induces advanced glomerulosclerosis with accelerated albuminuria triggered by mesangiolysis and podocyte injury in a murine model of DN.

**Funding:** Commercial Support - Daiwa Securities Health Foundation, Government Support - Non-U.S.

**PO0934**

**Overexpression of Nrf2 Increases Sglt2 Gene Expression and Exacerbates Dysglycemia and Nephropathy Progression in Diabetic Transgenic Mice**

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**Background:** Nuclear factor erythroid-2 related factor 2 (Nrf2), a transcription factor abundantly expressed in renal proximal tubule cells (RPTCs), possesses cytoprotective effects. However, clinical trial with Nrf2 activator (barbodoxolone methyl) in T2D patients increased mortality, heart failure rates, heightened hypertension and albuminuria without favorable effect on end-stage kidney disease (ESKD), though the underlying mechanism(s) remain unknown. We reported previously that Nrf2 deficiency ameliorates hyperglycemia and kidney injury in diabetic Akita (T1D) mice, and we identified putative Nrf2-binding sites in the promoter of SGLT2. We here hypothesized that overexpression of Nrf2 may upregulate Sglt2 expression and contribute to nephropathy progression in diabetes.

**Methods:** We generated Akita Nrf2−/−/Nrf2295TC-Tg mice by cross-breeding Akita Nrf2 knockout mice (Akita Nrf2−/−) with Nrf2 transgenic mice (Nrf2295TC-Tg) overexpressing Nrf2 in RPTCs, studying them until age 20 weeks. Immortalized human RPTC (1HK2) stably transfected with plasmid containing SGLT2 gene promoter were also used.

**Results:** Akita Nrf2−/−/Nrf2295TC-Tg mice had increased blood glucose, glomerular filtration rate, urinary albumin-to-creatinine ratio, tubulointerstitial fibrosis and Sglt2 expression as compared to their Akita Nrf2−/− littermates. In vitro, addition of oltipraz (a Nrf2 activator) or transfection of Nrf2 cDNA increased SGLT2 mRNA expression and promoter activity in 1HK2, these effects were blocked by small interference (si) RNA of NRF2. Deletion of Nrf2-responsive elements (NRF2-REs) in the SGLT2 promoter abolished the stimulatory effect of oltipraz on SGLT2 promoter activity. Nrf2 bound to NRF2-REs of SGLT2 promoter was seen on gel mobility shift and chromatin immunoprecipitation assays.

**Conclusions:** Our results identify a novel mechanism by which NRF2 mediates hyperglycemia (oxidative stress)-stimulation of SGLT2 expression and exacerbates dysglycemia and kidney injury in diabetes.

**Funding:** Government Support - Non-U.S.
Durable Euglycemia by Intraperitoneal Administration of Allogeneic Neo-Islets, 3D Organoids of Pancreatic Islet and Mesenchymal Stem Cells, Effectively Reduces Diabetic Nephropathy in Immune-Component Non-Obese Diabetic Mice

Background: We demonstrated that the i.p. administration of allologenic “Neo-Islets” (NIs), 3D organoids of culture expanded Pancreatic Islet (PI) and Mesenchymal Stem Cells (MSC), induces permanent euglycemia without the need for anti-rejection drugs in NOD mice with auto-immune Type Diabetes mellitus (T1DM). The NIs engraft in the omentum and physiologically deliver insulin and other islet hormones into the hepatic portal system, while providing auto- and allo-immune isolation, up regulate Tregs, stimulate angiogenesis, prevent apoptosis and inflammation. As a significant percentage of patients with T1DM develop diabetic nephropathy (DNP) and other end organ damage, we tested whether the induction of stable euglycemia in NOD mice would prevent or ameliorate DNP. Methods: Three Groups of adult mice (n=7 each; ~25 g b.wt.; age 12 weeks) were examined: (1) Non-diabetic, age and sex matched C57/B16 mice; (2) Vehicle treated NOD mice with fully developed auto-immune T1DM; (3) NI treated NOD mice with normal blood glucose levels. Animals were followed for 21 weeks post treatment (blood glucose levels, body weights, blood pressures, proteinuria, renal function). Results: At the termination of the study, kidneys from all groups were examined for glomerulosclerosis and interstitial fibrosis (Trichrome staining). The vehicle treated NOD mice showed (Group 2) 2 fold higher levels of proteinuria (mg/dl), 75% lost weight, had systolic hypertension and showed extensive interstitial fibrosis, glomerulosclerosis, proteinuria, hypertrophy and elevated SCR and BUN levels, while NI treated, euglycemic NOD mice (Group 3) showed significantly lower degrees of glomerulosclerosis, interstitial fibrosis, proteinuria, hypertrophy and better preserved renal function. All tested variables remained normal in non-diabetic Group 1 control mice. Conclusions: The presented data demonstrate that therapy-induced normalization of glycemia significantly improves the manifestations of DNP without fully correcting them when compared to non-diabetic controls. Modifications in NI treatment protocols are expected to further improve the development of DNP, which, if successful, would further strengthen the translational relevance of this novel therapy. (No U of Utah resources used.) Funding: Commercial Support - SymbioCellTech, LLC

IL-17A Deficiency Attenuates Autothaphagy Formation in Streptozoto- cin-Induced Rat Diabetic Nephropathy

Background: Diabetic nephropathy (DN) is one of the most important medical complications in diabetes mellitus. Autophagy is an important mediator of pathological responses and plays critical roles in inflammation during the progression of diabetic nephropathy. The Th-17 effector cytokine interleukin (IL-17A) can favorably modulate inflammation and autoimmunity. To study this, we examined whether IL-17A deficiency affects the autophagy process in streptozocin (STZ)-induced DN in kidney. Methods: The autophagic response for IL-17A in the nephrotoxicity of STZ was evaluated by observing STZ-induced functional and histological renal injury in IL-17A−/− mice. Results: IL-17A KO STZ-treated mice were developed more severe nephrophy, exhibiting increased albuminuria, glomerular damage and renal interstitial fibrosis at 12 weeks. IL-17A deficiency also increase the up-regulation of proinflammatory cytokine and fibrotic genes expression after STZ treatment. Meanwhile, autophagy-associated proteins were upregulated in STZ wild type mice however, IL-17A KO STZ-treated mice displayed a significant decrease in these protein expression. Especially, LC3 and ATG7, which play crucial role for autophagosome formation, is notably decreased in IL-17A KO STZ-treated mice compared with their wild type counterparts. Conclusions: These results suggested that autophagy is closely related to the increased cellular stress due to IL-17A deficiency. Our study demonstrate an important role of IL17A for autophagosome formation during the progression of DN and provide a potential therapeutic target for DN. Funding: Clinical Research Support, Government Support - Non-U.S.
Systemic Therapies Targeted to Ischemia in a Model of Diabetic AKI

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Background: There is a paucity of options to treat Diabetic Kidney Disease (DKD) in the clinical practice. Halosyn is a promising biological factor for DKD. However, the role of halosyn (HA) in the development and progression of DKD as well as the precise mechanisms and consequences of HA involvement in this pathology are still to be clarified.

Methods: In this study, we assessed the effects of halosyn synthesis inhibitor 4-Methylumbelliferyl-4-MU on the development of DKD. As a model, we used the diabetic and moderately hypertensive endothelial nitric oxide synthase/leptin receptor deficient (eNOS C57BLKS/Jp) double mutant mice.

Results: At 9 weeks old, the diabetic model mice were separated into two similar groups regarding sex, body weight, non-fasting plasma glucose concentrations, and eGFR. By continuous, rather than punctual measurement of signal intensity along the PT over time against the exact tubular volume, the filtrated volume per second was achieved by rapid reperfusion increased reactive macrophages and subsequent uptake of hydroxyl dendrimers. Given the high incidence of diabetic nephropathy and higher risk for AKI in these preparations by flow cytometry.

Conclusions: A diabetic model of AKI was successfully established to evaluate targeting of hydroxyl dendrimers to reactive macrophages. Prolonged ischemia followed by rapid reperfusion increased reactive macrophages and subsequent uptake of hydroxyl dendrimers. Given the high incidence of diabetic nephropathy and higher risk for AKI in these patients, these results provided a model and treatment strategy to evaluate targeted therapies with hydroxyl dendrimer drug conjugates to treat AKI and CKD.

Funding: Commercial Support - Ashvatha Therapeutics, Inc.
Conclusions: Treatment with CCR2 antagonist provides rapid renal protection in the db/db mice in a manner independent of GFR. This observation supports earlier findings that inhibition of chemokine receptors offers new therapeutic strategies for CKD.

PO0946
In Vitro Evaluation of [18F]Canagliflozin, a Potential PET Tracer for Imaging Tissue Distribution of the SGLT2 Inhibitor Canagliflozin in Type 2 Diabetes Patients In Vivo

Background: Sodium-glucose cotransporter 2 (SGLT2) inhibitors are guideline recommended for prevention of kidney and cardiovascular outcomes in patients with diabetic kidney disease. But not all patients benefit from these agents, possibly due to differences in SGLT2 inhibitor tissue distribution. Imaging studies can assist to quantify in vivo tissue drug distribution and SGLT2 density in patients in order to unravel the underlying determinants of this response variability. The objective of this study was firstly to synthesize [18F]Canagliflozin ([18F]CANA) for human use, and secondly, to confirm its affinity for SGLT2.

Methods: [18F]CANA was synthesized by GMP compliant automated substitution of a boronic ester precursor with [18F]fluoride. Its in vitro binding with SGLT2 was tested by incubating human kidney slices with [18F]CANA alone or together with canagliflozin or glucose and analyzing them with autoradiography. [18F]CANA binding sites were compared with SGLT2 distribution using immunohistochemistry on consecutive slices.

Results: [18F]CANA radiochemical yield was 2.0% ± 1.9% within 80 min, molar activity 5.20 GBq/μmol and radiochemical purity >99%. Autoradiography shows [18F]CANA binding in kidney slices with a significant reduction in binding in presence of canagliflozin and a clear trend in reduced binding in presence of glucose (Fig 1A and B). The pattern of [18F]CANA binding on autoradiography corresponds with the distribution of SGLT2 in the apical membrane of proximal tubules as shown with immunohistochemistry (Fig 1C).

Conclusions: We showed the successful automated synthesis of the SGLT2 inhibitor [18F]CANA and its specificity to the SGLT2. Given its unchanged structure compared to the marketed compound, canagliflozin tissue distribution and SGLT2 density can now be studied in vivo in human as determinants of between-patient response variability.

Funding: Private Foundation Support, Government Support - Non-U.S.

Figure 1. A and B: [18F]CANA binding in kidney sections with autoradiography. C: [18F]CANA binding using autoradiography compared with SGLT2 distribution using immunohistochemistry.

PO0947
Exploring New Targets of Diabetic Nephropathy by Bioinformatics Analysis
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Background: The pathogenesis of diabetic nephropathy has not been fully understood and the public platform contains mass data for bioinformatics analysis.

Methods: Difference analysis and weighted gene coexpression network analysis were carried out on GSE30529 to obtain target genes and perform functional enrichment analysis. Non-coding RNA analysis was studied to understand the potential mechanism of lncRNA expression of target genes. Using STRING database to build protein-protein interaction network. Nephroseq v5 database can access gene expression characteristics and clinical characteristics.

Results: From the GSE30529, 345 genes were identified through bioinformatics analysis. GO annotations of them included neutrophil activation, regulation of immune effector process and positive regulation of cytokine production. KEGG pathways included phagosome, complement and coagulation cascades and cell adhesion molecules. From the GSE30529, 345 genes were identified through bioinformatics analysis.

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Funding: Government Support - Non-U.S.
Methods: To test if APOC3, and the dyslipidemia it represents, play a role in diabetic kidney disease (DKD) we treated BTBR wildtype (WT) and leptin-deficient (OB; diabetic) mice with an antisense oligonucleotide (ASO) to APOC3 or a control ASO (cASO), all in the setting of human-like dyslipidemia (accomplished by administration of an LDLR ASO).

Results: APOC3 ASO treatment reduced triglycerides, triglyceride-rich lipoproteins, and prevented diabetes-accelerated atherosclerosis in the brachiocephalic artery and the aorta (aortic lesion was 9.3 ± 1.5 mm² in cASO-treated OB mice compared to 4.7 ± 0.93 mm² in APOC3 ASO-treated OB mice, p<0.001, n=7-10). Intriguingly, APOC3-ASO treatment reduced diabetes-associated urinary albumin excretion but had no effect on non-diabetic mice (WT mice: 108 ± 24.0 mg urinary albumin/day, OB cASO mice: 1076 ± 219 mg/day and OB mice with APOC3 ASO: 435 ± 63 mg/day, p<0.001, n=7-14). Diabetes resulted in a dramatic increase in glomerular neutral lipid levels. Triglycerides, triglyceride-rich lipoproteins, and APOC3-accumulation, which was attenuated by APOC3 ASO-treatment. Diabetes led to a doubling of glomerular volume (4512 ± 908 µm³/glomerular volume in OB mice vs. 21775 ± 1041 µm³ in WT mice, p<0.001, n=7-14), increased glomerular PAS-staining indicative of mesangial expansion (2494 ± 332 µm² PAS-positive matrix in OB mice and 822 ± 40 µm² in WT mice, p<0.001; or from 21% in WT to 28% in diabetes, p<0.01), and a significant loss of podocytes (80 ± 8 podocytes/10⁶ µm³/glomerular volume in OB mice and 230 podocytes/10⁶ µm³/glomerular volume in WT mice, p<0.001), all of which were in part reversed by APOC3 inhibition (glomerular volume in OB mice treated with APOC3 ASO 3633 ± 2240 µm³, p<0.05; PAS area 1761 ± 131 µm², p<0.01; and podocyte density 114 ± 9 podocytes/10⁶ µm³/glomerular volume, p=0.07, all compared to OB mice treated with cASO).

Conclusions: Together, this suggests that targeting APOC3 and diabetic dyslipidemia might be beneficial for both diabetes-accelerated atherosclerosis and DKD.

Funding: NIDDK Support

PO0949
Shen-Qi-Yan-Shen Formula Attenuates Diabetic Renal Lipid Deposition by Down-Regulating Proteoglycan Expression
Viny Li, Weijian Xiong. Chongqing Traditional Chinese Medicine Hospital, Chongqing, China.

Background: Renal lipid deposition is a crucial factor in the pathophysiology of diabetic nephropathy (DN). Proteoglycan (PG) is an important component of the extracellular matrix. Shen-Qi-Yan-Shen Formula (SQYSF) is a clinical empirical formula in treating DN. In this study, db/db mice are used to explore the potential mechanism of SQYSF by down-regulating PG expression.

Methods: We divide the mice into db/db normal control group, db/db model group, SQYSF treated group, captopril treated group, and SQYSF + captopril treated group. The groups of mice are given continuous administration of saline, SQYSF, captopril or SQYSF + captopril for 12 weeks, respectively.

Results: We have revealed that treating db/db mice with SQYSF protects them against renal injury. Our finding is supported by lower blood urea nitrogen and serum creatinine and less urinary albumin in the treated mice compared with the saline-treated db/db controls. Mice treated with SQYSF have significantly reduced protein levels of fasting blood glucose (FBG), HbA1c, TG, LDL-c and HDL-c. SQYSF markedly down-regulates protein expression of proteoglycan (PG), apoB and LDL receptor in the db/db mice. In addition, captopril exhibits a partial inhibitory effect on PG and other proteins, which can be enhanced by SQYSF.

Conclusions: SQYSF may protect db/db mice by relieving lipid deposition through the down-regulation of PG. These encouraging results corroborate SQYSF’s potential of becoming a novel therapeutic strategy for diabetic nephropathy.

Funding: Government Support - Non-U.S.

PO0948
Apolipoprotein C3 Inhibition Reduces Diabetic Kidney Disease and Atherosclerosis in a Mouse Model
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Background: Diabetes increases the risk of cardiovascular disease and kidney disease. Importantly, the majority of the excess cardiovascular risk in people with diabetes is observed in those who also have kidney disease. Apolipoprotein C3 (APOC3) is a small lipoprotein that is elevated by insulin-insufficiency and regulates plasma triglyceride levels.

Conclusions: Together, this suggests that targeting APOC3 and diabetic dyslipidemia might be beneficial for both diabetes-accelerated atherosclerosis and DKD.

Funding: NIDDK Support

PO0949
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Viny Li, Weijian Xiong. Chongqing Traditional Chinese Medicine Hospital, Chongqing, China.

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Methods: We divide the mice into db/db normal control group, db/db model group, SQYSF treated group, captopril treated group, and SQYSF + captopril treated group. The groups of mice are given continuous administration of saline, SQYSF, captopril or SQYSF + captopril for 12 weeks, respectively.

Results: We have revealed that treating db/db mice with SQYSF protects them against renal injury. Our finding is supported by lower blood urea nitrogen and serum creatinine and less urinary albumin in the treated mice compared with the saline-treated db/db controls. Mice treated with SQYSF have significantly reduced protein levels of fasting blood glucose (FBG), HbA1c, TG, LDL-c and HDL-c. SQYSF markedly down-regulates protein expression of proteoglycan (PG), apoB and LDL receptor in the db/db mice. In addition, captopril exhibits a partial inhibitory effect on PG and other proteins, which can be enhanced by SQYSF.

Conclusions: SQYSF may protect db/db mice by relieving lipid deposition through the down-regulation of PG. These encouraging results corroborate SQYSF’s potential of becoming a novel therapeutic strategy for diabetic nephropathy.

Funding: Government Support - Non-U.S.
Circulating MicroRNAs Associated with Hyperglycemia and Their Effects on Renal Function Decline in Type 2 Diabetes: Global miRNome Analysis

Background: It has been reported that microRNAs (miRNAs) play an important role in the pathogenesis of diabetic complications. We aimed to search for circulating miRNAs that were associated with hyperglycemia in type 2 diabetes (T2D) and examine their effects on renal function decline.

Methods: Using the next-generation sequencing-based HTG EdgeSeq miRNA platform, a total of 2,083 miRNAs were measured in baseline plasma specimens obtained from 73 subjects with T2D and normal renal function (discovery panel), and 136 subjects with T2D and impaired renal function (replication panel). Subjects in both panels were followed for 6-12 years to determine eGFR decline.

Results: We identified 11 candidate miRNAs that were strongly associated with elevated levels of glycated hemoglobin (HbA1c) in both screening and replication panels. Using bioinformatic analyses, we found that the candidate miRNAs targeted proteins of 6 pathways (the Ras signaling pathway, Signaling pathways regulating pluripotency of stem cells, the MAPK pathway, Glutamatergic synapse, the Rap 1 signaling pathway, and the AMPK signaling pathway). Importantly, 4 of these 11 miRNAs were significantly associated with risk of renal function decline.

Conclusions: There were few previous reports about the association between circulating miRNAs, hyperglycemia, and diabetic kidney disease in T2D. The present study comprehensively examined and identified hyperglycemia-regulated miRNAs in human samples. Our findings are novel in that circulating miRNAs regulated by hyperglycemia are associated with risk of eGFR decline in T2D.

Funding: Other NIH Support - National Institutes of Health (DK041526-23). Commercial Support - Novo Nordisk Foundation (NNF14OC0013659)

Longitudinal Changes in Plasma Biomarkers and Diabetic Kidney Disease Progression in VA NEPHRON-D
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1Johns Hopkins University, Baltimore, MD; 2Mount Sinai, New York, NY; 3VA Pittsburgh Healthcare System, Pittsburgh, PA; 4UMCG, Groningen, Netherlands.

Background: Pathways of inflammation are central to the pathogenesis of diabetic kidney disease (DKD). We previously reported in VA NEPHRON-D that higher baseline levels of soluble tumor necrosis factor receptors 1 and 2 (stTNFR1, stTNFR2) and kidney injury molecule-1 (KIM-1) were associated with DKD progression. Whether longitudinal changes in these and other promising biomarkers are also associated with subsequent kidney function decline is unclear.

Methods: We measured 6 plasma biomarkers (sTNFR1, sTNFR2, KIM-1, interleukin-18 [IL-18], monocytic chemotactic protein-1 [MCP-1], chitinase-3-like protein-1 [YKL-40]) at baseline and 12 mths. Using Cox models, we studied associations of each biomarker (at baseline, at 12 mths, and relative change from baseline to 12 mths) with kidney function decline (first occurrence of eGFR decrease ≥30 ml/min/1.73 m² or >50% if randomization eGFR ≥60 and <60, respectively, or ESRD), adjusting for biomarker, sex, race, treatment arm, BMI, HgbA1c, eGFR, UACR at baseline and 12 mths, systolic BP, eGFR, UACR at 12 mths. We excluded events before 12 mths (n=5).

Results: Of 754 VA NEPHRON-D participants with baseline and 12-mth plasma samples, mean eGFR=57 ml/min/1.73 m² and median UACR=0.8 g/g. Over a median follow-up of 2.5 yrs, 118 (16%) had kidney function decline. Compared to quartiles 2,3, the highest quartile of Delta stTNFR1, stTNFR2, KIM-1, and YKL-40 had 1.7 to 2.0-fold greater risks and the lowest quartile of delta MCP-1 had 52% lower risk of kidney function decline. Higher baseline and 12-mth biomarker levels were also associated with DKD progression [Figure].

Conclusions: Repeated measures of several plasma biomarkers in patients with DKD provided additional prognostic information even after adjusting for baseline biomarker levels, clinical variables, and time-updated eGFR and UACR.

Funding: NIDDK Support, Veterans Affairs Support
PO1053
Renal, Cardiovascular (CV), and Safety Outcomes of Canagliflozin (CANA) According to Baseline Albuminuria: A CREDENCE Secondary Analysis

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Background: Albuminuria is a risk factor for kidney disease progression and CV disease. We examined the relative and absolute effects of CANA by baseline albuminuria among CREDENCE participants.

Methods: CREDENCE was a double-blind, randomized study of 4401 participants with eGFR 30-<90mL/min/1.73m² and uACR >300-5000mg/g who demonstrated that CANA significantly reduced renal and CV outcomes, including the primary composite of end-stage kidney disease, doubling serum creatinine, or renal or CV death. We analyzed the effect of CANA on renal, CV, and safety outcomes by baseline uACR.

Results: At baseline, 2348 (53.4%), 1547 (35.2%), and 506 (11.5%) participants had uACR ≤300, >300–<1000, ≥1000–<3000, ≥3000mg/g. Higher uACR was associated with higher event rates (Figure). CANA reduced renal and CV endpoints, with no statistical variation by uACR (all p heterogeneity >0.17). CANA led to a greater absolute reduction in renal events in those with higher uACR (number needed to treat to prevent 1 episode of the primary composite: 22 and 8 for uACR >1000–<3000 and ≥3000mg/g). Rates of renal-related adverse events were lower with CANA, and the relative reduction was greater with higher uACR (p heterogeneity=0.003). CANA had no significant effect on acute kidney injury, volume depletion, hyperkalemia, urinary tract infections or hypoglycemia, with no differences by uACR (all p heterogeneity=0.12).

Conclusions: CANA safely reduces renal and CV events in people with type 2 diabetes and substantial albuminuria, with the greatest absolute renal benefit in those with uACR of 3000-5000mg/g.

Funding: Commercial Support - Janssen Scientific Affairs, LLC.

PO1054
Lower Cardiorenal Risk with SGLT2 Inhibitor vs. DPP4 Inhibitor in Type 2 Diabetes Patients Without Established Cardiovascular and Renal Diseases

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Background: Cardiorenal disease, defined by chronic kidney disease (CKD) or heart failure (HF), is a frequent disease manifestation associated with serious risks in T2D patients. We compared new use of sodium-glucose cotransporter-2 inhibitor (SGLT2i) vs. dipeptidyl peptidase 4 inhibitor (DPP4i) and the risk of cardiorenal disease in T2D patients without history of established cardiovascular and renal disease, defined as CRED-Rfree.

Methods: In this observational cohort study, patients were identified in health care databases in England, Germany, Japan, Norway, Sweden, and South Korea between the years 2012 and 2018. New users of SGLT2i were propensity score matched 1:1 with users of DPP4i. Unadjusted Cox regressions were used to estimate hazard ratios (HRs) for outcomes; cardiorenal disease, HF, CKD, stroke, myocardial infarction (MI) cardiovascular (CV) - and all-cause death (ACD).

Results: Baseline characteristics were well balanced between the treatment groups (n=105,130 in each group) with mean follow up of 1.5 years and 315,015 patient-years. The distribution of follow-up time for SGLT2i and DPP4i types was, dominated by dapagliflozin (91.7%) and sitagliptin/inagliptin (55.0%). SGLT2i was associated with lower risk of cardiorenal disease, HF, CKD, CV- and all-cause death, HR (95% CI) 0.56 (0.42-0.74), 0.71 (0.59-0.86), 0.44 (0.28-0.69), 0.67 (0.59-0.77) and 0.61 (0.44-0.85) respectively. No differences for stroke (0.87 [0.69-1.09]) and MI (0.94 [0.90-1.11]).

Conclusions: In this large multinational observational study of CRED-Rfree T2D patients, the unique preventive effects of SGLT2is on cardiorenal disease reported from clinical trials are confirmed in a real-world setting.

Funding: Commercial Support - AstraZeneca.

PO1055
In Patients with Biopsy-Proven Diabetic Nephropathy, 38% Have a Second Significant Diagnosis

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Background: AIM: determine the renal biopsy (Bx) incidence of a second kidney disease (2nd DX) in patients (Ps) with diabetic nephropathy (DN) Bx ed for various clinical indications.

Methods: Of 45,422 non-transplant cases received from 2001-2014 (2222 nephrologists, 39 states), 7,746 Pts with DN were found. 1,749 cases were excluded for insufficient data. 1,398 cases with FSGS were excluded (separate study). 4,599 cases were analyzed (age range: 8 - >89 years; males 53.5%). Bx indication: acute kidney injury (AKI), acute nephritic syndrome (ANS), rapidly progressive renal failure (RPRF), hematuria (Heme), suspect a non-DN renal disease (Non-DN), sudden increase in
PO0956

A Clinical and Pathological Study on Association of 4-Hydroxynonenal with Diabetic Kidney Disease
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Background: To explore the potential correlation between plasma 4-HNE level, tubulointerstitial 4-HNE deposition and DKD renal tubular atrophy during disease progression.

Methods: 59 patients with clinical diagnosis of DKD and 11 normal control were collected in the First Affiliated Hospital of Jinan University from Dec 2018 to Dec 2019. The 59 patients were divided into CKD phase 1-3, 4-5 according to the estimate glomerular filtration rate (eGFR). Oxidative stress indicators 4-HNE, superoxide dismutase (SOD) were measured in DKD patients. 34 cases of diabetic nephropathy (DN) diagnosed by biopsy in the hospital were divided into 3 groups (CKD 1-2, 3-4, 5-6). Biopsy cases were subjected to 4-HNE immunohistochemical staining. Univariate and multivariate logistic regression analysis was performed to identify independent risk factors of DKD incidence, and establishment of DKD eGFR multiple linear regression model was made.

Results: Compared with the normal group, oxidative stress index 4-HNE gradually increased in CKD phase 1-3, 4-5 groups, but SOD gradually decreased (P < 0.05). Logistic regression analysis found that plasma 4-HNE is an independent risk factor for DKD. (P < 0.008; OR = 1.003, 95% CI 1.001–1.006) Pearson correlation analysis showed that plasma 4-HNE levels were positively correlated with systolic blood pressure, mean arterial pressure, urea nitrogen, cystatin C and creatinine, and negatively correlated with hemoglobin and eGFR. The eGFR multiple linear regression model showed that eGFR is independently negatively correlated with tubulointerstitial 4-HNE expression (ß = 0.50, P < 0.001). Urea, history of hypertension, renal tubular atrophy, and independently positively correlated with hemoglobin (ß = 0.84, P < 0.001). Variance analysis revealed that there was a statistically significant difference between tubulointerstitial 4-HNE staining scores with the degree of renal tubular atrophy and interstitial infiltrates. (P < 0.05)

Conclusions: In the progression of DKD, tubular atrophy, anemia, hypertension were associated with oxidative stress, based on serum and staining of 4-HNE. Staining of 4-HNE can be used as a predictor of renal dysfunction, which may be related to tubular atrophy and interstitial infiltrates. 4-HNE is an independent risk factor for progression of DKD.

Funding: Clinical Revenue Support

PO0957

Association of Renal Pathological Lesions and Renal Prognosis in Patients with Diabetic Nephropathy and Effect Modification by Proteinuria
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Background: There are few detailed studies on renal pathological findings in diabetic nephropathy (DN) with low urinary protein (UP). We examined whether the association of renal histology with renal prognosis was modified by UP levels in DN diagnosed by renal biopsy.

Methods: The total of 396 participants diagnosed with DN by renal biopsy were divided into 2 groups by the level of UP; ≥0.5 g/day (high-UP group, n = 197) or <0.5 g/day (low-UP group, n = 199). The association of glomerular lesion (GL) and interstitial/tubular lesion (IFTA) with incidence of end-stage kidney disease (ESKD) was examined using Cox proportional hazard model with the adjustment for confounding factors in each proteinuria group.

Results: Compared to high-UP group, low-UP group had a higher eGFR (median [interquartile range (IQR)]; 66 [48, 89] mL/min/1.73m² vs 49 [31, 70], p < 0.001), lower systolic blood pressure (128 [112, 140] mmHg vs 140 [126, 154], p < 0.001), lower prevalence of severe GL (6.1% vs 56.8%, p <0.001) and IFTA (12.2% vs 61.3%, p <0.001). During a median [IQR] observation period of 8.3 [3.9, 17.6] years, 14 and 78 patients reached ESKD in low-UP and high-UP groups, respectively. Cox hazard model adjusted for confounding factors showed that both GL and IFTA were significantly associated with renal prognosis in the high-UP group, whereas only IFTA showed significant association in the low-UP group. The association of IFTA with renal prognosis was consistent (p for interaction = 0.45), but that of GL was significantly different between the two groups (p for interaction <0.01).

Conclusions: IFTA is consistently associated with renal prognosis regardless of UP levels, but GL is associated with renal prognosis only in patients with overt UP.

PO0958

Comprehensive Ultrastructural Analysis Strongly Predicts Kidney Function Decline in the Multicenter TRIDENT COHORT
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Background: While diabetic kidney disease (DKD) is responsible for more than half of all chronic and end stage kidney disease (ESKD), the association of light (LM) and electron microscopical (EM) structural changes with clinical parameters and prognosis in late stage DKD is not completely determined.

Methods: TRIDENT (Transformative Research in Diabetic Nephropathy) is a multicenter observational cohort aimed to identify changes associated with kidney function decline in an unbiased manner. Sixty-two patients diagnosed with biopsy-confirmed DKD were enrolled. Digital scans of biopsy slides and EM were scored for twelve LM and EM parameters and had the fastest eGFR decline, while cluster 1(N=25) had the slowest eGFR parameters. Demographic and clinical features of the patients were recorded at enrollment and patients were followed-up every six months.

Results: The median estimated glomerular filtration rate (eGFR) was 28.91(20.87 ml/min/1.73m²) and the urine protein to creatinine ratio (UPCR) at enrollment was 1.64(7.25) mg/mg. During a mean follow-up time of 10.6 months, the median change in eGFR was -25.8(58) % and median fold change in UPCR was 1.29(2.15) and 17 patients progressed to ESKD. Multiple linear regression analysis revealed that interstitial fibrosis independently associated with eGFR at enrollment. Glomerular lesions including global glomerulosclerosis and mesangiolysis were associated with eGFR decline. Foot process effacement significantly associated with UPCR at enrollment and mesangial hyalinosis predicted UPCR fold change. Unbiased clustering analysis identified three disease subgroups of which cluster 2(N=11) showed more pronounced damage by LM and EM parameters and had the fastest eGFR decline, while cluster 1(N=25) had the slowest eGFR decline and the least severe structural lesions. Cox regression analysis showed that the subjects in cluster 2 had the highest risk to reach ESKD (HR=14.8, 95%CI; 1.76-123.73, p=0.01).

Conclusions: This study confirms association of structural and clinical parameters even in late stage DKD. Furthermore, it highlights specific ultrastructural features that can strongly predict kidney function decline.
The Association Between Kidney Biopsy Findings in Diabetic Patients and Renal Replacement Therapy Initiation

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Background: Diabetic Kidney Disease (DKD) is the leading cause of Chronic Kidney Disease (CKD) worldwide. Nevertheless, about a third of type 2 diabetic patients with kidney involvement have Non-Diabetic Kidney Disease (N DKD). The distinction between DKD and N DKD can only be done accurately with kidney biopsy. There is lack of evidence in regards to the association between N DKD and CKD progression. The objective of the study was to evaluate the association of DKD, N DKD or both with Renal Replacement Therapy (RRT) initiation.

Methods: This is a retrospective study of patients with T2DM who underwent a kidney biopsy between 2006 and 2019 at the Department of Nephrology at the National Institute of Cardiology in Mexico City. The included patients were followed for five years or until start of RRT. According to presence of diabetic nephropathy and non-diabetic glomerular disease, three groups were identified: group 1: patients with DKD, group 2: patients with N DKD and group 3: patients with combined DKD and N DKD.

Results: A total of 141 DM patients were included, the mean age was age 52.4 ± 12.2 years and 48.2%. The main indication for kidney biopsy was nephrotic proteinuria in 46 patients (32.6%), rapidly impaired kidney function in 23 patients (16.3%), nephrotic syndrome in 24 patients (17%) and suspicion of other glomerulopathies in 4 patients (2.8%). Based on kidney biopsy findings, 53 (39.1%) had DKD, 13 (9.2%) had N DKD and 75 (53.5%) had both DKD and N DKD. One hundred and two (72%) of the RRT cases occurred within the first five years.

Conclusions: Kidney biopsies is this population could be of use in order to risk stratify this population. Subjects with the combination of DKD and N DKD have the worst renal prognosis.
Phosphorylated Akt (pAkt) and Myostatin: The Yin and Yang of the Muscle Response in Diabetes

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Background: Muscle wasting is common in patients with diabetic kidney disease (DKD). Both uremia and diabetes cause inflammation and insulin resistance in skeletal muscle, thus promoting wasting. However, the muscle response in DKD is not known yet. Our aim was to evaluate the intracellular signals controlling protein synthesis and degradation in muscle of patients with DKD.

Methods: We studied intracellular pAkt (a downstream effector of the insulin signal), myostatin (MSTN), p38MAPK, MURF and Atrogin in skeletal muscle of patients with diabetic CKD (DKCKD) (n=17, age 69 years ± 7, eGFR 9 ± 3 ml/min/1.73m²) as compared to non diabetic CKD (NDCKD) (n=32, age 67 years ± 11, eGFR 7.5 ± 2 ml/min/1.73m²) and controls (C) (n=24, age 67 years ± 11, eGFR 77 ± 13 ml/min/1.73m²).

Results: The expression of pAkt was significantly more downregulated in DKCKD as compared to NDCKD and C (P <0.05). MSTN expression was significantly lower in C as compared to DKCKD and NDCKD (P<0.05). MSTN mRNA was similarly upregulated in DKCKD and in NDCKD with respectively a 21- and a 18-fold increase compared to controls. Atrogin and Murf mRNA were both upregulated in DKCKD and in NDCKD; in DKCKD Murf mRNA presented a 18- and atrogin mRNA a 16-fold increase compared to controls. Atrogin and Murf mRNA were both upregulated in DKCKD and in NDCKD with respectively a 21- and a 18-fold increase compared to controls. The expression of pAkt was significantly more downregulated in DCKD as compared to NDCKD and C and western blot, mRNA expression (MSTN, Murf, Atrogin) by r-PCR.

Conclusions: With respect to non DKD, intracellular insulin signaling is particularly blunted in muscle of patients with DKD, while myostatin is similarly overexpressed. In diabetes, the abnormal pAkt levels in conjunction with myostatin overexpression are likely to orchestrate the wasting syndrome.

New Diagnostic Model for the Differentiation of Diabetic Nephropathy from Non-Diabetic Nephropathy in Chinese Patients

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Background: The differential diagnostic criteria of non-diabetic nephropathy (NDRD) and diabetic nephropathy (DN) usually depend on the 2007 KDOQI guideline, which is not accurate enough. Renal pathological biopsy is the gold standard for diagnosis, which is an invasive method and may cause several complications. This study aimed to construct a new noninvasive evaluation method for the differentiation of DN and NDRD.

Methods: We retrospectively screened 1030 patients (January 2005-March 2017). Variables were ranked in terms of importance, and random forest (RF) and support vector machine(SVM) were then used to construct the models. The final model was validated using an external group (338 patients, April 2017-April 2019), and compared with previous models.

Results: A total of 929 patients were assigned for model development. Ten variables were selected for model development. The area under the receiver operating characteristic curve (AUCROC) for the RF and SVM methods were 0.953 and 0.947. A total of 329 patients were analyzed for external validation. The AUCROC for the external validation of the RF and SVM method were 0.920 and 0.911.

Conclusions: We successfully constructed predictive model for DN and NDRD by machine learning methods, which were better than traditional ways.

Funding: Government Support - Non-U.S.

Performance for SVM and other models in external validation
PO0965

A Simulation Model for CKD Progression Among Patients with Type 2 Diabetes in the United States

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Background: Patients with type 2 diabetes (T2D) and chronic kidney disease (CKD) are at a higher risk of end-stage renal disease (ESRD), cardiovascular diseases and mortality. Modeling CKD progression in patients with T2D can help guide disease management for reducing clinical and economic burdens of CKD.

Methods: We developed a discrete-state and discrete-time microsimulation model for predicting changes of underlying risk factors over time and the progression of kidney disease, coronary heart disease, and cerebrovascular disease among patients with T2D and CKD. Transition probabilities were modeled as patient-level characteristics and risk factors, current disease state, and treatment status, with model parameters derived from individual-level data and summary data in published literature. Changes in risk factors for ESRD (urine albumin to creatinine ratio [UACR]), estimated glomerular filtration rate [eGFR]), and risk equations for ESRD, myocardial infarction (MI), congestive heart failure (CHF), stroke, and death without ESRD were developed using longitudinal data of a T2D subpopulation in the Chronic Renal Insufficiency Cohort (CRIC). This model underwent calibration and validation against the CRIC patients with T2D and CKD over a 7-year follow-up period.

Results: At baseline, 1,441 CRIC participants with T2D and CKD (mean age: 61.6 years) were available for model development and validation. Concordance between observed and predicted outcomes for the five risk equations ranged from 0.71 to 0.90. The simulated event rates of ESRD, CHF, MI and stroke using estimated changes in key risk factors, and the related 95% confidence intervals covered the observed event rates in CRIC.

Conclusions: The model provided reliable estimates of disease progression among T2D patients with CKD. Modeling disease progression in this population will allow assessment of the impact of early detection and interventions, which may alter the economic and quality of life burden of CKD.

Funding: Commercial Support - Bayer US LLC

PO0966

Joint Model of eGFR Slope: Data from LEADER in Patients with Type 2 Diabetes and High Risk of Cardiovascular Events

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Background: The LEADER cardiovascular (CV) outcome trial (NCT0179048) suggested liraglutide provides renal benefits vs placebo in patients with type 2 diabetes and high CV risk. Aiming to improve the modeling of eGFR slope (surrogate marker of renal outcomes), this post hoc analysis compared a joint model with the usual random slope model.

Methods: Two models were applied: 1) random slope model for eGFR using an effect modifier for treatment (liraglutide vs placebo) in change from baseline; 2) joint model using two processes (the same random slope model and a hazard model for time to a composite endpoint [all-cause death or ESRD]). These processes were correlated using a composite endpoint [all-cause death or ESRD]). These processes were correlated using a joint slope model. It did not change the liraglutide vs placebo treatment effect. Joint modeling may be useful in analyzing future trial data.

Funding: Commercial Support - Novo Nordisk A/S

PO0967

Large Database Longitudinal Assessment of Electrolyte Abnormalities in Diabetic Patients Receiving SGLT2 Inhibitors

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Background: In diabetic patients, the osmotic diuresis and natriuresis induced by sodium glucose co-transporter 2 (SGLT2) inhibitors produces changes in the level of electrolytes such as potassium, magnesium and calcium. Incidence of electrolyte abnormalities induced by these agents in a ‘real-world’ setting has not been studied.

Methods: We included all patients with diabetes who were prescribed canagliflozin, empagliflozin or dapagliflozin at our healthcare system between 2012-2019. Demographics, baseline medication use, comorbidities, and laboratory values were obtained by querying a centralized research repository. Serum electrolyte levels at SGLT2 inhibitor initiation were compared to electrolyte levels in the 6 months after initiation and the most extreme post-baseline levels were used to determine incidence of electrolyte abnormalities.

Results: In total, 1630 patients were included. Average age was 61 (SD 11) years, 63% identified as male, 71% as white. Hypertension was present in 85%, congestive heart failure in 20%; 18% had an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² and 12% had uncontrolled diabetes (A1C>10g/dL). ACE inhibitor/ARB use was present in 80% and 5% of patients (n=81) had elevated potassium (>5mEq/L) at baseline. In the first 6 months after drug initiation in patients without elevated potassium at baseline (n=1549), 12% experienced new hyperkalemia (>5 mEq/L) with 4% of patients experiencing a potassium level >5.5 mEq/L. Potassium >6 mEq/L was seen in 1%. Ten percent of patients with eGFR<60 mL/min/1.73 m² experienced hyperkalemia when compared to 21% of patients with eGFR>60 mL/min/1.73 m² (p<0.01). Hypomagnesaemia (<1.5 mg/dL) was present in 12% of patients, with values <1.30 mEq/L seen in 2%. Hypomagnesaemia (<1.5 mg/dL) was present in 3% and hypocalcemia (albumin-corrected calcium<7 mg/dL) was seen in 0.1%.

Conclusions: Patients with eGFR<60 mL/min/1.73 m² are particularly at high risk of developing hyperkalemia post-SGLT2 initiation. Effective monitoring and treatment strategies are needed to mitigate risks associated with hyperkalaemia.

Funding: Commercial Support - Relypsa Fellowship grant

Incidence of electrolyte abnormalities (%) (Table 1)

<table>
<thead>
<tr>
<th>Electrolyte Abnormality</th>
<th>Incidence (%)</th>
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<tbody>
<tr>
<td>Hyperkalemia (&gt;5 mEq/L)</td>
<td>12%</td>
</tr>
<tr>
<td>Hypokalemia (&lt;3 mEq/L)</td>
<td>1%</td>
</tr>
<tr>
<td>Hypomagnesaemia (&lt;1.5 mg/dL)</td>
<td>12%</td>
</tr>
<tr>
<td>Hypocalcemia (&lt;7 mg/dL)</td>
<td>0.1%</td>
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PO0968

Hyperkalaemia Risk and Mortality in Patients with Diabetes

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Background: Diabetes mellitus (DM) is associated with micro- and macrovascular complications, including chronic kidney disease (CKD) and cardiovascular events. Renin-angiotensin-aldosterone system inhibitors (RAASIs) are recommended for the management of these conditions; however, their usage may increase the risk of hyperkalaemia (HK), a potentially fatal electrolyte imbalance.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Methods: Patients with type 1 or 2 DM aged ≥18 years were identified from linkage primary and secondary care data from the UK Clinical Practice Research Datalink and Hospital Episode Statistics, respectively. DM and relevant complications/comorbidities (CKD, history of major adverse cardiovascular events [MACE] comprising arrhythmia, heart failure, myocardial infarction and stroke) were identified through READ codes recorded between 10/1999 to the index date (2008–June 2018) or the five-year look-back period (2003–2007). Index date was the latter of 1st January 2008 or initial DM diagnosis. Event rates (adjusted for age and sex) of HK (serum potassium [SK] ≥5.0 mmol/L; ≥5.5 and ≥6.0 mmol/L were also explored) and all-cause mortality (ACM) were estimated over the follow-up period (from the end of comorbidity assessment to the first of: death, loss to follow-up, end of study). Accumulation of complications/comorbidities over time resulted in re-classification.

Results: 288,871 DM patients were included with a mean follow-up of 5.87 years (standard deviation [SD] 3.23) years. Available follow-up (1,000 patient-years [PYs]) was 1,038 ± 5 years for DM + CKD + MACE and 89 for DM + CKD + MACE. ACM incidence increased in line with increasing comorbidity burden, to 146.73 ± 1.000 PYs in the DM + CKD + MACE cohort. At the SK threshold of ≥5.0 mmol/L, the incidence of HK was highest in patients with CKD (779.27±63.26 per 1,000 PYs with/without MACE, respectively) and lower in patients without CKD (384.13±2.65 per 1,000 PYS with/without MACE, respectively). The same between-cohort pattern was observed at thresholds of ≥5.5 and ≥6.0 mmol/L. CKD and/or CKD + MACE + ACM incidence increased with increased risk of HK and ACM. Routine monitoring of HK and prompt management of HK episodes could improve clinical outcomes in DM patients, particularly those with CKD and/or a history of MACE.

Funding: Commercial Support - AstraZeneca

PO0971
Advanced CKD Augments the Risk of Hypoglycemia with Insulin Use
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Background: Both insulin use and CKD are known risk factors for hypoglycemia in type 2 diabetes (T2D) but it is unclear whether advanced CKD augments the risk of hypoglycemia with insulin use.

Methods: We analyzed a national veteran cohort (N = 944,891) with T2D defined by ICD-9 codes and outpatient serum creatinine measurements from 1/2008 to 12/2010. Index date was defined as the date of first outpatient serum creatinine measurement. Duration of T2D was calculated by the first occurrence of ICD-9 codes for T2D; HbA1C >6.5% or use of anti-diabetic meds from 10/1999 to the index date. Baseline comorbidities were similarly defined by ICD-9 codes. Insulin use at index date was determined by prescription data. Hypoglycemic episodes requiring medical attention were defined by ICD-9 codes and ≥2 mmol/L decrease in HbA1C index date until 2/2016. A multivariate logistic regression model of basal insulin was used to relate baseline insulin use and CKD stages with subsequent hypoglycemic episodes in Cox regression models.

Results: Baseline mean age was 65.1±11 yrs, 19% black and mean eGFR 71±24. There were 16,648 of hypoglycemic episodes over 1,529, 224 years of follow up. There was a trend increase in incidence rate of hypoglycemic events by CKD stages and insulin use (Fig). In a Cox regression model adjusted for propensity scores as well as above covariates, compared to <eGFR 90 with no insulin use (Fig), the risk of serious hypoglycemic episodes was highest in the stage 4/5 CKD group on insulin (HR 4.79, 95% CI 4.13 to 5.32). Interaction p = 0.018 for insulin use and CKD stages for the risk of hypoglycemia.

Conclusions: Advanced CKD augments the risk of hypoglycemia with insulin use. Whether novel anti-diabetic agents are safer than insulin for the risk of hypoglycemia in advanced CKD needs to be studied.

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PO0972
The Effect of Microalbuminuria in Long-Term Outcomes in Elderly Patients with Diabetes
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Background: In current aging society, the number of elderly diabetes is rapidly growing worldwide. Despite strong evidence on the prognostic power of microalbuminuria in patients with diabetes, it remains uncertain that moderately increased urinary albumin excretion can identify elderly diabetes at high risk of ESRD (end stage renal disease) or mortality. This longitudinal study evaluated incidence of ESRD and mortality according to albuminuria amounts focusing on elderly diabetes.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PB - Publication Only

Underline represents presenting author.
Methods: We retrospectively identified 3,065 elderly (aged ≥65 years) diabetes. The primary outcomes were incidence of ESRD (considering competing risk with death) and all-cause death. The association between albuminuria (normoalbuminuria, urine albumin to creatinine ratio [uACR] <30 mg/g, microalbuminuria, uACR 30-300 mg/g, and macroalbuminuria, uACR >300 mg/g) and outcomes focusing on elderly (≥75 years) and very elderly (≥75 years) with diabetes were evaluated.

Results: The age was 71.1 (5.0) years and the duration of diabetes was 13.4 (8.7) years. Median follow-up duration was 89 (19.6) months. Overall, microalbuminuria and macroalbuminuria were observed in 25.5% and 9.4% of subjects, respectively. For normoalbuminuria, microalbuminuria, and macroalbuminuria, probability of ESRD and cumulative all-cause death at 8 years was 1.0%, 6.3%, and 29.7% (P<.0001), and 13.1%, 27.4%, and 31.7% (P<.0001), respectively. Using proportional-hazards regression models, albuminuria amounts were independently associated with increased risk of ESRD (fully adjusted hazard ratios [HR]: including kidney function: 3.92 [1.29-6.70] for microalbuminuria, 11.16 [6.47-19.24] for macroalbuminuria). The HR of all-cause death among subjects with BP levels 3 and 4 were 1.46 (1.21-1.76) for microalbuminuria and 1.42 (1.08-1.86) for macroalbuminuria. The associations between albuminuria amounts and the risk of ESRD and all-cause death were consistent in very elderly (≥75 years).

Conclusions: We demonstrated that microalbuminuria is a risk factor of incident ESRD and death even in elderly diabetes, as well as in very elderly. Further studies are needed to determine whether albuminuria can be a therapeutic target in this population.

PO0973
Risk of Cardiovascular Disease, CKD, and Cardiovascular Mortality According to 2017 ACC/AHA Blood Pressure Categories in Diabetes Miryung Kim, Jun Young Lee, Jae Won Yang, Seung-Ok Choi, Jae seok Kim, Minseob Eom, Hanwul Shin. Yonsei University Wonju College of Medicine, Wonju, Republic of Korea.

Background: The association between blood pressure (BP) and cardiovascular disease (CVD) and chronic kidney disease (CKD) in diabetes patients remains unclear.

Methods: By using an analysis based on the National Health Insurance Database of Korea, 8,922,940 persons were screened between 2009 to 2014. We determined the disease (CVD) and chronic kidney disease (CKD) in diabetes patients remains unclear.

Results: We demonstrated that microalbuminuria is a risk factor of incident ESRD and death even in elderly diabetes, as well as in very elderly. Further studies are needed to determine whether albuminuria can be a therapeutic target in this population.

Conclusions: We demonstrated that microalbuminuria is a risk factor of incident ESRD and death even in elderly diabetes, as well as in very elderly. Further studies are needed to determine whether albuminuria can be a therapeutic target in this population.

PO0974
Cardiovascular Disease and Medication Use by CKD Risk Groups in People with Type 2 Diabetes: A Post Hoc Analysis from CAPTURE Giuseppina Russo,1 Abdullah Aigiwaiyle,2 Fahri Bayram,3 Patrice Darmon,4 Timothy Davis,5 Kirsten T. Eriksson,6 Tian-Pei Hong,1 Margit S. Kaltoft,6 Csaba Lengyel,7 Jose Luis Arenas Leon,8 Ofri Mosenzon,9 Nicolai Rhee,11 Shimichiro Shirabe,12 Katerina Urbanova,13 Sergio Vencio,14 Guillermo Díez Deueide,15 University Hospital, Messina, Messina, Italy;1 King Saud University, King Saud University Medical City, Riyadh, Saudi Arabia;1 Erceyes University, Kayseri, Turkey;1 Hôpital de la Conception, Marseille, France;1 University of Western Australia, Fremantle Hospital, Fremantle, WA, Australia;1 Novo Nordisk A/S, Søborg, Denmark;1 Peking University Third Hospital, Beijing, China;1 University of Szeged, Szeged, Hungary;1 Centro de Atención e Investigación Cardiovascular del Potosí, San Luis Potosí, Mexico;1 Hadassah Medical Center, Diabetes Unit, Hebrew University, Jerusalem, Israel;1 Novo Nordisk Healthcare A.G, Zurich, Switzerland;1 H.E. C. Science Clinic, Yokohama, Japan;1 Dialisiologica Interno Ambulatorio S.r.o, Ostrava, Czechia;1 Instituto de Ciencias Farmaceuticas, Aparecida de Goiania, Brazil;1 Centro de Atención Integral en Diabetes, Buenos Aires, Argentina.

Background: The CAPTURE study estimated the contemporary (2019) prevalence of cardiovascular disease (CVD) in people with type 2 diabetes across 13 countries. This post hoc analysis describes the occurrence of CVD and medication use by chronic kidney disease (CKD) risk groups.

Methods: CAPTURE was a multinational, cross-sectional, non-interventional study conducted between December 2018 and September 2019. Data on CVD diagnoses, estimated glomerular filtration rate (eGFR), urine albumin level and glucose-lowering agents (GLA)/CVD medication use was collected during routine visits. Participants were categorized by CKD risk by eGFR and urine albumin thresholds according to the KDIGO classification.

Results: Of 9823 participants, 7923 (81%) had eGFR data, 6482 (66%) had urine albumin creatinine ratio (UACR) data, and 5829 (59%) had both measures available. The distribution by eGFR (>89, 60-89, 30-59, <30 ml/min/1.73m2) was 35%, 44%, 18% and 3%, respectively, and by UACR (<30, 30-300, >300 mg/g) 67%, 25% and 8%, respectively. By KDIGO risk group (low, moderate, high, very high), CVD prevalence was 29%, 44%, 53% and 59%, respectively. Use of GLA decreased with increasing CKD except for insulin which increased. Use of renin angiotensin aldosterone system inhibitors was 49–72% across risk groups (Table).

Conclusions: This post hoc CAPTURE analysis demonstrated a positive association between CVD prevalence and CKD risk. CVD medications with proven CVD benefits, including GLA, were underused.

Funding: Commercial Support - Novo Nordisk

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
PO0975
Cardiovascular Autonomic Dysfunction Is Associated with Decline in Kidney Function in Type 2 Diabetes and Healthy Controls
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Background: Cardiovascular autonomic dysfunction is a prevalent and severe complication in type 2 diabetes. We assessed the impact of cardiac autonomic dysfunction on change in kidney function and albuminuria in a cohort of persons with type 2 diabetes and healthy controls.

Methods: In 2013 we recruited 60 persons with type 2 diabetes and 30 controls. Estimated glomerular filtration rate (eGFR) and urinary albumin excretion rate (UAER) were measured at baseline and follow up. Cardiovascular reflex tests were performed, and continuous parameters of cardiovascular autonomic function was assessed from heart rate variability in a 5-minute resting ECG.

Results: For the follow up, 32 persons with type 2 diabetes and 21 controls were willing to participate and included in the analyses. Median [IQR] follow-up time was 6.2 [6.0, 6.3] years. At baseline, mean ± SD age was 60 ± 10 years, median known diabetes duration was 12 [5 to 21] years and mean HbA1c in the type 2 diabetes group was 54 ± 11 mmol/mol. At baseline, mean eGFR was similar between groups (type 2 diabetes: 79 ± 21 ml/min/1.73m² and controls: 86 ± 12 ml/min/1.73m² p=0.183) and median UAER was higher (p=0.001) in the type 2 diabetes group (33.5 [6.5 to 107.5] mg/24-h) than controls (5.5 [5.0 to 6.5] mg/24-h). During follow up, eGFR decreased in both groups (type 2 diabetes: -1.0 [95%CI: -1.4 to -0.5] ml/min/1.73m²/year p<0.001 and controls: -0.7 [95%CI: -1.1 to -0.3] ml/min/1.73m²/year p=0.001) and the change was similar between groups (p=0.179). Albuminuria did not change. After adjustment for age, sex, smoking, HbA1c, body mass index, heart rate, 24-hour systolic blood pressure, plasma cholesterol, baseline UAER and baseline eGFR, a lower response in heart rate variability during Valsalva (p=0.016) and a lower SDNN (p=0.029) were significantly associated with a steeper yearly decline in eGFR. Cardiovascular autonomic function was not associated with change in albuminuria.

Conclusions: Cardiovascular autonomic dysfunction as assessed by heart rate variability was associated with steeper decline in kidney function during 6 years of follow up. Autonomic autonomic dysfunction may be a T2D risk factor leading to higher risk of decline in eGFR. Whether there is a causal link remains to be established.

PO0976
Changes in Cardiac Microvascular Function in Persons with Type 2 Diabetes in Relation to Kidney Function
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Background: The myocardial flow reserve (MFR) reflects the function of both large epicardial arteries and the microcirculation. Coronary artery calcium score (CACS) is a measure of coronary atherosclerosis. Cardiac 82Rb PET/CT provides a measurement of both MFR and CACS, Knowledge on changes in MFR and CACS over time and the impact of kidney function on these changes is lacking.

Methods: In 2013 we recruited 60 persons with type 2 diabetes (T2D) and 30 non-diabetic controls (C); all free of overt cardiovascular disease. All underwent a cardiac PET/CT scan. In 2019, survivors (n=62) were invited for a repeated cardiac 82Rb PET/CT after a similar protocol. 29 with T2D and 19 C participated.

Results: Median [interquartile range] duration between visits was 6.2 [6.0–6.3] years. The Table summarizes kidney function, MFR and CACS at the 2 visits. MFR was lower in persons with T2D compared to C but not after adjustment (p=0.70). Increase in CACS was higher in men (p=0.03) but not after adjustment (p=0.07). Changes in MFR and CACS were not associated with other risk factors at baseline.

Conclusions: MFR was lower in T2D compared to C but did not change significantly in either of the groups when evaluated over 6 years. Kidney function had no independent impact on changes in MFR or CACS

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0978

The Predictive Value of Diabetic Retinopathy on Subsequently Diabetic Nephropathy in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Prospective Studies

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Background: Studies have already demonstrated diabetic retinopathy (DR) was associated with an increased risk of diabetic nephropathy (DN) in patients with type 2 diabetes (T2D), whereas the predictive value of DR on subsequent DN for T2D were not illustrated. Therefore, we conducted a meta-analysis of prospective cohort studies to assess the predictive value of DR on further DN risk in patients with T2D.

Methods: The PubMed, Embase, and the Cochrane library were systematically searched for eligible prospective cohort studies through March 2020. The predictive value of DR was assessed using sensitivity, specificity, positive and negative likelihood ratio (PLR and NLR), diagnostic odds ratio (DOR), and area under the receiver operating characteristic curve (AUC).

Results: Ten prospective cohort studies recruited a total of 635 patients with T2D were selected for this study. After pooling all studies, we noted the pooled sensitivity, and specificity of DR for predicted DN were 0.64 (95% CI: 0.54-0.73), and 0.77 (95% CI: 0.60-0.88), respectively. The pooled PLR and NLR of DR for predicted DN were 2.72 (95% CI: 1.42-5.19), and 0.47 (95% CI: 0.33-0.67), respectively. The summary DOR for the relationship between DR and subsequent DN for T2D patients was 5.53 (95% CI: 2.00-15.30), and the AUC of DR for predicted DN was 0.73 (95% CI: 0.69-0.77). The predictive value of DR for subsequent DN could affect by mean age, percentage male, and study quality.

Conclusions: This study found significant associations between DR and subsequent DN risk for patients with T2D, while the predictive value of DR was mild. Further prospective study should be assessed for the predictive value of DR on other conditions in T2D patients with specific characteristics.

Funding: Government Support - Non-U.S.

PO0979

Cellular Proteomic Phenotypes Underlying Plasma Signature of 10-Year Risk of Kidney Failure

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Background: A robust circulating proteomic signature of 10-year risk of kidney failure (KRIS) in a large prospective three-diabetes cohort study was recently identified (Niewczas et al, Nat Med 2019), but the source of the KRIS proteins remains unknown. Therefore, we aimed to evaluate potential contributions of the peripheral blood mononuclear cells (PBMC) and its subset, CD14, to the KRIS in a proteome-wide fashion.

Methods: Our study group consisted of a sample of Joslin Kidney Study participants with Type 2 Diabetes (n=16) with an average eGFR of 59±23 mL/min/1.73m^2 and median albuminuria of 57 (8, 312) at baseline. Within a median of 12 years, our study group experienced a median annual renal function decline of -1.4 (-2.6, -0.5) mL/min/1.73m^2/yr. We obtained PBMC and CD14 lysates using cell density and immunomagnetic separation techniques. Cell lysate samples were subjected to aptamer proteomics (1305 proteins).

Results: In the targeted evaluation, six out of 17 KRIS proteins in PBMC lysates were investigated for association to baseline DR score in the validation cohort and for step (RET2) or three-step (RET3) change in DR score according to the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol. Urinary peptide levels were correlated to development of DR endpoints. DIRECT-Protect studies were designed to assess the effect of candesartan in relation to development of DR endpoints. DIRECT-Protect 1 was considered the discovery cohort and DIRECT-Protect 2 the validation cohort. Endpoints were defined as a two-step (RET2) or three-step (RET3) change in DR score according to the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol. Urinary peptide levels were correlated to baseline DR score in the discovery cohort. In multivariate Cox regression analyses, lower alpha-1 type I collagen (COL1A1) (seq. LDGA~) and COL3A1 (seq. EDGK~) was significantly (p<0.05) associated to the development of RET2 and lower COL1A1 (seq. LDGA~) and COL3A1 (seq. EDGK~) to RET3. However, when attempting to validate these results, only a KER12 fragment was inversely associated to baseline DR in the validation cohort, as well as to development of RET3. Furthermore, lower levels of one COL3A1 fragment (seq. AFGS~) was associated to development of RET2 in the validation cohort.

Conclusions: Several urinary peptide fragments were associated to the presence and worsening of DR in type 1 diabetes. However, this could not be validated in type 2 diabetes, and the identified peptide fragments were not conclusively associated to deterioration of DR across both cohorts.

Funding: Government Support - Non-U.S.
Urinary Cubilin Shedding Predicts Progressive Diabetic Nephropathy in Persons with Type 1 Diabetes Mellitus

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Background: Diabetes mellitus (DM) is the leading cause of end-stage renal disease worldwide. Microalbuminuria (MA) is considered a gold standard to diagnose diabetic nephropathy (DN); however, its detection of early kidney damage is questionable. Therefore, there is an emergent need for novel biomarkers to capture early molecular alterations preceding MA. Cubilin is a 460 kDa protein lacking a transmembrane domain and is coexpressed with megalin facilitating albumin endocytosis in proximal tubule epithelial cells. We hypothesize that cubilin trafficking is compromised and is amenable to urinary shedding in DM. We propose that urinary cubilin shedding predicts DN.

Methods: This study assessed urinary IL-8, cubilin, monocyte chemoattractant factor (MCP-1), NGAL, VDBP levels by ELISA (normalized for creatinine) across three groups of individuals with type 1 diabetes (T1D): Group 1(n=9) preserved normal kidney function, group 2(n=10) developed proteinuria (albumin excretion >200 microgram/min) and group 3(n=9) developed progressive DN >40% decline in glomerular filtration rate (GFR) and proteinuria during follow-up of ~10 years. Urine samples for these assessments were obtained from the baseline examination of the Pittsburgh Epidemiology of Diabetes Complications (EDC) cohort. All patients had normal urine albumin excretion and kidney function. Duration of diabetes was comparable between groups (13.5 years±1). Mann-Whitney U and Kruskal Wallis tests were used to compare groups.

Results: Urinary IL-8 levels were (pg/ml) 229 ± 71, 270 ± 146 and 549 ± 41.5 (NS) respectively. Urinary cubilin excretion(pg/ml) was 237±1, 389.2±4 and 478±8 (p<0.05). A urinary cubilin excretion >30 pg/ml predicted progressive DN with a 67% sensitivity and 92% specificity of the ROC curve (p=0.05). Urinary MCP-1, NGAL and VDBP levels did not significantly differ across the groups.

Conclusions: We demonstrated that urinary cubilin shedding is a reliable biomarker for predicting progressive DN in T1D preceding microalbuminuria. Although not statistically significant, increased IL-8 levels were elevated in patients with significant proteinuria and decline in GFR. The role of urinary cubilin shedding as a biomarker for the diagnosis and treatment of diabetic nephropathy at an early stage should be examined in a larger patient population.

Comparison of Natriuretic Peptides as Risk Markers for Mortality and Cardiovascular and Renal Complications in Persons with Type 1 Diabetes

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Background: Assessment of natriuretic peptides, N-terminal pro-brain natriuretic peptide (NT-proBNP) and Midregional Proatrial Natriuretic Peptide (MR-proANP), represents a useful addition for evaluating risk of cardiovascular and renal complications. Only very few studies have compared these two risk markers. We compared the value of NT-proBNP and MR-proANP as risk markers for mortality and development of cardiovascular and renal complications in persons with type 1 diabetes (T1D).

Methods: Plasma NT-proBNP and MR-proANP were measured (using commercially available kits) in 664 persons with T1D and various degrees of albuminuria. Endpoints were traced through National Registers and laboratory records and comprised mortality (n=157), cardiovascular events (CV) (n=101) and renal events (CV) (n=101) and progression of kidney disease (ESKD, n=21) and decline in estimated glomerular filtration rate (eGFR) ≥30% (n=93). Median follow-up ranged from 5.1-6.2 years. From Cox regression models were used to compare groups.

Results: Of the 664 persons (53% male), mean age SD was 55±13 years, median (IQR) MR-proANP was 74 (49-116) pmol/L and NT-proBNP 70 (29-162) pg/L. Higher NT-proBNP level was associated with higher risk of mortality (HR 1.5 (1.2-1.8)), CVE (HR 1.3 (1.1-1.5)) and HF (HR 1.7 (1.3-2.1)) independent of cardiovascular risk factors (p<0.001) and MR-proANP (p=0.004). Higher MR-proANP level was associated with higher risk of mortality (HR 1.7 (1.1-2.7)), CVE (HR 1.6 (1.1-2.2)), HF (HR 2.8 (1.5-5.2)) and ESKD (HR 3.1 (1.2-7.8)) independent of cardiovascular risk factors (p=0.03), however, after addition of NT-proBNP significance for all endpoints was lost. None of the markers were significantly associated with decline in eGFR ≥30%.

Conclusions: Higher NT-proBNP concentration was independently associated with mortality and cardiovascular events. Our results suggest that NT-proBNP may be useful singly or in combination with MR-proANP for risk-stratification in persons with T1D.
Microscopic Hematuria Is a Risk Factor for ESKD in Patients with Biopsy-Proven Diabetic Nephropathy

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Background: Microscopic hematuria is rarely observed in patients with diabetic nephropathy (DN). Some studies have reported that hematuria is a risk factor for end-stage kidney disease (ESKD) in glomerulonephritis, but association of hematuria with renal prognosis in DN is unknown.

Methods: The present study is a retrospective cohort study of patients with DN confirmed by renal biopsy between June 1981 and December 2014. The participants were followed until October 2018 or death. Exposure of interest is the presence of hematuria (U-RBC >5) and main outcome was the occurrence of ESKD. The association of hematuria with ESKD was evaluated using Cox hazard model with adjustment for clinically relevant factors [age, sex, eGFR, proteinuria, body mass index, systolic blood pressure (SBP) and pathological evaluations]

Results: Patients who had microscopic hematuria at the time of renal biopsy were defined as the hematuria group (n = 91), and the remainder as the non-hematuria group (N = 306). Hematuria group had more proportion of male, higher SBP, more proteinuria, and lower eGFR compared with non-hematuria group. Pathological findings revealed that glomerular, tubulointerstitial, and vascular lesions in the hematuria group were significantly more severe than those in non-hematuria group. During a median follow-up period of 80 months, 44 and 52 patients developed ESKD in the hematuria group and non-hematuria groups, respectively. Survival analyses showed that incidence of ESKD was significantly higher in the hematuria group (P<0.0001). The significance remained robust even after adjustment for confounding factors (adjusted HR 1.64, 95% CI; 1.03-2.60).

In the subgroup analyses, the associations of hematuria with ESKD among male and overt proteinuria (≥0.5 g/day) were stronger than those among female and micro proteinuria (<0.5 g/day), respectively (P-values for interaction <0.1 and <0.03, respectively).

Conclusions: The presence of microscopic hematuria is an independent risk factor for ESKD in diabetic nephropathy.

Association Between TNFR-1, TNFR-2, and KIM-1 with Cardiovascular Outcomes: Results from the CANVAS Trial

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Background: Tumor Necrosis Factor Receptor (TNFR)-1, TNFR-2 and KIM-1 are blood-based biomarkers that are known to predict kidney outcomes in patients with diabetic kidney disease. We sought to examine the association of baseline TNFR-1, TNFR-2 and KIM-1 with cardiovascular (CV) and kidney outcomes in patients with type 2 diabetes mellitus (T2DM) in the CANagliflozin cardiovascular Assessment Study (CANVAS) study, and secondly, whether these markers modified the effect of the SGLT2 inhibitor canagliflozin (CAN) on these outcomes.

Methods: The CANVAS trial randomized participants with T2DM at high CV risk to CANA or placebo. Plasma TNFR-1, TNFR-2 and KIM-1 were measured with immunoassays (proprietary multiplex assay performed by Renalys/Al, NY, USA). Associations between the 3 biomarkers and the CV (nonfatal myocardial infarction, stroke, or CV death) and kidney outcome (40% eGFR decline, end-stage kidney disease, or renal death) were assessed using multivariable adjusted Cox regression.

Results: We included 3548 (82% of overall cohort of 4330) CANVAS participants with available baseline plasma samples (mean age 62.8 years, 33.3% female, mean eGFR 76.9 mL/min/1.73 m², median uACR 11.6 mg/g, median TNFR-1, TNFR-2 and KIM-1: 2578 pg/mL, 9684 pg/mL, and 110 pg/mL). During a mean follow-up of 5.6 y, 554 CV and 137 kidney outcomes occurred. After adjustment for demographics and clinical characteristics, each doubling of baseline TNFR-1, TNFR-2, KIM-1 was significantly associated with higher risk of kidney outcomes: TNFR-1, HR 3.74 (95% CI 2.28, 6.15); TNFR-2, HR 2.68 (95% CI 2.01, 3.57); KIM-1, HR 1.50 (95% CI 1.23, 1.82). The biomarkers were not associated with the CV outcome. The protective effect of CANA on the CV and kidney outcomes (HR 0.56, 95% CI 0.40, 0.78) was consistent regardless of baseline TNFR-1, TNFR-2, or KIM-1 (all P-interaction=0.10).

Conclusions: Higher levels of TNFR-1, TNFR-2 and KIM-1 were independently associated with a higher risk of kidney but not CV outcomes in patients with T2DM at high CV risk. The baseline biomarkers did not modify the effect of CANA on these outcomes.
PO0990

Virtual Patient Simulation in Diabetic Kidney Disease: Successful Strategy for Improving Recognition and Management

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Background: We sought to determine if virtual patient simulation (VPS)-based continuing medical education (CME) intervention could improve performance of nephrologists related to recognition and management of diabetes kidney disease (DKD).

Methods: The intervention comprised a patient presenting at two different time points in a VPS platform that allows learners to order lab tests, make diagnoses, and prescribe treatments in a manner matching the scope and depth of actual practice. Tailored clinical guidance (CG), based on current evidence and expert recommendation, was provided following each decision, followed by the opportunity for the learner to modify to their decisions. Decisions were collected post-CG and compared with each user’s baseline (pre-CG) decisions using a McNemar’s test to determine P values. The activity posted August 30, 2019; initial data was collected through November 7, 2019.

Results: 139 nephrologists completed the activity (all decisions within at least 1 case) and were included. Significant improvements were observed after CG: 1st Patient: Diagnosis CKD stage 3b: 28% absolute improvement (19% pre-CG vs 47% post-CG; P<.01) Diagnosis T2D: 33% absolute improvement (5% pre-CG vs 38% post-CG; P<.01) Initiate SGLT2 inhibitor: 53% improvement (17% pre-CG vs 70% post-CG; P<.01) Other patient education: 15% improvement (52% pre-CG vs 67% post-CG; P<.01) 2nd Patient: Diagnosis CKD stage 3a: 33% absolute improvement (24% pre-CG vs 57% post-CG; P<.01) Diagnosis T2D: 41% absolute improvement (10% pre-CG vs 51% post-CG; P<.01) Initiate SGLT2 inhibitor: 36% improvement (48% pre-CG vs 84% post-CG; P<.01) Initiate ACE inhibitor: 18% improvement (82% pre-CG vs 100% post-CG; P<.01) Other patient education: 14% improvement (59% pre-CG vs 73% post-CG; P<.01)

Conclusions: VPS that immerses and engages specialists in an authentic and practical learning experience can improve evidence-based clinical decisions related to patient identification and management of hyperkalemia.

Funding: Commercial Support - Janssen

PO0991

Effect of Multidisciplinary Care Models on Glomerular Filtration Rate for Patients with Diabetic Kidney Disease: Systematic Review and Meta-Analysis

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Background: Since 2015, the Kidney Disease Improving Global Outcomes guidelines advocate for comprehensive conservative care for diabetic nephropathy (DN) patients. Multidisciplinary care (MCD) models are such strategies that offer integrated care to delay renal disease progression, reduce micro- and macrovascular complications of diabetes, increase the quality of life, and reduce associated costs. Prior reviews have assessed the effect of MCDs in all-cause mortality, hospitalization rate, and need for temporal or permanent renal replacement therapy. However, to date, there are no reviews on their impact on glomerular filtration rate (GFR).

Methods: We conducted a systematic search of observational and randomized trials on DN GFR assessments. We searched Ovid and PubMed databases. Following the STROBE and CONSORT recommendations, we assessed the quality of evidence and any selection/information bias from our resulted pool of evidence. Our primary outcome was GFR quantifications between MCD vs. non-MCD DN treated patients. We performed a meta-analysis of these measurements using random and fixed effects models and examined inter-study heterogeneity with meta-regression models.

Results: There were 93 records from our systematic search. We screened titles and abstracts and retrieved eight records (9,892 participants) for qualitative and quantitative assessments. By subgroup analyses, MCD had a statistically significant effect on GFR among younger patients (<65 years, x.53-fold increase in GFR vs. non-MCD) with longer follow-up (>2 years, x.57-fold increase in GFR vs. non-MCD) (Table).

Conclusions: Based on eight records with significant sample size, MCDs might have a positive effect on GFR if implemented earlier (preferably before age 65). However, this benefit might not be seen immediately, rather in the long-term. We suggest implementing these approaches as standard of care for DN.

PO0992

Outcomes of Diabetic vs. Non-Diabetic Patients in the GCC Dialysis Outcomes and Practice Patterns Study

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Background: Diabetes is a common comorbidity among hemodialysis (HD) patients in the Gulf Cooperation Council (GCC) countries, higher than any other region participating in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Objectives of the analysis were to describe the prevalence of glycated-hemoglobin (HbA1c) measurement, distribution of HbA1c with mortality among participants in the GCC DOPPS.

Methods: 2,274 HD patients were analyzed from 6 GCC (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates) participating in DOPPS phase 5 (2012-2015) and 6 (2015-2018). Diabetic status was based on cause of ESKD or medical diagnosis. Cox regression was used to assess the associations of diabetes (among all GCC patients) and baseline HbA1c (among diabetic patients) with mortality adjusted for demographics, comorbidities, creatinine, and Kt/V.

Results: Overall 60% of GCC DOPPS participants were diabetic (country prevalence ranged from 45% in Saudi Arabia to 74% in Kuwait). Compared to non-diabetic patients, patients with diabetes were older (60 vs. 47) on dialysis fewer years (1.5 vs. 3.0), and had higher BMI (27.6 vs. 24.9). Diabetes was associated with elevated mortality, adjusted HR(95% CI)=1.69 (1.21-2.34). Measurement of HbA1c within the four months prior to enrollment was variable – ranging from 0% in Bahrain and 33% in Saudi Arabia to 60-78% in the other GCC countries. Among diabetic patients with HbA1c measured, median [IQR] HbA1c was 6.8 [5.8-7.1]. A moderate U-shaped relationship with HbA1c and mortality was observed after adjustment.

Conclusions: Although diabetes is highly prevalent in the GCC HD population, measurement of HbA1c remains variable among this population. The relationship of HbA1c with mortality appears similar to that in see in other DOPPS regions. Further investigation related to frequency of measurement and control of HbA1c via treatment is warranted.

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PO0993

Self-Management and Progression of Patients with Diabetic Kidney Disease (DKD): A Retrospective Cohort Study

Yifan Wu,a Ping Wang,a Li Luo,a Min Zhang,a Bingqing Xia,a Lizzie Fu,a Fang Tang,a Xiangling Zhang,a Xusheng Liu,a Fuhua Lu,a 1Renal Division, the Second Affiliated Hospital of Guangzhou University of Chinese Medicine (Guangdong Provincial Hospital of Chinese Medicine), Guangzhou, China; 2Department of Internal Medicine, Yanfu Hospital with elevated mortality, adjusted HR(95% CI)=1.69 (1.21-2.34). Measurement of HbA1c within the four months prior to enrollment was variable – ranging from 0% in Bahrain and 33% in Saudi Arabia to 60-78% in the other GCC countries. Among diabetic patients with HbA1c measured, median [IQR] HbA1c was 6.8 [5.8-7.1]. A moderate U-shaped relationship with HbA1c and mortality was observed after adjustment.

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PO0994
Attitude Toward Care and Dietary Patterns Differ in CKD and Transplant Patients with and Without Diabetes
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Background: Diabetes mellitus requires dietary changes and increased interaction with the health-care team over that required by kidney disease alone. We compared dietary adherence and attitudes in pts with kidney disease with and without diabetes in inner-city Brooklyn.

Methods: A face-to-face survey was conducted in a random convenience sample of pts from CKD (23) and transplant (33) clinics. Diet was studied by 24-hour recall using ASA24 software. Healthy Eating Index was calculated using the HEI-15 score. The Beliefs in Medicine Questionnaire (BMQ) was used to elicit attitudes toward the healthcare environment. Comparisons were by t-test.

Results: 15 (45%) transplant (TXP) and 13 (57%) CKD pts had diabetes (DIAB). DIAB were older than pts without diabetes (NODIAB) (62.1±4.2 vs 59.4±2.4 yrs, p<0.0001) but age did not correlate with any finding. Mean creat was 1.8±0.1 mg/dl and did not differ between CKD and TXP, or DIAB and NODIAB. Mean HbA1c was 8.0±0.28, time with diabetes was 97.7±20.3 months and did not differ between clinics. DIAB were more likely to agree that their health depends on medications in the future (1.36±0.12 vs 2.00±0.26, p=0.024), less likely to believe that if doctors had more time, they would prescribe fewer medications (3.61±0.25 vs 2.79±0.28, p=0.034) and less likely to believe that medicines are poisons (4.5±1.04 vs 3.93±0.23, p=0.039). DIAB pts ate fewer carbohydrates (137.4±11.6 vs 212.8±13.4, p<0.0001), less sugar (44.7±5.6 vs 89.4±9.5, p<0.0001), less fiber (10.9±1.1 vs 16.1±1.4, p<0.005), less vitamin C (54.2±9.9 vs 110.2±23.3, p=0.031), less fruit (0.3±0.1 vs 1.9±0.6, p=0.015) and less refined grains (3.0±0.43 vs 4.6±0.59, p=0.035). There was no difference for HEI score, total caloric or protein intake.

Conclusions: In our population: 1. Approximately 50% of our pts had diabetes. 2. Pts with diabetes had a more positive opinion of the healthcare environment and ate fewer carbohydrates, sugars and refined grains but less fresh fruit, fiber and vitamin C. 3. Education of our pts with kidney disease and diabetes should reinforce their attitudes towards the healthcare environment while encouraging an eating plan that includes fruits and vegetables, as pts appear to be focusing on restricting sugar and carbohydrates and less fresh fruit, fiber and vitamin C. 4. Education of our pts with kidney disease and diabetes should reinforce their attitudes towards the healthcare environment while encouraging an eating plan that includes fruits and vegetables, as pts appear to be focusing on restricting sugar and carbohydrates and less fresh fruit, fiber and vitamin C.

PO0995
Racial and Ethnic Similarities of Adherence to Diabetic Hemoglobin A1c Testing and Control Measures Between Providers and Patients in Federally Qualified Health Centers in Eastern North Carolina
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Background: Type 2 Diabetes is a chronic metabolic disorder that occurs when there is a dysregulation of insulin production and cellular insulin response, leading to hyperglycemia. The test for glycated hemoglobin, Hba1C, is the basic blood test used for diagnosis. There is limited exploration of the relationship between adherence to Hba1c testing, diabetes control, and congruent provider/patient race and ethnicity. This study examined the correlations among Hba1c testing, provider race/ethnicity, and patient race/ethnicity.

Methods: Twelve consecutive monthly diabetes reports and dashboards compiled by the Rural Health Group, starting on October 1, 2018, were retrieved and analyzed in the investigation of the racial and ethnic similarities of Hba1c adherence to diabetic testing and control measures between providers and patients in the Federal Qualified Health Center in eastern North Carolina. Comparative statistical analyses permitted the juxtaposition of the comparison groups of patients and providers: White, Black, Hispanic, or other.

Results: As per adherence with the order of testing, there were no statistically significant differences found for White, Black, or Hispanic patients when they were seen by different providers. However, as per adherence to diabetes control measures, Black patients seen by Black providers were much more likely to have an Hba1c < 7% (52% when seen by a Black provider vs. only 45% when seen by a White provider, p-value = 0.0001, 95% confidence interval). Similarly, White patients had an Hba1c < 7% 50% of the time when seen by White providers, but only 43% of the time when seen by Black providers (p-value < 0.05). Therefore, patients who are the same race as their providers are statistically more likely to have an Hba1c, which reflects adherence to diabetes control measures.

Conclusions: Patients who are the same race/ethnicity as their providers did not play a significant role on Hba1c testing than patients who are the same race/ethnicity as their provider. However, patients who are the same race/ethnicity as their provider were more likely to have a Hba1c < 7%, which was statistically significant and reflected adherence to diabetes control measures. This finding was particularly true of White patients to White providers and with Black patients to Black providers.

PO0996
Low Serum Transferrin Saturation Is Associated with Incident Diabetes in Veterans with CKD
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1George E. Wahlen Department of Veterans Affairs Medical Center, Salt Lake City, UT; 2University of Utah Health, Salt Lake City, UT.

Background: Chronic kidney disease (CKD) is associated with increased risk for new-onset diabetes. Decreased circulating iron, as expressed by low transferrin saturation (Sat), is associated with diabetes in the general population, but it has not been investigated if Sat or ferritin is independently associated with incident diabetes in CKD.

Methods: We developed a historical cohort using the Veterans Affairs Informatics and Computing Infrastructure. We identified non-diabetic Veterans with CKD (MDRD eGFR <60 mL/min/1.73m2) with at least one set of iron indices between 2006-2015. Veterans with diabetes, end-stage renal disease, genetic or chronic disorders affecting iron metabolism, or those who received intravenous iron or erythropoietin stimulating agents within 3 months of the iron indices were excluded. A generalized additive Cox model was applied to the cohort to explore the joint dose-response relationship of the hazard for incident diabetes following the iron assay. A contour surface plot relating the covariate-adjusted hazard for incident diabetes to both Sat and ferritin was developed using cubic regression splines.

Results: Of the 1,159,371 Veterans with CKD, 54,990 met the inclusion criteria. The meansSD for age and eGFR were 73.8 ± 11.8 years and 43.8 ± 10.4 mL/min/1.73 m2, respectively. The median (IQR) Sat and ferritin values were 23.0 (16.9, 29.7) % and 112.1 (56.0, 210.0) ng/mL. Over the mean follow-up period of 4 years, the risk of diabetes was inversely associated with Sat, while it was positively correlated with serum ferritin. The surface contour map suggests that lower Sat range (~20%) has a stronger relationship with diabetic risk than serum ferritin.

Conclusions: In Veterans with pre-dialysis CKD, decreased Sat is closely associated with incident diabetes risk, while increased ferritin exacerbates the risk.

Funding: Veterans Affairs Support
**PO0997**

**Association of Glomerular Hyperfiltration with Glycemic Control and Serum Uric Acid Among NHANES Participants with Diagnosed Diabetes Mellitus**

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**Background:** Glomerular hyperfiltration (GH) is the earliest sign of diabetic kidney disease (DKD) even prior to the development of albuminuria. Some studies have reported that improvement in glycemic control reduces GH. Since elevated serum uric acid (SUA) level may herald worse diabetes outcomes including a higher likelihood of DKD, we sought to examine the association of GH status with glycemic control and SUA among diabetics.

**Methods:** We examined the National Health and Nutritional Examination Survey (NHANES) data from 1999 through 2016, comprising adults (age ≥ 20 years, n= 47,133, projected to N=214.9 million US population). We defined diagnosed diabetes cases as those who reported being diagnosed by a doctor or using glucose-lowering medications (n= 5,783, N=19.3M) and defined GH as eGFR ≥120 ml/min/1.73m2 (CKD-EPI) vs. normal/filtration as ≤ 60 eGFR <120 (GH: n=110, non-GH: n=3115). Cases with eGFR<60 were excluded (n=2,558). We assessed the association of GH with average glycemic control (HbA1c) and SUA levels adjusted for demographic characteristics, diabetes duration, and diabetes treatment, using univariable and multivariable regression models.

**Results:** The prevalence of GH in persons under 10 years of diabetes was 2.7% but significantly less after 10 years (1.1%, p = 0.003). GH was more likely in younger age, female sex, Hispanic ethnicity, higher A1c, higher SUA, and those with no diabetes treatment. In the multivariable model, female sex was the strongest predictor followed by Hispanic ethnicity, higher SUA, and younger age [Table].

**Conclusions:** GH is more common in the first 10 years of diabetes and associated with higher SUA. It is more common among females, Hispanic race, and younger diabetes patients. Further studies should examine the potential role of sex, ethnicity, age, and SUA in the mechanism of GH among persons with diabetes.

Regression model for variables associated with Glomerular Hyperfiltration (GH) among patients with diagnosed diabetes:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs old)</td>
<td>0.91 (0.89, 0.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (female vs. male)</td>
<td>1.04 (0.99, 1.09)</td>
<td>0.11</td>
</tr>
<tr>
<td>Ethnicity (Hispanic vs. white)</td>
<td>1.01 (0.97, 1.05)</td>
<td>0.50</td>
</tr>
<tr>
<td>HbA1c (per SDU)</td>
<td>1.09 (1.09, 1.10)</td>
<td>0.06</td>
</tr>
<tr>
<td>SUA (hyperuricemia vs. reference)</td>
<td>2.82 (1.3, 4.62)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**PO0998**

**Continuous Glucose Monitoring in a Diabetic Hemodialysis Patient**

Elisa Park,1 Kamary Kalantar-Zadeh,1 Amy S. You,1 David A. Price,2 Connie Rhee,1 1University of California Irvine, Irvine, CA; 2DexCom Inc, San Diego, CA.

**Introduction:** Diabetes is the leading cause of end stage renal disease (ESRD) in the US. Patients with diabetic kidney disease (DKD) are susceptible to hypo- and hyperglycemia via multiple pathways. Continuous glucose monitoring (CGM) provides automated, less invasive glucose measurements (updated every 5 minutes) and more comprehensive glucose data vs. conventional self-monitored blood glucose (SMBG), and glycemic benefits for CGM use have been established. However, CGM use has been limited in diabetic hemodialysis (HD) patients as devices are not currently approved for use in this population.

**Case Description:** We describe a 48-year old male with ESRD due to DKD receiving HD. At the age of 26, the patient was diagnosed with diabetes after presenting with recurrent skin infections and unexplained weight loss. He was initially treated with glyburide which was changed to metformin, and was later transitioned to an insulin pump. Over time he developed DKD which progressed to ESRD by the time he was 41 years old. His diabetes was also complicated by neuropathy and retinopathy with right eye blindness. For two decades, the patient utilized SMBG with capillary fingerstick evaluation demonstrated creatinine 2.7 mg/dL, glucose 245 mg/dL, urine protein-creatinine (uPCR) of 8.5, hemoglobin A1c of 7.5%, and negative serum and urine protein electrophoresis. Echocardiogram revealed severe left ventricular hypertrophy. CT of his abdomen demonstrated a 4 x 4 cm pancreatic cystic mass which had been biopsied 15 years previously and showed no malignant cells. Due to persistent gastrointestinal complaints, imaging was repeated 2 years later and demonstrated an increase in the pancreatic mass size to 5.8 x 5.1 cm without any evidence of metastasis. Further laboratory evaluation demonstrated C-peptide 2.4 ng/ml (normal) and glucagon 1766 ng/L (normal <208 ng/L). Elevated pancreatic polypeptide and chromogranin A levels confirmed the diagnosis: glucagonoma. He declined surgery and was intolerant of octreotide. Although uPCR decreased to a nadir of 1.5 with improved blood pressure control, his kidney function progressively declined and he required hemodialysis (HD). HD only minimally improved his nausea and vomiting. His physical condition declined over the course of a year, until he entered hospice and expired. At time of death, his pancreatic lesion measured 6 cm.

**Discussion:** Glucagonomas are rare tumors with an incidence of approximately 0.1 cases per 100,000, most commonly presenting in the 5th decade of life. Secondary causes of DM should be considered in patients without obesity, normal C-peptide levels despite advanced disease, and/or a pancreatic mass. Additionally, glucagon excess or mechanical obstruction by a pancreatic mass may cause gastrointestinal complaints attributed to uremia or diabetic gastropathy. Timely diagnosis and resection could prevent this disease cascade of diabetes, nephropathy, and end-stage kidney disease.
PO1000
Effects of Canagliflozin on Cardiovascular, Renal, and Safety Outcomes by Baseline Loop Diuretic Use: Data from the CREDENCE Trial
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Background: Canagliflozin (CANA) reduces the risk of cardiovascular (CV) events and kidney failure in people with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD). Inherent in its mechanism of action is enhanced natriuresis and osmotic diuresis. It is unclear if the efficacy or safety of CANA is modified by concomitant diuretic use.

Methods: CREDENCE randomized participants with T2DM and CKD to CANA or matching placebo. The primary outcome was a composite of end-stage kidney disease, doubling of serum creatinine, CV or renal death. We estimated effects on key efficacy and safety outcomes by baseline use of loop diuretics.

Results: Of 4401 CREDENCE participants, 955 (21.7%) received loop diuretics at baseline. These participants were older (mean age 63.5 vs 62.7 y; P=0.01), with a longer diabetes duration (17.0 vs 15.5 y), lower eGFR (49.7 vs 58.0 mL/min/1.73m²), and were more likely to have a history of heart failure (27.6 vs 11.3%; all P<0.001). Unadjusted event rates were higher in those using loop diuretics (Figure). Effects of CANA on the primary outcome and other CV and renal outcomes were consistent irrespective of loop diuretic use. The risk of renal-related adverse events, acute kidney injury, and volume depletion was not elevated by loop diuretic use (data not shown; all P>0.05).

Conclusions: CANA reduces the risk of CV and renal outcomes in people with T2DM and CKD irrespective of baseline use of loop diuretics, without additional adverse effects.

Funding: Commercial Support - Janssen Scientific Affairs, LLC

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

Figure. Effect of canagliflozin on cardiovascular and renal outcomes by baseline use of loop diuretics

PO1001
Acute Declines in eGFR During Treatment with Canagliflozin (CANA) and Its Implications for Clinical Practice: Insights from CREDENCE
Hiddo J. I. Heerspink,12 Megumi Oshima,1 Meg J. Jardine,4 Rajiv Agarwal,9 George L. Bakris,8 Christopher P. Cannon,4 David M. Charytan,8 Dick de Zeeuw,7 Robert Edwards,10 Tom Greene,11 Adeera Levin,12 Kenneth W. Mahaffey,5 Bruce Neal,1 Carol A. Pollock,14 Norm Rosenthal,10 David C. Wheeler,11 Hong Zhang,15 Bernard Zinman,16 Vladko Perkovic,1 The George Institute for Global Health, Sydney, NSW, Australia; 2Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands; 3Department of Nephrology and Laboratory Medicine, Kanazawa University, Kanazawa, Japan; 4Concord Repatriation General Hospital, Sydney, NSW, Australia; 5Indiana University School of Medicine and Veterans Affairs Medical Center, Indianapolis, IN; 6Department of Medicine, University of Chicago Medicine, Chicago, IL; 7Cardiovascular Division, Baim Institute for Clinical Research, Boston, MA; 8Nephrology Division, NYU School of Medicine and NYU Langone Medical Center, New York, NY; 9Baim Institute for Clinical Research, Sydney Medical School, University of Sydney, Royal North Shore Hospital, St Leonards, NSW, Australia; 10Indiana University School of Medicine and Veterans Affairs Medical Center, Indianapolis, IN; 11Department of Medicine, University of British Columbia, Vancouver, BC, Canada; 12Department of Population Health Sciences, University of Utah, Salt Lake City, UT; 13Stanford Center for Clinical Research, Stanford, CA; 14Kolling Institute of Medical Research, Sydney Medical School, University of Sydney, Royal North Shore Hospital, St Leonards, NSW, Australia; 15Department of Renal Medicine, UCL Medical School, London, United Kingdom; 16Renal Division of Peking University First Hospital, Beijing, China; 17Lunenfeld-Tanenbaum Research Institute, Mt Sinai Hospital, University of Toronto, Toronto, ON, Canada; 18Kolling Institute of Medical Research, Sydney Medical School, University of Sydney, Royal North Shore Hospital, St Leonards, NSW, Australia.

Background: CANA slows progression of chronic kidney disease (CKD) in people with type 2 diabetes. CANA also induces a reversible acute decline in estimated glomerular filtration rate (eGFR), which is believed to be a hemodynamic effect. Predictors of the initial decline and its association with long-term eGFR trajectories and safety outcomes are unknown.

Methods: This post hoc study of CREDENCE included 4289 patients with type 2 diabetes and CKD who had eGFR measured at both baseline and week 3. Participants were categorized by percentage decline in eGFR at week 3: greater than 10% decline (n=349, 8%); between 0 and 10% decline (n=1434, 33%); and no decline (n=2506, 59%). Long-term eGFR decline was calculated as a linear mixed effects model and Cox regression analysis adjusted for laboratory measures and medication use.

Results: More participants in the CANA (956 [45%]) versus placebo (PBO) group (450 [21%]) had an acute eGFR decline (>10% p<0.001). A >30% decline occurred infrequently (89 [4%] with CANA and 39 [2%] with PBO; p<0.001). In the CANA but not in the PBO group, older age (OR CANA 1.17, 95% CI 1.05–1.31; per 10 years) and diabetes duration (17.0 vs 15.5 y), lower eGFR (49.7 vs 58.0 mL/min/1.73m²), and were

Figure: Cardiovascular comorbidities include cardiovascular death, myocardial infarction, stroke and hospitalization for unstable angina; MACE: major adverse cardiovascular events; CV: cardiovascular; HFr: hospitalization for heart failure; ESKD: end-stage kidney disease; MI: myocardial infarction; HR: hazard ratio; CI: confidence interval.
upregulated in fibrosis. In the current study, we investigated the impact of canagliflozin and its biomarkers of COL III formation (PRO-C3) and degradation (C3M) in the CANVAS trial.

**Methods:** COL III formation was assessed with the PRO-C3 enzyme-linked immunosorbent assay (ELISA), detecting the cleaved pro-peptide released upon digestion on the extracellular matrix. COL III degradation was assessed with the C3M ELISA, detecting a neo-epitope fragment released after MMP-9 mediated degradation. The change in biomarker measurements at year 3 from baseline were compared between placebo and canagliflozin in plasma (n=2156) and urine (n=2137) samples using a linear model to assess whether biomarker levels were significantly affected by treatment. Urine biomarker levels were corrected for urine creatinine.

**Results:** Treatment with canagliflozin compared to placebo resulted in significantly lower plasma PRO-C3 levels (-0.52 ng/mL (p=0.0054; 95% CI: -0.88, -0.15), with mean levels rising in the placebo group (0.48 ng/mL) but remaining stable in the intervention group (0.04 ng/mL). Urinary PRO-C3 levels were increased 293.19 ng/mmol (p<0.001; 95% CI: 158.87, 427.51), with mean levels increasing 24.23 ng/mmol in the placebo group and 31.42 ng/mmol in the intervention group. Urinary C3M levels were increased 84.25 ng/mmol (p=0.001; 95% CI: 481.12, 1184.74), with mean levels decreasing -337.71 ng/mmol in placebo and increasing -330.30 ng/mmol on treatment. There was no correlation between the change in plasma and urine PRO-C3 (r=0.07).

**Conclusions:** The reduction in PRO-C3 levels in plasma and the increase in urinary C3M levels following treatment with canagliflozin suggest an anti-fibrotic effect of canagliflozin. Further research is necessary to understand the mechanism for canagliflozin’s effects on fibrosis.

**Funding:** Commercial Support - Janssen Research & Development, LLC

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**PO1003**

**Canagliflozin Treatment Reduces Formation and Increases Degradation of Collagen Type III in the Canagliflozin Cardiovascular Assessment Study (CANVAS)**

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**Background:** The CANVAS trial investigated the effects of canagliflozin in T2D patients at high risk of cardiovascular (CV) disease. Collagen type III (COL III) is one of the main components of the interstitial extracellular matrix that is significantly affected by canagliflozin.

**Methods:** Treatment with canagliflozin reduced COL III formation and increased COL III degradation in plasma and urine samples. COL III formation was assessed with the PRO-C3 enzyme-linked immunosorbent assay (ELISA), detecting the cleaved pro-peptide released upon digestion on the extracellular matrix. COL III degradation was assessed with the C3M ELISA, detecting a neo-epitope fragment released after MMP-9 mediated degradation. The change in collagen type III formation and degradation at year 3 from baseline were compared between placebo and canagliflozin groups using a linear model to assess whether biomarker levels were significantly affected by treatment. Urine biomarker levels were corrected for urine creatinine.

**Results:** Treatment with canagliflozin compared to placebo resulted in significantly lower plasma PRO-C3 levels (-0.52 ng/mL (p=0.0054; 95% CI: -0.88, -0.15), with mean levels rising in the placebo group (0.48 ng/mL) but remaining stable in the intervention group (0.04 ng/mL). Urinary PRO-C3 levels were increased 293.19 ng/mmol (p<0.001; 95% CI: 158.87, 427.51), with mean levels increasing 24.23 ng/mmol in the placebo group and 31.42 ng/mmol in the intervention group. Urinary C3M levels were increased 84.25 ng/mmol (p=0.001; 95% CI: 481.12, 1184.74), with mean levels decreasing -337.71 ng/mmol in placebo and increasing -330.30 ng/mmol on treatment. There was no correlation between the change in plasma and urine PRO-C3 (r=0.07).

**Conclusions:** The reduction in PRO-C3 levels in plasma and the increase in urinary C3M levels following treatment with canagliflozin suggest an anti-fibrotic effect of canagliflozin. Further research is necessary to understand the mechanism for canagliflozin’s effects on fibrosis.

**Funding:** Commercial Support - Janssen Research & Development, LLC
PO1005
Canagliflozin and Risk of Skin and Soft Tissue Infections in People with Diabetes Mellitus and Kidney Disease in the CREDEEN Trial

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Background: The skin’s hypertonic microenvironment has a protective antimicrobial function that may be disrupted by sodium glucose cotransporter 2 inhibitors (SGLT2i). We aimed to describe skin and soft tissue infections (SSTI) in the CREDEEN trial and determine whether canagliflozin affects the risk of SSTIs.

Methods: We performed a post-hoc analysis of the CREDEEN trial that randomised people with type 2 diabetes and albuminuria stage 2 and 3 chronic kidney disease to either canagliflozin 100mg daily or placebo. Adverse events were assessed by trained trial coordinators following predetermined criteria for SSTI with discrepancies resolved by consensus. We analysed the risks of SSTIs in the on-treatment population as the more conservative approach, with sensitivity analyses conducted in the intention-to-treat population, for serious events only and for participant subgroups. Univariable time-to-event regression models were assessed.

Results: Overall 373/4397 (8.5%) participants experienced 478 events comprising 252 bacterial skin infections (including 2 episodes of necrotising fasciitis), 94 fungal skin infections, 109 other skin infections and 23 soft tissue infections. Of these, 136/478 (28%) were serious. Canagliflozin did not increase the risk of SSTI (HR 0.85 [95% Confidence Interval (CI) 0.69-1.04] p=0.11), with similar results in the intention-to-treat population (HR 0.88 [95% CI 0.73-1.07] p=0.20), in analyses confined to serious SSTI (HR 0.83 [95% CI 0.58-1.21] p=0.33) and participant subgroups (all p interaction <0.10). Both cases of necrotising fasciitis were in patients assigned to canagliflozin and the participants recovered after drug was withdrawn.

Conclusions: Canagliflozin did not increase the risk of skin and soft tissue infections overall or in any subgroup, in CREDEEN trial participants with type 2 diabetes mellitus and albuminuric chronic kidney disease.

PO1006
Early Change in Albuminuria with Canagliflozin (CANA) Predicts Kidney and Cardiovascular (CV) Outcomes

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Background: The association between early changes in albuminuria and kidney and CV events is primarily based on trials of renin-angiotensin system blockade. It is unclear whether this relationship is similar with sodium-glucose cotransporter 2 inhibitors.

Methods: In this post-hoc analysis of the CREDEEN trial in patients with type 2 diabetes and chronic kidney disease, we assessed the effect of CANA versus placebo on albuminuria at week 26, and the association of early changes in urinary albumin/creatinine ratio (UACR) for the first 26 weeks with kidney and CV outcomes using multivariable Cox regression. Kidney and CV outcomes were defined as (1) end-stage kidney disease, doubling of serum creatinine or death due to kidney disease, (2) major adverse cardiovascular events (MACE) and (3) hospitalization for heart failure (HFH) or CV death.

Results: This analysis included 3836 participants (87.2%) with complete data for early changes in UACR. CANA lowered UACR by 31% (95% CI 27–36%) at week 26 and increased the likelihood of achieving a 30% UACR reduction (OR 2.69, 95% CI 2.35–3.07). We observed log-linear associations of early changes in UACR during 26 weeks with kidney and CV outcomes (all p trend <0.001, Table). Each 30% UACR reduction was independently associated with a lower hazard for clinical outcomes, overall and in each treatment arm (all p <0.001).

Conclusions: In people with type 2 diabetes and CKD, canagliflozin results in early and sustained reductions in albuminuria, which was independently associated with long-term kidney and cardiovascular outcomes.
**Kidney Effects of Empagliflozin in People with Type 1 Diabetes**

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**Background:** Empagliflozin lowers the risk of cardiovascular and kidney events in type 2 diabetes (T2D). In the empagliflozin in type 1 diabetes (T1D) clinical program (EASE), glycemic control, weight and blood pressure improved with empagliflozin as adjunct to insulin treatment, though diabetic ketoacidosis risk was higher with use of the 10 and 25mg doses vs the 2.5mg dose. The kidney effects of empagliflozin in T1D remain incompletely understood.

**Methods:** Here we report changes in kidney parameters in phase 3 placebo-controlled trials EASE-2 (empagliflozin 10/25mg; 52-week; n=730) and EASE-3 (empagliflozin 2.5/10/25mg; 26-week; n=975).

**Results:** Means/SD baseline estimated glomerular filtration rate (eGFR in mL/min/1.73 m²) in EASE-2/EASE-3 was 97.5±18.2 and 98.5±18.2 and median (interquartile range) baseline urinary albumin-to-creatinine ratio (UACR in mg/g of creatinine) was 6.2 (2.7,14.1) in both studies. After 26 weeks of treatment in EASE-3, mean placebo-corrected eGFR changes with empagliflozin 2.5mg (n=230), 10mg (n=228) and 25mg (n=234) were -0.14 (p=0.87), 2.57 (p=0.004) and -3.56 (p<0.0001), respectively. Mean placebo-corrected eGFR changes with empagliflozin 10mg and 25mg were ≤0.02 (p=0.87; n=226) and ≤-2.0 (p=0.002; n=228) after 52 weeks in EASE-2, respectively.

Changes in eGFR 3 weeks after end of therapy (FU) returned to above baseline levels. In participants with UACR >30mg/g, no significant changes in urinary albumin-to-creatinine ratio (UACR) were observed. In a pooled analysis (EASE-2 + EASE-3), in participants with baseline UACR ≥30mg/g, UACR decreased by 16% (p=0.27) and 30% (p=0.002) with empagliflozin 10mg (n=71) and 25mg (n=77 vs placebo (n=65), respectively, at 26 weeks. In EASE-3, in people with baseline UACR ≥30 mg/g, treatment with empagliflozin 2.5mg (n=36) for 26 weeks did not significantly attenuate UACR vs placebo (n=34). Hematocrit and serum albumin increased in EASE-2 and EASE-3 with empagliflozin treatment while serum uric acid decreased; changes in these parameters returned to near baseline values at the FU visit after 26 and 52 weeks of treatment.

**Conclusions:** In conclusion, empagliflozin doses >2.5 mg/day as adjunct therapy to insulin in T1D resulted in short-term changes in kidney markers comparable to changes observed with SGLT2 inhibitor use in T2D.

**Funding:** Commercial Support - Boehringer Ingelheim & Eli Lilly and Company Diabets Alliance

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**Emapril Lins Is Associated with Increased Plasma Lipid Metabolites in Type 1 Diabetes**

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**Background:** Sodium glucose cotransporter-2 (SGLT2) inhibition reduces the risk of cardio renal complications in people with diabetes, possibly by altering energy substrate pathways. It has been hypothesized that SGLT2 inhibitors improve mitochondrial efficiency and may induce a shift towards increased lipid utilization as an energy substrate. In this exploratory, post-hoc analysis, we investigated the effects of SGLT2 inhibition on plasma lipid and tricarboxylic acid (TCA) cycle metabolites in patients with type 1 diabetes (T1D).

**Methods:** In the ATIRMA trial (NCT01392560), patients with T1D were assessed under clamped euglycemia and hyperglycemia at baseline and after 8 weeks of empagliflozin treatment. Plasma samples from the ATIRMA trial were analyzed for lipid and TCA cycle metabolites using the ZipChip method.

**Results:** Of the 15 lipid metabolites, 5 increased during clamped euglycemia in response to empagliflozin (Figure) while 1 increased after treatment during clamped hyperglycemia. Of the 3 TCA cycle metabolites, 2 increased during clamped euglycemia in response to empagliflozin. None of the metabolites decreased significantly after empagliflozin treatment.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline represents presenting author.**
PO1011
Comprehensive Effectiveness of SGLT2 Inhibitors, GLP1 Receptor Agonists, DPP4 Inhibitors, and Sulfonylureas on Risk of Kidney Outcomes: Emulation of a Target Trial Using Healthcare Databases

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Background: The comparative effectiveness of SGLT2i, GLP1, DPP4, and sulfonylureas on risk of kidney outcomes among people with type 2 diabetes mellitus is not known.

Methods: We built a cohort of 216,558 US Veterans initiated on SGLT2i, GLP1, DPP4, or sulfonylureas and followed them for up to 3 years. The outcome was defined as the risk of the major adverse kidney events (MAKE) of estimated glomerular filtration rate (eGFR) decline ≥50%, end stage kidney disease, or all-cause mortality. Risks were estimated using survival models adjusted for pre-defined covariates as well as covariates identified by a high-dimensional variable selection algorithm through application of generalized propensity scores.

Results: During follow up, there were 14612 (6.75%) MAKEs. Adjusted KM curve showed a lower risk of MAKE in the entire range of renal function. The comparative effectiveness of SGLT2i, GLP1, and DPP4 vs. other classes of glucose-lowering drugs (oGLD) was associated with lower risk of ESRD and all-cause death.

Conclusions: In this large nationwide study of Korean patients with T2D, initiation of SGLT-2i vs. oGLD was associated with lower risk of ESRD and all-cause death.

Funding: Commercial Support - AstraZeneca

PO1012
Renal Outcomes and All-Cause Death Associated with SGLT-2 Inhibitor vs. Other Glucose-Lowering Drugs (CVD-REAL 3 Korea)

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Methods: Using data from the Korean National Health Insurance Service database from January 2014 to December 2017, a total of 701,674 patients were identified with T2D. We divided these patients into new-users of SGLT-2i and new-users of other glucose-lowering drugs (oGLD). Using propensity scores, patients in the two groups were matched 1:1. We examined the risk of end-stage renal disease (ESRD) and all-cause death.

Results: There were 45,016 patients in each group, and baseline characteristics were well-balanced between groups: mean age 58.1 ± 10.6 years; mean estimated glomerular filtration rate (eGFR) 92.9 ± 27.4 ml/min/1.73 m²; 8% of patients had proteinuria. We identified 167 incident ESRD and 1,070 all-cause deaths during follow-up. Use of SGLT-2i versus oGLD was associated with a lower risk of ESRD (HR: 0.47; 95% confidence interval [CI]: 0.34 to 0.65) and all-cause death (HR: 0.82; 95% CI: 0.73 to 0.93). In a subgroup analysis by eGFR, initiation of SGLT2i vs. oGLD was associated with lower risk of progression to ESRD among patients with eGFR 60-90 and <60 ml/min/1.73 m² and lower risk of all-cause death associated with SGLT-2i versus oGLD was observed across the entire range of renal function.

Conclusions: In this large nationwide study of Korean patients with T2D, initiation of SGLT-2i vs. oGLD was associated with lower risk of ESRD and all-cause death.

Funding: Veterans Affairs Support
PO1015 Correlation of Anti-Albuminuric Effect by SGLT2 Inhibitor with Tubulointerstitial Impairment
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Background: This study aimed to examine the anti-albuminuric effect of SGLT2 inhibitor (SGLT2i) in patients with or without renal dysfunction, and to investigate factors associated with the effect of SGLT2i.

Methods: Patients with diabetic nephropathy were enrolled and received 50 mg of Iplagliatin. Their blood and urine were sampled at 0 M, 1 M and 12 M. Patients with renal dysfunction (DF; eGFR < 60) and with normo-renal function (NF; eGFR ≥ 60) were separately analyzed.

Results: In all patients (n=22), urine albumin-to-Cr ratio (ACR) was reduced at 1M and maintained until 12M (median: 236.2 at 0M, 115.0 mg/gCr at 1M), however, eGFR was not changed. In DF, ACR was also decreased (median: 311.8 at 0M vs 107.0 mg/gCr at 1M, n=10). In NF, ACR was similarly decreased at 1M. Next, the patients in DF and NF were divided by %ACR reduction (high responder: HR, low responder: LR). In NF, only %change of eGFR at 12M was significantly different (-6.5±6.8% in HR vs +5.0±7.6% in LR). In DF, MCP-1 at 1M (-33.0±7.3% in HR vs +45.9±33.1% in LR) and %change of NAG at 12M showed significant difference (-33.6±13.5% in HR vs -6.8±28.3% in LR), however, there was no difference in eGFR. Univariate analysis showed significant correlation between %ACR reduction and %MCP-1 at 1M (R=0.734, p=0.016) or %NAG at 12M (R=0.714, p=0.047) in DF whereas no significant correlation was observed in NF. Multivariate analysis confirmed the results.

Conclusions: In patients with normo-renal function, restoring glomerular hyperfiltration might be important for anti-albuminuric effect of SGLT2i. However, in patients with renal dysfunction, the effect of SGLT2i seemed to be associated with reduced tubulointerstitial damages.

PO1014 Comparative Effectiveness of SGLT2 Inhibitors vs. Other Antihyperglycemics on Risk of Kidney Outcomes: A Cohort Study
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Background: In randomized controlled trials, sodium-glucose co-transporter-2 inhibitor (SGLT2i) reduced the risk of adverse kidney outcomes. We aimed to examine the comparative effectiveness of SGLT2i and other antihyperglycemics on the risk of major adverse kidney events (MAKE) of estimated glomerular filtration rate (eGFR) decline >50%, end-stage kidney disease, or all-cause mortality.

Methods: We built a cohort of 379,191 new users of SGLT2i or other antihyperglycemics. Risk of MAKE during follow up served as the primary outcome. Pre-defined covariates and covariates identified by a high-dimensional variable selection algorithm were used to build a propensity score. Linear mixed models were used to estimate the longitudinal change of eGFR and body mass index (BMI) and survival analyses were used to estimate the risk difference of MAKE.

Results: Compared to other antihyperglycemics, SGLT2i use was associated with 0.98 (0.48, 1.53) ml/min/1.73m2 less annual reduction in eGFR, 0.24 (0.17, 0.32) kg/m2 more annual decrease in BMI, and reduced risk of MAKE (HR=0.64 (0.60-0.70)), and in analyses that required concurrent use of metformin in at least the first 90 days of follow up (HR=0.63 (0.57-0.69)).

Conclusions: Among people with diabetes mellitus type 2, SGLT2i use was associated with eGFR preservation, greater decline in BMI, and reduced risk of MAKE compared to other antihyperglycemics.

Funding: Veterans Affairs Support

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Underline represents presenting author.

PO1016 SGLT2i Prescribing for Type 2 Diabetes and Comorbid Conditions Among 24 US Healthcare Organizations
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Background: Sodium glucose cotransporter-2 inhibitors (SGLT2i) are among several glucose-lowering therapies available. Clinical guidelines for type 2 diabetes recommend use of SGLT2i for people with ASCVD, heart failure (HF), or Ckd when eGFR is adequate, to control glycemia, reduce cardiovascular risk, and slow progression of kidney disease.

Methods: Using an EHR-derived dataset from 24 AMGA member health care organizations (HCOs), we identified 248,469 patients with type 2 diabetes aged 18–85 who had ≥1 ambulatory encounter with a primary care provider and ≥1 prescription for a glucose-lowering medication other than metformin and insulin in the past year (9/2018–8/2019). Patients with end stage kidney disease or hospice care were excluded. We explored the proportion of patients with an SGLT2i prescribed in the past year, and used logistic regression to describe differences by eGFR category, comorbid conditions, and specialist visits, adjusted for all predictor variables, age, sex, race, ethnicity, financial class, and HCO.
Results: Across HCOs, median proportion of patients with an SGLT2i prescribed was 22% (range, 12–39%). Prescribing decreased with eGFR category from G1 to G4 (Figure 1). SGLT2i prescribing was lower for patients with HF and those who saw a nephrologist, marginally higher for patients with ASCVD and those who saw a cardiologist, and substantially higher for patients who saw an endocrinologist.

Conclusions: There was significant variation in SGLT2i prescribing across HCOs. While guidelines emphasize use of SGLT2is among patients with ASCVD, HF, or CKD, our findings suggest these recommendations have not been widely adopted in clinical practice. Endocrinologists may play an important role in prescribing new glucose-lowering medications, while nephrologists may be hesitant to prescribe medications for type 2 diabetes.

Table: Kidney-function-related outcomes with dulaglutide 1.5 mg treatment

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Dulaglutide 1.5 mg</th>
<th>Placebo</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite outcome</td>
<td>76% (13.7%)</td>
<td>80% (16.2%)</td>
<td>0.89 (0.63, 1.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sustained eGFR decline</td>
<td>155 (3.2%)</td>
<td>214 (4.5%)</td>
<td>0.43 (0.25, 0.73)</td>
<td>0.002</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>31 (0.5%)</td>
<td>40 (0.6%)</td>
<td>0.78 (0.40, 1.51)</td>
<td>0.55</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>16 (0.3%)</td>
<td>21 (0.4%)</td>
<td>0.96 (0.42, 2.35)</td>
<td>0.96</td>
</tr>
<tr>
<td>Sustained eGFR decline</td>
<td>69 (2.7%)</td>
<td>72% (1.7%)</td>
<td>0.39 (0.19, 0.78)</td>
<td>0.072</td>
</tr>
</tbody>
</table>

Dulaglutide Treatment in Patients with Type 2 Diabetes and Moderate-to-Severe CKD Improves Kidney Fibrosis Biomarker Levels

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Background: The AWARD-7 clinical trial demonstrated that once-weekly dulaglutide slowed the decline in estimated glomerular filtration rate (eGFR) and decreased urine albumin/creatinine ratio compared to insulin glargine in patients with type 2 diabetes and moderate-to-severe chronic kidney disease (CKD). Lower levels of urinary C3M (a marker for type III collagen degradation) and increased level of serum PRO-C6 (a marker for type VI collagen formation) are reported to correlate with CKD progression and lower eGFR.

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Underline represents presenting author.
PO1021

Hemoglobin A\textsubscript{1c} Reduction with the GLP-1 Receptor Agonist Semaglutide Is independent of Baseline eGFR: Post Hoc Analysis of SUSTAIN and PIONEER Programs

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Background: Hyperglycemia is an established risk factor for the development and progression of chronic kidney disease. The glucagon-like-peptide-1 receptor agonist semaglutide is approved for the treatment of type 2 diabetes (T2D) across a wide range of estimated glomerular filtration rates (eGFRs). We investigated whether baseline eGFR affected glycated hemoglobin (HbA\textsubscript{1c}) reduction with semaglutide.

Methods: This post hoc, trial-level analysis considered all SUSTAIN (1–10) and PIONEER (1–10) trials where renal impairment was not an exclusion criteria and where the number of subjects receiving semaglutide with eGFR <60 mL/min/1.73m\textsuperscript{2} was >10. It included data for once-weekly subcutaneous semaglutide (SUSTAIN 4–6, pooled 0.5 and 1.0 mg; PIONEER 5 and 6). Within each trial, absolute estimated change in HbA\textsubscript{1c} from baseline to end of treatment (EOT) was compared between eGFR subgroups using a linear mixed model.

Results: Mean HbA\textsubscript{1c} at baseline ranged from 7.9% to 8.7% across the subgroups. Semaglutide significantly reduced HbA\textsubscript{1c} at a comparable magnitude across eGFR subgroups in all trials (mean reduction of 1.0–1.7% from baseline to EOT; p<0.148 for difference between eGFR subgroups within each trial; Figure).

Conclusions: Semaglutide (subcutaneous and oral) is an effective glucose-lowering agent in subjects with T2D, independently of baseline eGFR, including in those with chronic kidney disease.

Funding: Commercial Support - AstraZeneca

PO1022

Effects of Semaglutide on CKD Outcomes: A Post Hoc Pooled Analysis from the SUSTAIN 6 and PIONEER 6 Trials

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Background: The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated a benefit on kidney disease with subcutaneous (s.c.) once-weekly (OW) semaglutide vs placebo (PBO) in subjects with type 2 diabetes (T2D) at high CV risk. The PIONEER

Funding: Commercial Support - AstraZeneca

PO1020

Once-Weekly Exenatide Effects on eGFR Slope and Urine Albumin-to-Creatinine Ratio (UACR) as a Function of Baseline UACR: An EXSCEL Post hoc Analysis

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Background: GLP-1 RA effects on major kidney outcomes in unselected T2D patients at high cardiovascular (CV) risk are modest or neutral. However, GLP-1 RA may provide renal benefits in those at high risk of worsening kidney disease. We examined once-weekly exenatide (EQW) effects on eGFR slope and UACR change, as a function of baseline UACR, in a subset of EXSCEL participants.

Methods: Of 14752 EXSCEL participants, eGFR slope was assessed in those with baseline UACR and a post-baseline eGFR (n=3503 [23.7%]) via mixed model repeated measures (MMRM) analysis (median follow-up 3.3 years). UACR percent change from baseline to first post-baseline measurement (median time 8.9 months) was assessed in those with baseline and a1 follow-up UACR (n=2829 [19.2%]) via ANCOVA of log-transformed UACR, with baseline UACR as a covariate.

Results: Participants with baseline UACR measurements were generally similar to the overall EXSCEL population, and balanced across treatment arms. EQW improved eGFR slope, compared with placebo, in patients with baseline UACR<100mg/g (+0.79 mL/min/1.73m\textsuperscript{2}/year [95% CI 0.24–1.34]) and UACR>200mg/g (+1.32 mL/min/1.73m\textsuperscript{2}/year 95% CI [0.57–2.06], but not at lower UACR thresholds (Figure A). No difference in EQW effect on eGFR was observed as a function of baseline eGFR, CV disease history, RAAS inhibitor use, or SBP. EQW, compared with placebo, reduced UACR by 28.2% in patients with baseline UACR>30 mg/g. This effect was consistent in subgroups with higher baseline UACR (baseline UACR<100 mg 22.5%; baseline UACR<200 mg 34.5%) (Figure B).

Conclusions: This post-hoc EXSCEL analysis suggests that EQW reduces UACR, with improvement in eGFR slope specifically in participants with elevated baseline UACR.

Funding: Commercial Support - AstraZeneca
6 CVOT reported CV safety with oral once-daily (OD) semaglutide in a similar cohort. This post hoc analysis evaluated the potential benefit of semaglutide vs PBO on chronic kidney disease (CKD) outcomes.

**Methods:** Data from 6,480 subjects (SUSTAIN 6: N=3,297; median follow-up: 2.1 years; mean baseline [BL] estimated glomerular filtration rate [eGFR], 76 mL/min/1.73 m²; PO1024: N=3,183; median follow-up: 1.3 years; mean BL eGFR, 74 mL/min/1.73 m²) were pooled for semaglutide (0.5 and 1.0 mg s.c. OW, 14 mg oral OD) or PBO. Time to onset of persistent eGFR reduction (≤30, ≤40, ≤50% [corresponding to doubling of serum creatinine]) was evaluated overall and by BL eGFR subgroup (≤30–60, ≤60 mL/min/1.73 m²). Analyses adjusted for proportional-hazards model with treatment group and eGFR subgroup and interaction between both as fixed factors stratified by trial.

**Results:** In the overall population, hazard ratios (HRs) for onset of persistent eGFR reductions with semaglutide vs PBO were not statistically significantly different from 1, but estimated HRs were <1.0, favoring semaglutide. Estimated HRs for semaglutide vs PBO in the eGFR at ≤30–60 mL/min/1.73 m² subgroup were generally lower than in the overall population; semaglutide significantly reduced the risk of developing a persistent 30% eGFR reduction vs PBO (p<0.03; Figure). No significant interactions between treatment and eGFR subgroup were observed.

**Conclusions:** This analysis of semaglutide CVOTs supports the possibility of a smaller magnitude of eGFR decline with semaglutide vs PBO and suggests a potential kidney disease benefit of semaglutide vs PBO in people with T2D and established CKD.

**Funding:** Commercial Support - Novo Nordisk

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**POI024**

**AKI Associated with Semaglutide**

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**Introduction:** Recently there have been post-marketing reports of AKI and worsening CKD in patients taking glucagon-like peptide-1 (GLP-1) receptor agonists. Clinical details of these patients have not been published. Herein we report two patients who suffered rapid worsening of renal function after being prescribed semaglutide (Ozempic).

**Case Description:** Patient 1. An 83-year-old woman with diabetes, hypertension, and CKD was seen in Apr 2020 for increasing leg edema. In Nov 2019 she had been prescribed weekly semaglutide injections. At that time serum creatinine was 1.59 mg/dL (eGFR 30 mL/min/1.73m²) and serum albumin 3.3 g/dL. Rate of decline of eGFR for the previous 6 years had been 1.5 mL/min/1.73m²/yr. Attempts to increase the dose of semaglutide from 0.25 mg to 0.5 mg resulted in nausea and vomiting the day following the injection, so the drug was stopped at the end of March 2020. She had no intercurrent illnesses, hospitalizations, or change in other medications. Examination revealed BP 162/82 and 3+ peripheral edema. Serum creatinine was 3.50 mg/dL (eGFR 11), serum albumin 2.9 g/dL, and urine protein/creatinine ratio (UPCR) 4.9 g/g. Urinalysis revealed 3+ protein. Renal biopsy showed diffuse and nodular glomerulosclerosis with acute interstitial lymphocytic and eosinophilic infiltration and acute tubular injury. There has been no recovery of renal function in the 2 months since semaglutide was discontinued.

**Patient 2.** A 65-year-old male with diabetes, hypertension, and CKD was initially seen in 2012 for CKD management. BP was well controlled and eGFR stable in the 30-35 range with UPCR of 400-500 mg/g for the next 7 years. In Nov 2019 he was started on weekly semaglutide 0.25 mg increased after 2 weeks to 0.5 mg, after which eGFR decreased to 22 in Mar 2020 accompanied by an increase in UPCR to 1333. The patient denied GI symptoms but did complain of decreased appetite and fatigue. Semaglutide was stopped with resolution of symptoms. His most recent eGFR is 24.

**Discussion:** AKI has been observed in both clinical trials with GLP-1 receptor agonists and post-marketing clinical experience. Most of these events have occurred in patients who experience adverse GI symptoms. To our knowledge, Patient 1 is the first reported case with biopsy findings. Patients developing new symptoms after starting semaglutide should have laboratory tests performed and the drug discontinued if there is worsening renal function.

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**POI025**

**Association of Atrasentan Plasma Exposure with Variability in Responses in Proxies of Kidney Protection and Fluid Retention: A Post Hoc Analysis of the SONAR Trial**

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**Background:** Atrasentan reduced urinary albumin/creatinine ratio (UACR) and the risk of kidney failure in patients with type 2 diabetes and chronic kidney disease in the SONAR trial. However, in this high risk population, atrasentan was also associated with fluid retention in some patients. We evaluated whether plasma exposure to atrasentan could explain between-patient variability in UACR response, a surrogate for kidney protection, and in B-type natriuretic peptide (BNP), as a biomarker of fluid expansion.

**Methods:** Patients received 0.75 mg atrasentan for six weeks in the active run-in (enrollment) period. Individual area under the concentration time curve (AUC) was used to populate a pharmacokinetic model. Subsequently, the association between atrasentan AUC as well as baseline clinical characteristics with UACR and BNP response was estimated with linear regression in univariable and multivariable analyses.

**Results:** The median atrasentan AUC was 43.8 ng.h/mL which varied considerably among patients (3.5%-97.5% percentiles: 12.6 to 197.5 ng.h/mL). Median UACR change at the end of enrollment was -36% and BNP change was 8.7%, which also varied among patients [UACR: 2.5%-97.5% percentiles: -76.2 to 44.5%; BNP: -71.5 to 300.0%]. Atrasentan AUC, along with certain clinical characteristics at baseline such as age, eGFR, and hemoglobin, was independently associated with greater UACR reduction (β=-7.0% per ng.h/mL AUC; p<0.01) and greater BNP increase (β=4.5% per ng.h/mL AUC; p<0.01).

**Conclusions:** Atrasentan plasma exposure varied among individual patients and in addition to other patient characteristics, explained the between-patient variability in UACR and BNP response.

**Funding:** Commercial Support - The SONAR trial was sponsored by Abbvie
PO1026

Effect of Oral Supplementation with Curcumin in Diabetic Subjects with Proteinuric Kidney Disease: A Randomized Controlled Trial
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Background: Proteinuria remains one of the most important risk factors associated with kidney disease progression. Curcumin is a powerful antioxidant, and different studies have demonstrated the increased expression of cytoprotective proteins through the Keap1/Nrf2 pathway. We conducted a randomized controlled trial in proteinuric diabetic patients to assess the effect of curcumin on proteinuria.

Methods: The trial was conducted between May 2016 and September 2019. We included diabetic patients over 18 years of age, with an estimated GFR by CKD EPI ≥ 15 mL/min/1.73 m2 and proteinuria >1 g/g despite optimal dose or contraindication to RAAS blockade. We excluded patients without DM, renal replacement therapy, kidney transplantation, or pregnancy. The study group received 3.22g of turmeric powder equivalent to 1.67g of curcumin, divided into three doses every 8 hours for 24 weeks. Primary outcome was proteinuria at the end of follow up. Secondary outcomes included eGFR and blood pressure control. Our power calculation estimated a total of 100 patients. Results were analyzed on an intention to treat basis.

Results: 100 diabetic patients were included. The mean age was 58.1 ± 10.3 years, 67% were female, 98% were hypertensive and the mean eGFR and 24h proteinuria were 58.9 ± 10.3 mL/min/1.73 m2 and 44.8 ± 24 g/g, respectively. After 24 weeks follow up, no significant differences were observed between groups for proteinuria, eGFR or blood pressure control (Table 1).

Conclusions: In this randomized double blinded controlled trial in diabetic subjects with nephrotic range proteinuria and moderate CKD, curcumin administration was not effective in proteinuria reduction or eGFR preservation. ClinicalTrials.gov Identifier: NCT03198488

Funding: Government Support - Non-U.S.

Table 1. Results

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender (%)</th>
<th>Hypertension (%)</th>
<th>Baseline eGFR (mL/min/1.73m2)</th>
<th>Final eGFR (mL/min/1.73m2)</th>
<th>Baseline 24h proteinuria (g/g)</th>
<th>Baseline 3 month 3 proteinuria (g/g)</th>
<th>Final Proteinuria (g/g creatinine)</th>
<th>Baseline SBP (mmHg)</th>
<th>Final SBP (mmHg)</th>
<th>Baseline DBP (mmHg)</th>
<th>Final DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58.9 ± 10.3</td>
<td>39.67 ± 21.6</td>
<td>69.8 ± 20.8</td>
<td>35.9 ± 16.5</td>
<td>33.7 ± 15.4</td>
<td>4.1 ± 3.8</td>
<td>4.2 ± 2.5</td>
<td>3.5 ± 2.6</td>
<td>138 ± 19</td>
<td>139 ± 19</td>
<td>81 ± 12</td>
<td>73 ± 12</td>
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</tbody>
</table>

PO1027

Effect of Praligacuat, a Once-Daily, Oral Soluble Guanylate Cyclase Stimulator, on Albuminuria in Patients with Diabetic Kidney Disease: A Randomized, Double-Blind, Phase 2 Trial
John P. Hannahan,1 Ian H. de Boer,1 George L. Bakris, Thibe Wilson,1 James D. Wakefield,1 Jelena P. Scerovici,1 Jennifer Chickinger, Michael Carmesman,4 Mark Currie,4 George T. Milne, Albert T. Profy,1 Cyclerion Therapeutics, Cambridge, MA; 1The University of Washington, Seattle, WA; 2The University of Chicago Medical Center Comprehensive Hypertension Center, Chicago, IL; 3Covance Inc, Princeton, NJ.

Background: Impaired nitric oxide (NO) signaling has been implicated in the progression of diabetic kidney disease (DKD). Praligacuat (PRL) is a soluble guanylate cyclase stimulator that amplifies NO signaling in vitro and reduces proteinuria and fasting plasma glucose in the ZDF rat model of DKD.

Methods: We evaluated the safety and efficacy of PRL in adults (25-75 y) with type 2 diabetes, eGFR 30-75 mL/min/1.73 m2, sleep apnoea and moderate DKD. PRL was administered PO 20 mg daily for 12 weeks. Two first morning void specimens for UACR were collected at baseline and weeks 1, 4, 8, 12. Adverse events, 24 h BP and serum chemistry were also assessed. The primary efficacy endpoint was change from baseline (CBF) in UACR to weeks 8 and 12 analyzed by mixed-effects repeated measures model to compare pooled PRL vs PBO.

Results: A total of 156 participants enrolled and 140 completed treatment. Of the 156, 66% were men, 71% were White, 24% Black, and 54% Latino. Model estimates of mean UACR CBF [90% CI] [intent-to-treat (ITT)] were -28% [-36, -18] for pooled PRL and -15% [-27, 0] for PBO; PBO-adjusted UACR CBF was -15% [-31, 4] (p=0.17). Quality checks identified a site with data inconsistent with that from the overall study population. In a post-hoc sensitivity analysis excluding this site, PBO-adjusted UACR CBF for PRL was -20% [-33, 5], normal p=0.03. PBO-adjusted CBF for other variables at week 12 (ITT) were: 24 h systolic BP +4.2 mmHg [7.5, -8.0], 24 h heart rate 3.4 bpm [1.6, 5.2], HbA1c -0.27% [-0.50, -0.03], and cholesterol -10.1 mg/dL [-19.2, -1.0]. Mediation analyses indicated that ~75% of the UACR decline was independent of SBP decrease. Both praligacuat doses were well tolerated.

Conclusions: PRL did not significantly reduce UACR in the primary ITT analysis, but favorable trends in UACR, BP, and metabolic variables warrant further clinical study of PRL in DKD.

Funding: Commercial Support - Cyclerion Therapeutics

PO1028

Preexisting CKD Increases Risk of Metformin Monotherapy Failure in US Veterans with Type 2 Diabetes
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Background: Metformin (MET) is increasingly used for treatment of type 2 diabetes (T2D) in patients with chronic kidney disease stage 3 (CKD3); however, it is unknown if rates of MET monotherapy failure differs in patients with and without CKD3.

Methods: This was a retrospective study including 21,142 US Veterans with T2D and estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73m2 who initiated MET monotherapy and were followed for 3 yrs. Preexisting CKD was present in 1,363 (6.5%) patients. Baseline patients' characteristics were similar between two groups except CKD patients were older (68.7 vs. 59.3 yrs in non-CKD) and had lower eGFR (<60 mL/min/1.73 m2) and proteinuria >1 gram/g despite optimal dose or contraindication to RAAS blockade. Two groups except CKD patients were older (68.7 vs. 59.3 yrs in non-CKD) and had lower eGFR (<60 mL/min/1.73 m2) and proteinuria >1 gram/g despite optimal dose or contraindication to RAAS blockade. Cox regression analyses adjusted for case-mix.

Results: The mean ± age for the total cohort was 59.9 ± 10.2 yrs, 94.3% were males, 79.7 and 17.3% were Whites and Blacks, respectively. Preexisting CKD was present in 1,363 (6.5%) patients. Baseline patients' characteristics were similar between two groups except CKD patients were older (68.7 vs. 59.3 yrs in non-CKD) and had lower eGFR (54.1 vs. 87.4 mL/min/1.73 m2 in non-CKD). In Kaplan-Meyer analysis there were no difference in rates of MET discontinuation or addition of 2nd HA in patients with and without CKD3.

Conclusions: In newly treated patients with T2D the presence of preexisting CKD stage 3 was associated with increased risk of MET monotherapy failure. MET discontinuation may be expected in CKD3 patients with the progression of CKD; however, our findings of the increased risk of addition of 2nd HA warrant further studies to understand whether hypoglycemic efficacy of MET monotherapy is reduced in CKD stage 3.

Funding: Commercial Support - AstraZeneca

PO1029

Utilization of Glucose-Lowering Medications Among US Medicare Beneficiaries with CKD Between 2007 and 2016
Julie Zhao,2 3 Eric D. Weinhandl,4 Angelina M. Carlson,1 Wendy L. St. Peter,1 1University of Minnesota, Minneapolis, MN; 2Chronic Disease Research Center, Minneapolis, MN.

Background: Selecting effective and safe glucose-lowering medications for chronic kidney disease (CKD) patients is challenging. Twelve classes of glucose-lowering medications are on the US market today. Information regarding utilization of glucose-lowering medications in patients with CKD is limited.

Methods: We evaluated the safety and efficacy of PRL in adults (25-75 y) with type 2 diabetes, eGFR 30-75 mL/min/1.73 m2, sleep apnoea and moderate DKD. PRL was administered PO 20 mg daily for 12 weeks. Two first morning void specimens for UACR were collected at baseline and weeks 1, 4, 8, 12. Adverse events, 24 h BP and serum chemistry were also assessed. The primary
Methods: We evaluated an adult CKD population from Medicare 5% random sample 2007-2016, provided by the United States Renal Data System. Yearly cohorts of patients with CKD and type 2 diabetes were created. Descriptive statistics were used to report proportions of patients using glucocorticoid and renin-angiotensin system blockade therapy. Results are presented as percentages. Patient characteristics of patients using glucocorticoid therapy were compared using a Student's t-test for continuous variables and chi-square test for categorical variables. Significance level was set at 0.05.

Results: Of the 3,520,825 patients, 944,006 (27.0%) had CKD and type 2 diabetes. Between 2007-2016, the percentage of patients with CKD and type 2 diabetes treated with glucocorticoid therapy increased from 31.7% to 38.7% (p<0.0001). There were significant differences in patient characteristics of patients using glucocorticoid therapy compared to patients not using glucocorticoid therapy. These differences included older age, higher body mass index, higher rates of anemia, and higher rates of diabetes complication.

Conclusion: The results of this study highlight the increasing use of glucocorticoid therapy in patients with CKD and type 2 diabetes over the study period. Further studies are needed to determine the effectiveness and safety of glucocorticoid therapy in this population.
Methods: TRCA-301E is a multicenter, Phase 3, randomized, blinded, placebo-controlled trial in 196 pts with CKD (eGFR 20-49 mL/min/1.73 m²) and MA (serum bicarbonate 12-20 mEq/L) who were treated for up to 1 yr with veverimer or placebo, with dose titration targeted to achieve a normal serum bicarbonate.

Results: Compared with placebo, veverimer significantly increased serum bicarbonate and significantly improved physical function as reported on the Kidney Disease and Quality of Life-Physical Function Domain (KDQOL-PFD) and the 5-times repeated chair stand test (RCS) with a safety profile that was similar to placebo (Wesson, The Lancet 2019). In the subgroup with diabetes (n=70; veverimer; n=57; placebo), mean age was 63 years, mean baseline eGFR was 28.5 mL/min/1.73 m², and mean serum bicarbonate was 17.3 mEq/L; 16% were on background oral alkali. In the veverimer group, at Week 52, mean serum bicarbonate increased by 4.39 mEq/L (P=0.05 vs placebo) and significantly more pts had a ≥4 mEq/L increase or normalization of serum bicarbonate (64% vs 33%; P=0.01). Pt-reported limitations of physical function (KDQOL-PFD) (e.g. walking several blocks, climbing a flight of stairs) significantly improved in the veverimer group (+12.5 vs +0.3; P<0.001) as did objective physical performance on the RCS at Week 52 (P=0.0001). There was no significant effect of the presence or absence of diabetes on the effect of veverimer on improvement in either measure of physical function.

Conclusions: Few interventions for CKD have improved QOL or physical functioning. Our study demonstrates that veverimer is an effective treatment for diabetic pts with MA in CKD. Treatment with veverimer significantly improved these pts felt and functioned.

Funding: Commercial Support - Tricida, Inc.

PO1034

Monocyte-to-Lymphocyte Ratio, an Independent Risk Factor of Survival and Cardiovascular Disease in Hemodialysis Patients: Results from the International MONDO Consortium

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Background: Patients with ESRD have a high prevalence of chronic inflammation and higher risk of death. Monocytes have a crucial inflammatory role, but there has been limited study to date. This analysis studied the independent relationship between MLR, all-cause and cardiovascular (CV) mortality in a large and ethnically diverse hemodialysis population.

Methods: Four cohorts were described by phases of hemodialysis exposure. Kaplan-Meier (KM) curves were applied to explore the association between MLR quartiles with all-cause and CV mortality in the 4 cohorts. Cox proportional hazards models with spline terms (adjusted for age, gender, race, body mass index, diabetic (DM) and congestive heart failure (CHF)) were applied to explore the association between MLR levels and all-cause mortality in the cohorts.

Results: 21,095 patients were included in acute phase cohort; 19,240 in the early-stable phase cohort, 16,680 in the mid-stable cohort, and 13,839 in the late-stable phase cohort. Notably, patients with higher baseline MLR by quartile tended to be older, male and with a higher percentage of DM and CHF as comorbidities. Lower lymphocyte count and higher neutrophil count, NLR, CRP were associated with higher MLR quartile, and with a higher percentage of DM and CHF as comorbidities. Lower lymphocyte count and higher risk of death. Monocytes have a crucial inflammatory role, but there has been limited study to date. This analysis studied the independent relationship between MLR, all-cause and CV mortality across all phase cohorts, including long-term follow-up in this large and ethnically diverse hemodialysis population. Higher prevalence of DM and CHF are seen in patients with higher levels of MLR. This work supports findings made previously in more restricted cohorts and warrants further mechanistic investigation.

Conclusions: There is a positive relationship between higher levels of MLR and adjusted all-cause and CV mortality across all phase cohorts, including long-term follow-up in this large and ethnically diverse hemodialysis population. Higher prevalence of DM and CHF are seen in patients with higher levels of MLR. This work supports findings made previously in more restricted cohorts and warrants further mechanistic investigation.
Variations in the Thrombin Generation Profile and Clotting Factor Levels in the Patients Undergoing Maintenance Hemodialysis

Fakhira Siddiqui, Emily Bontekoe, Debra Hoppensteedt, Walter Jeske, Vinod K. Bansal, Jawed Fareed, Loyola University Medical Center, Maywood, IL.

Background: Chronic kidney disease (CKD) patients are at high risk of cardiovascular disorders and thrombosis. CKD-V patients undergoing maintenance hemodialysis exhibit varying degrees of hemostatic dysregulation. Endogenous thrombin potential (ETP) is important to the pathogenesis of vaso-occlusive complications. This study investigated ETP and its relevance to circulating coagulation factor levels in CKD-V patients.

Methods: Citrated blood samples from 95 patients with CKD-V were collected prior to and after maintenance hemodialysis. Normal human plasma (NHP) was used for referencing purposes. Plasma levels of coagulation factor VII, IX, X and XIII were measured by ELISA. ETP was measured using a kinetic fluorogenic method. Such parameters as peak thrombin, lag time (LT) and area under the curve (AUC) were calculated. Correlation analysis between peak thrombin and coagulation factors was carried out by using GraphPad Prism software.

Results: CKD patients did not show any significant difference in factor VII levels (110.6% vs 112.5%) and factor X (81.5% vs 88.2%). Factor IX levels were elevated (126.3%) in the CKD-V group compared to NHP (100.5%). Similarly, factor XIII levels were significantly higher in CKD-V (104.8%) in comparison to NHP (82.3%). In the ETP studies, CKD-V patients showed a wide variation in ETP parameters. Peak thrombin levels (107.1 mU/ml vs 168.3 mU/ml) and AUC (589.0 mU/min vs 815.7 mU/min) were lower while lag time was higher (2.89 min vs 2.17 min) in the CKD-V group in comparison to NHP. Coagulation factor VII, IX and X correlated with peak thrombin levels (r > 0.3) whereas factor XIII did not show any significant correlation.

Conclusions: These studies demonstrate that CKD-V patients exhibit a decreased generation of endogenous thrombin with simultaneous consumption of coagulation factors suggesting an ongoing activation of coagulation system. Almost 10% of the CKD-V patients exhibit increased levels of peak thrombin values which correlated with relatively higher levels of clotting factors suggesting a decreased activation of ETP. These studies suggest that majority of CKD-V patients are in a sustained state of ongoing thrombin generation which may contribute to the observed thrombotic complications in these patients.

Impact of Age on the Association of Pre-ESRD Uric Acid with Post-Transition Mortality Among US Veterans

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Background: Elevated uric acid is a marker for dropout and higher mortality in kidney disease patients. In a prior analysis we demonstrated that higher pre-dialysis uric acid was associated with higher post-transition outcomes. As higher uric acid is more commonly found in older patients, we examined the differences in the association between pre-dialysis uric acid and mortality post-transition to dialysis across age groups.

Methods: From US veterans who transitioned to dialysis between 10/2007-03/2015, we identified 9,110 patients with a uric acid measured 3 months before transitioning to ESRD. We examined the association of pre-ESRD uric acid category with all-cause mortality post-transition using Cox proportional hazards models adjusted for case-mix covariates and additional adjustments for laboratory values and eGFR, separately in patients less than 65 or >= 65 years.

Results: The mean age of the cohort was 66±11 years, 2% female, and 36% African American. The 3-month prelude uric acid average was 8.13 ± 2.29 mg/dL, 4.521 patients were during follow-up (median follow up time of 25 months). Compared to the reference group (7<8mg/dL), in the fully adjusted model, lower uric acid led to a lower risk and the highest category of uric acid had an 18% higher risk of mortality in those 65 years or older. There was no significant association between uric acid and mortality among patient younger than 65. Wald Test for interaction showed a significant difference in association (p value: 0.0029).

Conclusions: Elevated uric acid pre-transition is associated with a higher risk of mortality post-transition among older Veteran patients. In older patients, prelude uric acid can be informative of post-transition outcomes. Further study of this relationship is warranted to determine if uric acid should be more closely monitored in patients transitioning to dialysis and to further understand why age modifies the clinical impact of uric acid.

Hemodiafiltration Reduces All-Cause Mortality in Korean Hemodialysis Patients: A Propensity-Matched Cohort Study

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Background: On-line hemodiafiltration (OL-HDF) is currently the most advanced hemodialysis modality. Several studies have found that high convection volume OL-HDF reduces the mortality in dialysis patients compared with that of conventional hemodialysis(HD). Most randomized controlled trials are in patients receiving MHD. Until randomized controlled trials assess whether PA improves survival in HD patients, it should be considered as part of the clinical management of HD patients.

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OL-HDF on survival benefit have failed. To date, the survival rate of OL-HDF has not been investigated in a large number of Koreans.

**Methods:** Using data from the Korean Society of Nephrology. The total 85,643 patients undergoing hemodialysis between 2014 and 2019 were divided into two groups receiving only conventional HD and only OL-HDF with thrice sessions per week, dialysis vintage 2 months, and 1-year follow-up. Demographic characteristics, hemodialysis patterns, and overall survival were analyzed between the groups.

**Results:** The study included 8,959 patients (750 OL-HDF, 2,805 conventional HD) with a median follow-up of 2.58 (interquartile range 0.50–4.66) years. The mean age was younger for males gender, and the dialysis vintage was slightly longer in patients with OL-HDF group compared with those of conventional HD group. We performed propensity score matching in 1:1 with the covariate of age, gender, cause of ESRD, and dialysis vintage. Compared with conventional HD, OL-HDF was associated with improved all-cause mortality/hazard ratio 0.639 (95% confidence interval 0.465 to 0.934). In cardiovascular mortality, no statistical difference was observed between the groups.

**Conclusions:** Our results indicate that OL-HDF was associated with reduced mortality without harmful effects on nutritional status across patient subgroups of age, sex, and cause of ESRD, dialysis vintage.

**Comparison of cumulative probabilities of survival between HD and HD groups**

**PO1041**

**Energy Homeostasis Gene Polymorphisms and Survival of Hemodialysis Patients**

Monika K. Swiderska, Adrianna Mostowska, Pawel P. Jagodziński, Alicja E. Grzegorzekowa, E. University Medyczny imienia Karola Marcinkowskiego in Poznań, Poznam, Poland.

**Background:** Patients who undergo hemodialysis (HD) therapy have an increased risk of death compared to the general population. Single nucleotide variants (SNVs) of energy homeostasis influence the susceptibility to diabetes mellitus (DM), dyslipidemia, and coronary artery disease (CAD). We investigated whether selected SNVs related to energy homeostasis are associated with mortality risk in HD patients.

**Methods:** The study included 271 HD patients who were tested for 11 SNVs in FOXO3, IGFBP3, FABP1, PCSK9, ANGPTL6, and ANGPTL8 genes using HRM analysis and TaqMan assays. FOXO3, IGFBP3, L-FABP, PCSK9, ANGPTL6, and ANGPTL8 plasma concentrations were measured by ELISA in 71 HD patients. The Kaplan-Meier method and Cox proportional hazard models were used for survival analyses.

**Results:** Patients with ANGPTL8 rs733737 CC genotype had over 3-fold increased risk of death compared with the carriers of the major allele (log-rank test p=0.002; HR 3.4; 95%CI 1.5–7.7; p=0.003). rs733737 CC genotype was in particular a risk factor for cardiac (2e-4; 5.5; 2-15.1; SE-4) and cardiovascular deaths (0.004; 4; 1.5–10.7; 0.007). The association mentioned above remained significant after adjustment for gender, DM, CAD, age at RRT onset, BMI and CRP (p=0.03, 0.04 and 0.02 for overall survival, cardiac and cardiovascular deaths, respectively). ANGPTL8 rs733737 was also associated with an increased risk of diabetic nephropathy (OR 1.895; CI 1.1–2.9; p=0.02). Plasma ANGPTL8 levels were increased in patients diagnosed with CAD (p=0.028). Carriers of ANGPTL8 rs3110697 variant A allele had increased risk of cardiovascular mortality (HR 1.3; 95%CI 1.1–1.6; p=0.03, adjusted p=NS). IGFBP3 rs3110697 positively correlated with the diagnosis of CAD (p=0.006), myocardial infarct (p=0.01) and dyslipidemia (p=0.02) as well as with CRP concentrations (p=0.005). Carriers of FOXO3 rs4946936 CT genotype had increased risk of cardiac death (HR 1.6; 95% CI 1.1–2.4; p=0.03, adjusted p=NS), whereas FOXO3 rs2802292 TT genotype was associated with decreased risk of vascular mortality (HR 0.8; 95% CI 0.2–0.8; p=0.005). The association remained significant after adjustment (p=0.002). The analyzed proteins did not correlate with the survival probability of HD patients.

**Conclusions:** ANGPTL8 rs733737, IGFBP3 rs3110697, FOXO3 rs2802292, and rs4946936 are prognostic factors of survival among HD patients.

**Funding:** Government Support - Non-U.S.

**PO1042**

**Short-Term Association of Pre-Dialysis Calculated Serum Osmolality and Its Per-Quartile Change with Mortality in Maintenance Hemodialysis Patients**

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**Background:** Homeostatic regulation of serum osmolality (SOsm) is critical for normal cellular function. Since kidney plays an important role in maintaining homeostasis, patients with kidney dysfunction might be unable to maintain homeostasis. However, it is unknown if SOsm can predict risk of mortality in maintenance hemodialysis (HD) patients.

**Methods:** We identified 16,402 patients who transitioned to maintenance HD in a large U.S. dialysis organization over 5 years (2007-2011) and had available calculated pre-dialysis SOsm Sodium and Potassium and blood urea nitrogen (BUN) and Glucose at baseline. We used the equation with the best fit between measured and calculated SOsm as follows: 2x([Na, in mmol/L]+[K, in mmol/L])+[Glucose, in mg/dL/18]+[BUN in mg/dL]/2.8. We divided the patients into ten groups based on their calculated SOsm (SOsm updated at quarterly intervals as a proxy of short-term exposure): <300, 300–<304, 304–<307, 307–<309, 309–<311, 311–<313, 313–<315, 315–<317, 317–<321 (reference group) and ≥321 mOsm/Kg, and calculated SOsm’s per quarter change from the date of first dialysis: <-8.0, -8.0–<-6.0, -6.0–<-4.0, -4.0–<-2.0, -2.0–<0, 0–<+2.0 (reference group), <+2.0–<+4.0, +4.0–<+6.0, +6.0–<+8.0, +8.0 mOsm/Kg. All-cause mortality risk was estimated using multivariable Cox models.

**Results:** The patients were 56% male, 48% non-white, and the mean age was 63 ± 13 (mean ± SD) years. Those with low calculated SOsm tended to be older. In time-varying analysis, the association between all-cause mortality and per quarter change in calculated SOsm was significant after adjusted hazard ratio: +8.0, 8.0–<10.0, 10.0–<12.0, 12.0–<14.0, 14.0–<16.0, 16.0–<18.0, 18.0–<20.0, 20.0–<22.0, 22.0–<24.0, 24.0–<26.0, 26.0–<28.0 (reference group), +2.0–<+4.0, +4.0–<+6.0, +6.0–<+8.0, +8.0 mOsm/Kg. Higher calculated SOsm was associated with higher mortality risk (Figure B).

**Conclusions:** This result suggests that short-term and a wide range of changes in serum osmolality may increase the risk of all-cause mortality in hemodialysis patients.

**PO1043**

**Survival Differences Among ESRD Patients in the Mainland United States, Hawaii, and Pacific Islands**

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**Background:** Asians and Native Hawaiians and other Pacific Islanders (NHOPIs) have a high prevalence of kidney disease risk factors, there are sparse data

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examining ESRD outcomes in these populations. As Hawaii is among the states with the highest representation of Asians and NHOPIs, we compared ESRD survival among Asians, NHOPIs, and other racial groups residing in the mainland US vs. Hawaii and the Pacific Islands.

Methods: Using United States Renal Data System (USRDS) data, we examined the impact of geographic residence in the mainland US vs. Hawaii and the Pacific Islands on associations of race and mortality among incident ESRD patients who transitioned to dialysis over 2010-16. HRs for all-cause mortality were estimated using Cox models adjusted for sociodemographics, comorbidities, dialysis characteristics, pre-ESRD nephropathy care, laboratory tests, and mortality risk factors. We included 152,625 patients. Mean age was 60.8 years, 59% were white, male, smokers with hypertension as the cause of ESRD. Patients with AAA are less likely to have diabetes as an etiology of ESRD. AAA is associated with a decreased risk of mortality. Our aim was to establish and evaluate a personal scoring system in which we included associated comorbidities, age and, other HD related factors known to predict mortality.

Results: Incident dialysis patients from 2005–2014 from the USRDS were queried. Incident dialysis patients from 2005–2014 from the USRDS were queried. Compared with White incident ESRD patients residing in the mainland US, Asians and NHOPIs in the mainland US had lower mortality risk: HRs (95% CIs) 0.67 (0.66-0.67) and 0.72 (0.70-0.73), respectively. When examining Asians and NHOPIs residing in Hawaii and the Pacific Islands, survival benefit was attenuated in Asians and was diminished to the null in NHOPIs (ref: White incident ESRD patients in mainland US): HRs (95% CIs) 0.77 (0.74-0.79) and 1.00 (0.96-1.03), respectively. Conclusions: In the mainland US, Asians and NHOPIs had lower mortality risk compared with Whites. However, in Hawaii and the Pacific Islands, this survival benefit was diminished in Asians and was mitigated in NHOPIs. Further studies are needed to determine the factors contributing to the differential ESRD mortality risk across racial groups residing in the mainland US vs. Hawaii and the Pacific Islands.

Funding: NIDDK Support

PO1045 Risk Factors and Mortality in Dialysis Patients with Abdominal Aortic Aneurysm


Background: In the general population, abdominal aortic aneurysm (AAA) is associated with increased mortality. Once diagnosed, AAA can be followed noninvasively or corrected surgically. Vascular disease is common in dialysis patients, but there is limited information on the incidence and outcomes for AAA in this population. To address this question, we queried the United States Renal Data System (USRDS) for risk factors associated with diagnosis of AAA, survival of patients diagnosed with AAA, and overall risk factors for mortality.

Methods: Incident dialysis patients from 2005–2014 from the USRDS were queried. ICD-9 and ICD-10 codes were used to define a diagnosis of AAA and identify clinical co-morbidities. Cox proportional hazards (CPH) modeling was used to determine the adjusted hazard ratio (aHR) and 95% confidence intervals (CI) for death.

Results: From a total cohort of 968,799, we identified 22,121 subjects with a diagnosis of AAA. When compared to patients without the diagnosis, AAA patients were older and had higher percentages of white race, male gender, tobacco use, Charlson comorbidity index (CCI), and hypertension as end stage renal disease (ESRD) etiology, but lower percentages of diabetes as ESRD etiology. A bivariate CPH model of survival showed that AAA patients had significantly increased mortality compared to patients without a AAA diagnosis (HR=1.29, p-value<0.0001). However, in the final CPH model, patients with a AAA diagnosis had a decreased risk of mortality (aHR=0.85, 95% CI 0.844-0.860), after controlling for age, CCI, and other demographic and comorbid variables.

Conclusions: ESRD patients with a diagnosis of AAA are more likely to be older, white, male, smokers with hypertension as the cause of ESRD. Patients with AAA are less likely to have diabetes as an etiology of ESRD. AAA is associated with a decreased risk of death, which suggests that AAA in the ESRD population by itself may not increase mortality, but the comorbid factors that come with it do.

Funding: Private Foundation Support

PO1046 Composite Comorbidity Scoring System to Predict Mortality in a Saudi Dialysis Population


Background: Most uremic patients starting hemodialysis (HD) have multiple comorbidities, resulting in a high risk of mortality. Our aim was to establish and evaluate a personal scoring system in which we included associated comorbidities, age and, other HD related factors known to predict mortality.

Methods: All patients referred to DaVita-KSA, from October 2014 to December 2019, to continue hemodialysis therapy, were included in this analysis. Cox proportional hazards model was used to identify factors influencing all-cause mortality. A personal scoring system was established based on the score assigned to each factor, according to its weight as predictor of death, judged on the value of the relative risk generated in the preliminary analysis. An index of co-morbidity was calculated for each patient that corresponded to the sum of scores assigned to each factor. Patients were divided into 4 groups according to percentile rank of their comorbidity index (Group 1: low risk, Group 2: moderate, Group 3: high, Group 4: very high) and compared in terms of global and annual mortality rates and survival using Log rank analysis.

Results: 3983 patients (2177 males, 55%) were included with a mean age of 52.5± 16.8 years. Diabetic and hypertensive nephropathies accounted for 78.1% of all causes of ESRD. After a cumulative follow-up period of 7635 years, 15.3% of patients were transferred to other facilities, 8.7% were transplanted and 14.5% were deceased.

Funding: Commercial Support - Fresenius Medical Care North America

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PO1047
Mortality and Cost Track Yearly Changes in ESRD Quality Incentive Program Performance
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Background: Patients treated in dialysis facilities that receive payment reductions under the ESRD QIP experience higher mortality and cost (Medicare payments) during the same performance year. We asked whether these outcome measures track with yearly changes in the QIP payment reduction.

Methods: Mortality and cost per patient year were analyzed using claims files for dialysis patients enrolled in the traditional Medicare fee-for-service program for performance years 2010-2016.

Results: The table displays index-year mortality and cost (columns) according to the facility QIP payment reduction (PR) for the prior year (rows) and the direction of the change in QIP PR in the index-year (worse, unchanged, better). In almost all cases, mortality and cost were higher when patients in facilities that did worse in QIP and lower for patients in facilities that did better. For example, patients treated in dialysis facilities that received a 1.5% QIP PR in the prior year experienced 18.7% mortality if the index-year PR was unchanged, 16.9% mortality if the index-year PR was lower (≤1%) and 24.5% mortality if the index-year PR was higher (≥2%).

Conclusions: Patient mortality and average Medicare payments track with changes in facility QIP PRs. The findings suggest that facility efforts to improve QIP performance may translate into improved mortality and lower costs to Medicare. Moreover, it is unlikely that the observed association between outcome measures and QIP is attributable to unmeasured patient case-mix, which tends to be relatively stable from year to year. The findings suggest that the ESRD QIP captures meaningful aspects of quality and value.

Funding: Other U.S. Government Support

PO1048
Comparison of ESRD Quality Incentive Program (QIP) Performance and Dialysis Facility Compare (DFC) Star Rating
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Background: The DFC quality of patient care star rating system reached its 5-year mark in 2020 and the ESRD QIP surpassed its 10-year mark. Both programs have undergone considerable changes in a continuing effort to help patients make informed care in most cases.

Results: Facilities with higher PY 2020 QIP scores tended to receive higher star ratings. Among facilities with no PR (N=3,920), 78.4% received 4 or 5-stars and 91.7% of facilities with a 2% PR received 1 or 2-stars. The average facility TPS decreased by approximately 10 points with each decrease in star rating, with significant differences between all categories (Table 1).

Conclusions: The ESRD QIP and the star rating program have distinct goals which have led to differences in their design and methodology, such as the use of the small facility adjuster in the ESRD QIP and non-overlapping measures between the two programs. Nevertheless, there is strong overall correspondence between the two programs in their assessments of facility quality of care. These results are reassuring, in that QIP scores and star ratings are providing a consistent message about dialysis facility quality of care in most cases.

Funding: Other U.S. Government Support

Table 1. Mean TPS by PY 2020 QIP Payment Reduction and CY 2018 5-star rating (N=103)

<table>
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<th>PR</th>
<th>Facility %</th>
<th>Mean TPS (SD)</th>
<th>Star Rating</th>
<th>Facility %</th>
<th>Mean TPS (SD)</th>
</tr>
</thead>
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<td>74.2* (9.7)</td>
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<td>24.0%</td>
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<td>20.9%</td>
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<td>12.0%</td>
<td>42.7* (8.3)</td>
<td>3</td>
<td>33.6%</td>
<td>53.4* (8.9)</td>
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<td>7.5%</td>
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<td>1.3%</td>
<td>23.9* (5.7)</td>
<td>5</td>
<td>2.6%</td>
<td>36.1* (13.0)</td>
</tr>
</tbody>
</table>

*test with pr 0.001 vs. adjacent category.

PO1049
Comparison of 5-Year Survival Rate Between Hemodialysis and Peritoneal Dialysis Patients: A Prospective Cohort Study with Propensity Score Matching
Mami Miyazaki,1 Shigehiro Doi,1 Ayumu Nakashima,1 Toshiki Doi,2 Takao Masaki.1 Hiroshima Daigaku Byoin, Hiroshima, Japan; 2Harada Hospital, Hiroshima, Japan.

Background: Chronic Kidney Disease patients who require dialysis have increased worldwide. However, whether hemodialysis (HD) or peritoneal dialysis (PD) independently affects prognosis is still controversial.

Methods: A multicenter prospective observational study was conducted from 1 January 2012 to 31 March 2018. Total of 646 HD patients and 72 PD patients were enrolled from Hiroshima Chronic kidney disease outcomes cohort study (Hi-COCS) in Japan. We excluded patients whose follow-up period was less than 3 months. One to one propensity score matching was performed to compare the survival rates between HD and PD patients and to find the factors that would affect prognosis.

Results: Of 621 HD patients and 71 PD patients, the mean average age was 74.2±12.5, 49.7% patients had DM, and 19.2% patients had CVD. The median follow-up period was 41 months. Total of 130 patients were selected with 1:1 propensity score matching (65 HD patients and 65 PD patients). In the PS matched cohort, there was no difference between the two groups in the 5-year survival rates of the overall events. (HD 71.2% vs PD 71.2%, respectively, P = 0.97) PD group had better survival rate of cvd outcome which was significantly different between the two groups (P = 0.043). Multivariate Cox proportional hazard model showed that adjusted hazard ratio (HR) of overall events and CVD events were 1.06 (95% confidence interval (CI); 0.53-2.10, P = 0.96) and 4.90 (95% CI 1.37-15.38, P = 0.014), respectively. Age, non-HDL cholesterol and CRP were associated with prognosis in overall events. Only non-HDL cholesterol was associated with prognosis in CVD events.

Conclusions: In this study, we found out that 5-year survival rate was not significantly different between the HD and PD patients in overall events. However, PD group had better survival rate of CVD events than that of HD patients. It suggests that PD may potentially have treatment advantage for patients who have high risk factors of CVD events.

PO1050
Effects of Dialysate Magnesium Concentrations on Mortality: Results from the MONDO Initiative
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Background: Dialysate magnesium (DMg) is known to be positively associated with serum Mg levels in hemodialysis (HD) patients (pts). We aimed to study the associations between different DMg levels and mortality in HD pts.

Methods: We conducted a retrospective cohort study to examine the associations of different DMg levels (1.0, 1.5, or 2.0 mEq/L) and all-cause mortality. In-center HD pts treated in KH and MONDO with constant DMg levels during their first year of observation were studied. The primary outcome variable was a 1-year mortality risk. In a second step, we used 1:1 propensity score matching (based on age, gender, calendar, and vintage) to create 4 matching groups: 1)DMg 1.0 versus 1.5 mEq/L (KH and MONDO), 2)DMg 1.5 versus 2.0 mEq/L (only KH), 3)1.0 versus 2.0 mEq/L (only KH). The associations between different DMg levels and mortality after matching were evaluated by Cox proportional hazards models, Kaplan Meier survival curves, and the Log Rank test, respectively.

Results: We studied 32,117 pts from KH (69 years, 64% males, 42% diabetics, 48% cathereter; DMg 1.0: 31,460 (98%), DMg 1.5: 395 (1%) and DMg 2.0: 262 (1%)); 15,211 pts from MONDO (57 years, 58% males, 41% diabetics, 24% catheter; DMg 0.75: 2,481
Risk of Hypokalemia in Hyperkalemic Hemodialysis Patients

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Background: Combined pre- and post-dialysis hypokalemia is associated with increased mortality risk. The Phase 3b DIALIZE study (NCT03030352I) showed that sodium zirconium cyclosilate (SZC) reduces pre-dialysis serum potassium (sK) and is well tolerated in hemodialysis patients (pts) with hyperkalemia. In this post-hoc safety analysis of DIALIZE, we report hypokalemia events in the SZC and placebo (PBO) arms.

Methods: In DIALIZE, 196 pts were randomized blindly 1:1 to receive PBO (n=99) or SZC (n=97) 5 g starting dose once daily on non-dialysis days (4 days/week [wk]) for 8 wks, comprising a 4-wk SZC or PBO dose-escalation phase (max 15 g) to achieve target pre-dialysis sK: 4.0–5.0 mmol/L, and a 4-wk stable-dose evaluation phase. In this post-hoc analysis, the proportions of pts with hypokalemia (sK <3.5 mmol/L) pre-dialysis, post-dialysis, and combined pre- and post-dialysis at the same visit were tabulated by visit. Pts’ current pre-dialysis sK by post-dialysis sK (a3.5 vs <3.5 mmol/L) at the previous visit was also assessed.

Results: The frequency of pre-dialysis hypokalemia was comparable between SZC and PBO, with 5 pts in each arm accounting for 7 and 5 events, respectively. The proportion of pts with post-dialysis hypokalemia at each visit was greater with SZC than PBO. For all but 2 SZC pts with post-dialysis hypokalemia, pre-dialysis sK<5 returned to a3.5 mmol/L at the next visit (Figure). In each arm, 1 pt had combined pre- and post-dialysis hypokalemia.

Conclusions: Despite the efficacy of SZC in lowering pre-dialysis sK, SZC was not associated with a clinically significant increase in the frequency of pre-dialysis hypokalemia. Treatment with SZC vs PBO did not increase the frequency of combined pre- and post-dialysis hypokalemia which is associated with increased mortality risk.

Funding: Commercial Support - AstraZeneca

Poster

PO1052
Electrolyte Changes in Contemporary Hemodialysis: An Analysis of the Monitoring in Dialysis (MID) Study

Simon Correa,1,2 Katherine M. Scovnier,1,2 James A. Tumlin,3 Prabir Roy-Chaudhury,4 Finnian R. McCausland,1,2 David M. Charytan.1 Monitoring in Dialysis Study Group1 Brigham and Women’s Hospital, Boston, MA; 2 Harvard Medical School, Boston, MA; 3 New York University School of Medicine and NYU Langone Medical Center, New York, NY; 4 UNC Kidney Center, Chapel Hill, NC and WG (Bill) Hefner VA Medical Center, Salisbury, NC.

Background: There is a paucity of data examining electrolyte concentrations during and immediately after hemodialysis (HD) sessions. We describe these changes and provide predictive nomograms based on HD prescriptions and post-HD electrolytes.

Methods: We leveraged patient (n=66) and HD session-level pre- and post-HD laboratory data (n=1,713) from the Monitoring in Dialysis study and fit mixed effects regression models to analyze differences between pre-, 15-minutes post-, and 30-minutes post-HD levels (compared with immediately post-HD) of electrolytes, blood urea nitrogen, creatinine, and albumin as well as the association of post-HD values with dialysate prescriptions.

Results: Serum bicarbonate, calcium, and albumin increased (mean increase 4.9 mEq/L at 0.3, 0.7 mEq/L at 0.1, and 0.4 g/dL at 0.03, respectively), and potassium, magnesium, and phosphorus decreased immediately post-HD (mean -1.2 mEq/L at 0.1, -0.3 mEq/L at 0.03, and -3.0 mEq/L at 0.2, respectively). Hypokalemia and hypophosphatemia were present in 34% and 67% of immediately post-HD samples, respectively. Changes were observed in electrolyte concentrations at 15- and 30-minutes post-HD compared to immediately post-HD (Fig. A: observed changes; Fig. B: predictive nomograms of post-HD electrolytes).

Conclusions: Contemporary HD results in marked changes in electrolyte concentrations during and after the treatment. We report a high frequency of post-HD hypokalemia and hypophosphatemia and present predictive nomograms relating post-HD changes to dialysate prescriptions. Whether the abnormalities observed in potassium and phosphorus post-HD predispose to adverse symptoms and arrhythmia is unclear and requires further research.
PO1053

Metabolomic Analysis Fails to Identify Uremic Solute Associated with Pruritus in Hemodialysis Patients

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Background: Uremic pruritus is a debilitating symptom in hemodialysis (HD) patients. That uremic solutes contribute to pruritus is suggested by the improvement after transplantation. We aimed to identify solutes associated with pruritus using metabolomic analysis comparing plasma of HD patients with severe pruritus and mild/no pruritus.

Methods: Plasma and ultrafiltrate (UF) samples from 12 HD patients with severe pruritus (Itch) and 24 HD patients with mild/no pruritus (No Itch) were analyzed. Pruritus was assessed using a 100-mm visual analogue scale with severe defined as >70 mm. Plasma and UF were analyzed using a metabolomics platform (Metabolon Inc.). Solutes were first identified as uremic based on the finding of higher average peak areas in all 36 HD patients than in 16 controls with normal kidney function. Solutes were deemed uremic if their HD/control ratio was >4 in plasma and/or UF with a false discovery rate of <0.05. Peak areas of each solute in the Itch and No Itch HD patients were then compared to identify uremic solutes associated with pruritus.

Results: HD vintage, spKt/Vurea, and lab values were similar in both groups (Table). Metabolomic analysis identified 593 uremic solutes. No difference in the levels of these uremic solutes was found between the Itch and No Itch patients using a false discovery rate <0.05 (Figure).

Conclusions: Metabolomic analysis did not reveal any uremic solutes associated with pruritus in HD patients. The role of uremic solutes in pruritus remains to be established.

Funding: Veterans Affairs Support

PO1054

Combined Value of Geriatric Nutritional Risk Index, Body Composition, and Bone Mineral Density for Predicting Mortality of Hemodialysis Patients

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Background: Prognostic utility of the geriatric nutritional risk index (GNRI) and the association between body mass index and bone mineral density (BMD) in hemodialysis (HD) patients are uncertain. We assessed the combined predictive value of GNRI, body composition, and BMD in HD patients.

Methods: Pre-dialysis laboratory data, same-day post-dialysis body composition parameters by the Body Composition Monitor (Fresenius), and radius, lumbar spine, and femoral bone mineral density (BMD) using dual energy X-ray absorptiometry were assessed in HD patients at baseline. The data were compared according to GNRI tertiles (T). Logistic regression analysis was used to assess GNRI T1. Kaplan-Meier survival and Cox proportional hazard analyses were conducted. Comparison of multiple receiver operating characteristic curves was performed to assess whether mortality prediction accuracy improved after adding GNRI, body composition, and BMD to established risk factors.

Results: Among 264 patients (male: 65%, diabetes: 42%), mean age was 65±12 years and the median dialysis vintage was 79 (39-144) months. GNRI T1, T2, T3 were 88 (85-91), 94 (93-95), 98 (97-101), respectively. GNRI T1 patients showed older age, lower male frequency, and lower serum albumin, body cell mass index (BCMI), lean tissue index, fat tissue index (FTI), lumbar spine, femoral, renal and right distal mid-third BMD, but higher overhydration/extracellular fluid than patients with GNRI T2 or T3 (P<0.05). FTI (OR: 0.88), femoral neck BMD (OR: 0.95), age (OR: 1.03), C-reactive protein (OR: 1.37) and hemoglobin (OR: 0.70) were significant predictors of GNRI T1 (P<0.05). Patients with GNRI T1 showed significantly lower 2-year survival and GNRI T was significant predictor for 2-year all-cause mortality [Hazard ratio (T1-2): 2.07 (0.56-8.93), (T1-3): 5.59 (2.45-3.39x37), P<0.05]. Area-under-the curve for all-cause mortality using established risk factors (age, sex, diabetes, serum phosphate) was 0.66, improving to 0.79 by adding GNRI alone or to 0.81 by adding GNRI, FTI, and femoral neck BMD (P<0.05).

Conclusions: Associations of GNRI, body composition, and BMD were confirmed in HD patients. Combining GNRI, body composition, and BMD to established risk factors improved mortality prediction in HD patients.

Funding: Private Foundation Support

PO1055

Predicting Intradialytic Hypotension with Continuous Hemodynamic Monitoring Throughout Hemodialysis

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Background: Intradialytic hypotension (IDH) remains one of the most common complications associated with hemodialysis (HD). The CritLine Monitor (CLM) measures relative blood volume (RBV) and blood oxygen saturation (O2 Sat), but uncertainties remain in application of these parameters for predicting IDH. We looked at differences in CLM parameters based on whether an IDH episode was imminent or not as a function of time into a HD session to investigate whether their prognostic ability is dependent on the time into HD.

Methods: We studied routinely collected data from 17 US dialysis clinics. IDH was defined by systolic blood pressure (SBP) below 90 mmHg. The CLM directly measures RBV and O2 Sat, interpreted as arterial O2 Sat (Sao2) for all sessions with a fistula or graft and as central venous oxygen saturation (Scvo2) for those with a central venous catheter. For sessions with Scvo2, we also calculated estimated upper body blood flow (euBBF). We extracted each parameter every 30 minutes through each treatment. We compared
variables dependent on whether IDH occurred in the subsequent 30 minutes. Separate linear mixed-effects models were used for each CLM parameter as the dependent variable, IDH status as a dummy-coded predictor and subject as a random effect to account for repeated measures on individuals.

Results: We studied 2,791 patients and 197,526 sessions, 160,094 (81%) with SaO2 and 37,432 (19%) with ScvO2 data. IDH occurred in 13% of sessions. RBV was not different in the first 90 minutes for patients approaching IDH compared to those who were not, but was lower thereafter. Differences between the groups were observed throughout HD for ScvO2 and eUBBF, but not SaO2.

Conclusions: The ability for RBV to predict IDH depends on the time of onset. ScvO2 and eUBBF better predict IDH than SaO2, reflecting the dependence of ScvO2 on cardiac output while SaO2 more reflects pulmonary function.

**PO1056**

**Time of Hemodialysis and Risk of Intradialytic Hypotension and Intradialytic Hypertension**

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Background: Blood pressure (BP) fluctuates throughout the day following a circadian pattern. BP control is of utmost importance in patients with ESRD undergoing hemodialysis (HD), and both intradialytic hypotension (IDH) and intradialytic hypertension (HTN) are associated with adverse CV events and death. Whether the risk of IDH and intradialytic HTN varies according to the time of the day of the HD session is unknown.

Methods: Random effects logistic regression models examined the association of HD start time (before 9:00 am [timecat1], 9:00 am to 12:00 pm [timecat2], and after 12:00 pm [timecat3]) with IDH and intradialytic HTN among adults undergoing thrice-weekly maintenance HD (N=1,938 patients; n=64,503 sessions from the Hemodialysis [HEMO] Study, and N=3,408 patients; n=33,590 from a contemporary large dialysis organization [LDO]). IDH was defined as nadir intra-HD SBP <90 mmHg if pre-HD SBP <160 mmHg or <100 mmHg if pre-HD SBP ≥160 mmHg, and intradialytic HTN was defined as any increase in post-HD SBP compared to pre-HD SBP. Models were adjusted for demographics, CV comorbidities, HD dose, HD flux, pre-HD BUN, pre-HD SBP, UFR, HD vintage and HD session length.

Results: Mean age was 55 years and 56% were female in HEMO; mean age was 63 years and 42% were female in LDO. Compared to timecat1, timecat2 and timecat3 were associated with a 9% (aOR 0.91, 95% CI 0.82-1.01) and a 17% (aOR 0.83, 95% CI 0.75-0.94) lower risk of IDH in HEMO, respectively (Fig 1A). Conversely, compared to timecat1, a monotonic increase in the risk of intradialytic HTN was observed for timecat2 (aOR 1.14, 95% CI 1.05-1.24) and timecat3 (aOR 1.40, 95% CI 1.28-1.53) in HEMO (Fig 1B). These findings were consistent in LDO (Fig 1).

Conclusions: In two diverse and large cohorts of HD, we observed a monotonic decrease in the risk of IDH and a monotonic increase in the risk of intradialytic HTN as HD start time progressed throughout the day. Whether HD treatment allocation to certain times of the day in hypertensive-prone or hypertensive-prone patients improves outcomes deserves further investigation.

**PO1057**

**Association Between Pulse Pressure and Extracellular to Intracellular Water Ration in Hemodialysis Patients**

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Background: Optimal fluid management is a challenge in patients with end-stage kidney disease (ESRD) on maintenance hemodialysis (HD). Multifrequency bioimpedance spectroscopy (MBIS) is a non-invasive method to estimate body composition, including estimates of extracellular water (ECW) and intracellular water (ICW) and the ratio between both spaces (ECW/ICW). Pulse pressure is a significant risk factor of cardiovascular disease and death in general and dialysis population. Our study aimed to analyse the correlation between systolic, diastolic and pulse pressure with body composition status in ESRD patients before HD.

Methods: We performed a retrospective single-centre cohort study in 93 HD patients. The body composition was measured using the portable whole-body MBIS device, Body Composition Monitor-BCM (B) (Fresenius Medical Care, Bad Homburg, Germany). Blood pressure was measured with OMRON monitors.

Results: The mean age of patients was 64 ± 13 years, mean diastolic value 63 (1-352) months, 61% were men, all patients had arteriovenous fistula as vascular access. Sixty-nine (74.2%) patients were fluid overload (FO) with > 1.1 L of overhydration. Other data are presented in table 1. We found a statistically significant correlation between the pulse pressure and ECW/ICW ratio (r=0.258; P=0.033) in FO patients. In contrast, there was no significant correlation between systolic, diastolic blood pressure and ECW/ICW ratio in non-FO patients.

Conclusions: Only pulse pressure and not systolic or diastolic blood pressure values measured before HD are associated with ECW/ICW ratio in FO patients.

**PO1058**

**Plasma Refill Rate: A Potential Hemodynamic Marker of Intradialytic Hypotension During Hemodialysis**

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Background: Intradialytic hypotension (IDH) is difficult to predict. Continuous hemocrit monitoring (CHM) measures relative blood volume to provide non-invasive dynamic monitoring during hemodialysis (HD). We used CHM data with time-updated ultrafiltration rate (UFR) to estimate plasma refill rate (PRR), a potential mediator of hemodynamic status, and studied its relationship to IDH.

Methods: We used CHM performed at 17 Renal Research Institute HD units from 2017 to 2019 to calculate intradialytic PRR standardized to weight and height. We defined IDH as 1) systolic blood pressure (SBP) <90 mmHg and 2) a drop in SBP ≥20 mmHg or in mean arterial pressure a 10 mmHg associated with symptoms. IDH-prone was defined as having >20% of treatments with IDH. Un- and multivariable mixed-effects logistic regression were used to evaluate factors associated with low initial PRR (lower quartile) within the first 10 minutes of HD. Bi- and multinomial logistic regression were used to evaluate the relationship between initial PRR and IDH. Data are presented as mean±SD or aOR; 95% CI.

Results: We studied 2,637 patients (61±15 yrs, 57% male, 51% white) with 184,044 total treatments, interdialytic weight gain (IDWG) 2.1±1.4 kg, and UFR 9.3±4.6 ml/kg/h. IDH occurred in 13.7% and 15.8% of treatments by definitions 1 and 2, respectively. PRR (ml/kg/h) over all sessions was 5.0±8.8, 8.4±6.0, 7.9±7.2, and 7.4±11.4 at 10, 1h, 2h, and 3h, respectively, with substantial variability at both patient and treatment levels. Older age, low BMI, female sex, black race, low albumin, and multimorbidity were associated with low initial PRR. Patients with low initial PRR were more likely to be IDH-prone by definition 1 (aOR 1.95; 1.01-3.72) and definition 2 (aOR 1.50; 0.87-2.56). Patients with low initial PRR were more likely than patients with high initial PRR to be IDH-prone by definition 1 (aOR 2.12; 1.50-2.74).

Conclusions: The dynamics of PRR vary during an HD session and has promise as a marker of hemodynamic instability. We found that several patient and treatment factors classically associated with IDH were also associated with low initial PRR, independent of MBIS= multifrequency bioimpedance spectroscopy; HD=hemodialysis.
PO1059

Hypoadosteronism in Chronic Hemodialysis Patients Causes Intradialytic Hypotension and Is Improved with Fludrocortisone

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Background: Intradialytic hypotension (IDH) affects up to 30% of chronic hemodialysis (CHD) pts and hypoadosteronism (HA) is common in these pts. Aldosterone (aldo) exerts potent non-genomic hypertensive effects via its arterial aldo receptor & enhanced sympathetic nervous system activity.

Methods: We identified 11 consecutive CHD pts with severe IDH & normal cosypotin stimulation tests that had HA. Mean PRA was 3.3 +/-7.7 ng/mL/hr & serum aldo was 2.9 +/- 0.6 ng/dL. All pts had failed low temperature dialyze, UF & Na modeling and maximum doses of midodrine. We studied pre & post HD SBP & DBP, number of episodes of systolic BP <100 & mean UF volume (kg) for the 13 dialysis treatments pre fludrocortisone (FC), 1 month post FC & 6 months post FC. FC dose was 0.1 mg BID. The mean pt age was 69 +/-11 years & dialysis duration was 5.1 +/-2.3 years.

Results: The mean +/- SD pre & post HD SBP & DBP & the mean number of hypotensive episodes were significantly improved at 1 & 6 months post-FC (Table 1). No changes occurred in UF volume. 4 pts remained on FC for 2 years or more without side effects and with sustained good results.

Conclusions: Refractory IDH is associated with HA in CHD pts. FC therapy decreases IDH episodes as well as improves pre & post SBP & DBP & can be used safely in CHD pts.

Table 1. Results for pre & post HD SBP & DBP, Hypotensive episodes & UF volume.

<table>
<thead>
<tr>
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<th>Pre-FC Mean BID</th>
<th>Pre-FC Mean mg/L</th>
<th>Post-FC Mean BID</th>
<th>Post-FC Mean mg/L</th>
<th>Mean (with BID vs. post FC)</th>
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<tr>
<td>SBP</td>
<td>115 (29.3)</td>
<td>131 (16.8)</td>
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<tr>
<td>DBP</td>
<td>70 (14.5)</td>
<td>72 (14.5)</td>
<td>72 (14.5)</td>
<td>72 (14.5)</td>
<td></td>
</tr>
<tr>
<td>UF kg</td>
<td>5.4 (9.1)</td>
<td>3.2 (2.2)</td>
<td>3.2 (2.2)</td>
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PO1060

Feasibility and Benefits of Hemodialyzer Filtration of Contaminated Water in Poor Rural Communities in Ghana

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Background: Contaminated water supplies for drinking water are a source of health problems in poor communities. Hemodialyzers with a pore size of 0.003 micrometers have been known to be effective in preventing transfer of bacteria and most viruses. Our NGO, “Easy Water for Everyone,” investigated prospectively the incidence of diarrea, before and after implementation of water treatment utilizing reused hemodialyzers in poor villages lacking electricity and sanitation in Ghana.

Methods: Data were collected monthly regarding the incidence of diarrea and death in households of 8 villages that have no electricity during February to November 2018. In a "study" villages the main source of drinking water (river), was processed after the first 5 (pre) months through a set of 8 hemodialyzers that produced purified water at ~250 L per hour. River water was pumped weekly into an elevated holding tank to be drawn by gravity through the dialyzers whenever the faucet was opened. Manual back flushes (4x/ day) by trained villagers maintained high output of clean water. The same data collection in a "control" villages where the polluted water was not (yet) treated during the same 10 month period. We also assessed the function of the devices over ~21 months of use in 9 villages.

Results: [1] Monthly rates of diarrhea in the study villages decreased from 18 to 5 per 100 villagers from the pre to the post period for a rate reduction by 72% (rate ratio = 0.27). In the control villages the monthly rate during the same calendar months decreased by 23% (p >0.05) from the first to the second 5 months. After >11 months of daily filtration in 9 villages (population ~2000) none of the filters had to be replaced, suggesting that daily back-flush management prevented hemodialyzer clogging.

Conclusions: We demonstrated feasibility and success of sustaining a simple and effective water treatment program on entire villages including those without available electricity. The continuous function over >11 months indicates low cost of the device over time. The reduction in diarrea from before to after initiation of the hemodialyzer filtration device is large. The simplicity of hemodialyzer filtration by gravitational feed, low cost and relative case suggest wider application to other needy villages.

Funding: Private Foundation Support

PO1061

Combining a Heparin-Graded Dialyzer with a Citrate-Enriched Dialysate Offers Acceptable Dialysis Adequacy Avoiding Systemic Anticoagulation: Results of the Randomized Noninferiority Evoxet Study

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Background: The combined use of a heparin-graded membrane with a citrate-enriched dialysate is a hemodialysis (HD) strategy with low circuit cloting rates while avoiding systemic anticoagulation. Its adequacy in comparison to HD using systemic anticoagulation is unknown.

Methods: Prevalent HD patients were recruited for a randomized crossover non-inferiority trial powered at >90% to detect a prespecified non-inferiority threshold of 10% spKt/Vurea (NCT03887468). HD using a heparin-grafted dialyzer in combination with a 1.0 mmol/L citrate-enriched dialysate (“evohep”) was compared to HD using a heparin-grafted, systemic unfractrated heparin and bicarbonate-based dialysate (“evohep”). Each treatment arm lasted 4 weeks: 3x4hours HD/week with fixed blood and dialysate flow rates and midweek biological analyses.

Results: 26 patients received 617 HD sessions: 307 evoct and 310 evohep sessions. Mean spKt/Vurea was 1.46±0.23 for evoct and 1.50±0.24 for evohep sessions (p=0.06). The mean paired difference of spKt/Vurea was 0.04 with a 95% CI of -0.002 to 0.08, the upper bound of the estimate lying within the prespecified non-inferiority threshold (i.e. <0.15). Ultrafiltration reduction rate (URR) was 71.5±5.9% vs 72.1±5.7% and beta2microglobulin RR 37.4±6.8% vs 37.8±8.5% for evoct and evohep sessions. Processed blood volume was 75.4±3L vs 75.8±5.1L and online Ki was 47.3±5L vs 48.3±4L for all evoct and evohep sessions.

Conclusions: HD avoiding systemic anticoagulation using a heparin-grafted dialyzer with a citrate-enriched dialysate offers recommended spKt/Vurea dose and is not inferior to HD using systemic anticoagulation in terms of spKt/Vurea. Circuit clotting complications occurred at low rates during evoct sessions and did not have clinically significant repercussions on dialysis efficacy.

Funding: Private Foundation Support, Government Support - Non-U.S.

PO1062

Cinacalcet Use and the Risk of Gastrointestinal (GI) Bleeding Among Hemodialysis Subjects with Secondary Hyperparathyroidism (SHPT) in the Dialysis Outcome and Practice Patterns Study (DOPPS)


Background: Cinacalcet is an oral calcimimetic for the treatment of SHPT in US adult hemodialysis (HD) patients. We conducted an observational study to evaluate the potential association between cinacalcet and fatal and non-fatal GI bleeding using data from DOPPS, an observational longitudinal data system of a random sample of patients from dialysis facilities in more than 20 countries.

Methods: The eligibility criteria for study cohort inclusion was individuals a18 years of age with ESRD receiving in-center hemodialysis at a DOPPS facility for a minimum of four months during calendar years 2009-2015, in the following countries: Australia, New Zealand, Canada, France, Germany, Italy, Spain, Sweden, Japan, the UK, and the US. The nested within the cohort, we conducted a matched case-control study (1:4 matching ratio) to estimate the association between cinacalcet use and GI bleeding events. We used a set of sampling and matching rules on the following: (1) duration of follow-up (same number of days), (2) time on dialysis (±1 year, >1 year), (3) age (±11 year), and (4) sex. Multivariable conditional logistic regression models were used to generate adjusted odds ratios (ORs) and 95% confidence intervals (CIs), accounting for baseline comorbidities.

Results: A total of 9,349 HD patients with SHPT met the eligibility criteria for the cohort study, 4,399 subjects from the United States and 4,950 subjects from countries outside the United States. We estimated the incidence rate of hospitalization or death due to GI bleeding (per 1,000 person-years [PY]) in the US as 10.2 (95% CI: 7.9, 13.3); and outside the US as 23.5 (95% CI: 21.7, 25.9) in our study population, our number was association between cinacalcet exposure and GI bleeding (fatal or nonfatal events) in HD patients with SHPT in the US (adjusted OR: 0.68 [95% CI: 0.47, 1.00]) and ex-US (adjusted OR: 0.75 [95% CI: 0.50, 1.12]) populations.

Conclusions: Cinacalcet use was not associated with an increased risk of GI bleeding events in HD patients with SHPT in the US and ex-US adult hemodialysis subjects with SHPT. The study results are broadly generalizable to adult subjects with ESRD receiving center-based hemodialysis in the US and selected countries outside the US.

Funding: Commercial Support - Amgen
PO1063 Medium Cut-Off Dialyzer Improves Erythropoiesis-Stimulating Agent Resistance in a Hepcidin-Independent Manner in Maintenance Hemodialysis Patients

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Background: The response to erythropoiesis stimulating agents (ESAs) is affected by inflammation linkaged to middle molecules in hemodialysis (HD) patients. We evaluated the effect of a medium cut-off (MCO) dialyzer on ESA resistance in maintenance HD patients.

Methods: Forty-nine patients who underwent high-flux HD were randomly allocated to the MCO or high-flux group. The primary outcome was the changes of erythropoietin resistance index (ERI; U/kg/wk/g/dL) between baseline and 12 weeks. The biomarkers associated with iron metabolism and inflammation at 12 weeks were compared between groups.

Results: The MCO group showed significant decrease in the ESA dose, weight-adjusted ESA dose, and ERI compared to the high-flux group at 12 weeks (all p < 0.05). In the MCO group, the ESA dose, weight-adjusted ESA dose, and ERI did not change until 8 weeks compared to those at baseline, but decreased significantly at 12 weeks (all p < 0.01). Serum iron and transferrin saturation were higher in the MCO group at 12 weeks (both p < 0.05). The MCO group showed a greater reduction in TNF-α and lower serum TNF-α level at 12 weeks compared to the high-flux group (p = 0.025 and p = 0.027), whereas no differences were found in the reduction ratio of hepcidin and serum levels of erythropoietin, erythroferrone, soluble transferrin receptor and hepcidin between groups.

Conclusions: HD with MCO dialyzer improves ESA resistance compared to high-flux HD in maintenance HD patients. The MCO dialyzer provides superior removal of the inflammatory cytokine such as TNF-α and thus improves iron metabolism in a hepcidin-independent manner.

The iron metabolism regulatory pathway Blue arrows indicate dominant effects.

PO1064 Recent Trends in Acute Care Admissions Among Medicare Beneficiaries Undergoing Dialysis

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Background: While the rate of hospital admissions has been a bedrock measure of morbidity among dialysis patients, patients today may receive acute care during a hospital admission, observation status, or an emergency department (ED) visit. There are no public reports summarizing the composite rate of these encounters among dialysis patients. We used claims data to estimate rates of acute care admissions in dialysis patients with Medicare fee-for-service coverage.

Methods: Using Medicare Limited Data Sets, we identified all patients with Medicare Part B claims documenting outpatient dialysis from January 2014 to December 2017. For each calendar week (Monday to Sunday), we identified patients with at least one outpatient dialysis session, who were alive at the end of the week, and who were not hospitalized at the last midnight of the week. We calculated the proportion of patients who were admitted to the hospital, observation status (with discharge to home), or an ED (with discharge to home) during the subsequent calendar week. From the time series of weekly admission risks, we fit an autoregressive integrated moving average model, both overall and within strata defined by concurrent enrollment in Medicaid.

Results: From 2014 to 2017, mean weekly incidence of acute care admission increased from 5.8% in 2014 to 6.0% in 2017 (p < 0.01 from test of secular trend), as displayed. The incidence of hospital admission was unchanged (p = 0.35), whereas the incidence of both observation status admissions and ED visits increased (p < 0.01). In 2017, 49% of acute care admission volume was attributed to observation status admissions and ED visits. In patients with Medicare coverage alone and patients with concurrent enrollment in Medicaid, mean weekly incidence of acute care admission increased to 5.2% and 6.9%, respectively, in 2017.

Conclusions: From 2014 to 2017, the incidence of acute care admission increased in dialysis patients with Medicare fee-for-service coverage, mostly because of increasing incidence of observation status admissions and ED visits.

Funding: Commercial Support - Fresenius Medical Care

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO1065 Poor Vitamin K Status Associates with Worse Clinical Outcome Independent of Coronary Artery Calcium and Aortic Valve Calcium in ESRD

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Background: Patients with end-stage renal disease (ESRD) are at high risk of vitamin K deficiency and vascular calcification. The association between vitamin K status and vascular calcification is non-affirmative in clinical observations. We investigated the association of vitamin K status with all-cause mortality in ESRD and the modification effect of vascular calcification in this scenario.

Methods: We studied 493 stable ESRD patients (median age 55 years, 66% males) comprising non-dialysis patients (n=321), prevalent peritoneal dialysis (n=122) and hemodialysis patients (n=50). Plasma dephosphorylated-uncarboxylated matrix-Gla protein (dp-ucMGP), a circulating marker of vitamin K deficiency, and other relevant clinical and biochemical data were determined at baseline. A cohort of 553 controls (median age years, 45% males) was referred to estimate vitamin K status in healthy subjects. Vascular calcification was estimated with coronary artery calcium (CAC) and aortic valve calcium (AVC).

Results: Plasma dp-ucMGP (median 1445 pmol/L) levels were substantially elevated in ESRD patients compared to healthy subjects (median 376 pmol/L). During median 42 months’ follow-up, 92 patients died (19%) and 128 patients (26%) underwent renal transplantation. There was a significant trend of increased all-cause mortality (1.19 (1.01-1.40), sub-hazard ratio (95% confidence interval)), with adjustment for age, sex, presence of cardiovascular disease, diabetes, body mass index, inflammation, handgrip strength and dialysis. In subgroup analysis further adjusted for presence of CAC or AVC, dp-ucMGP remained as an independent risk factor of mortality (1.27 (1.03-1.56) and 1.36 (1.05-1.66), respectively). In multivariate linear regression model, increased dp-ucMGP levels were associated with increased all-cause mortality (1.27 (1.03-1.56) and 1.36 (1.05-1.66), respectively). Multivariate linear regression model, increased dp-ucMGP levels were associated with increased all-cause mortality (1.27 (1.03-1.56) and 1.36 (1.05-1.66), respectively). Multivariate linear regression model, increased dp-ucMGP levels were associated with increased all-cause mortality (1.27 (1.03-1.56) and 1.36 (1.05-1.66), respectively).

Conclusions: Vitamin K deficiency is evident in ESRD and strongly associated with an increased risk of mortality which is not modified by the presence of vascular calcification. Plasma dp-ucMGP was not an independent risk factor of calcification quantified by CAC and AVC.
PO1066 Calcium Carbonate-Pre-Added Cheese to Improve Compliance, Nutrition, and Metabolic Balance of Patients on Renal Replacement Treatment Gianluigi Ardissono,1 Valentina Capone,1 Elisabetta Margiotta,2 Isabella Capano,1 Francesca Raffiotta,2 Giovanni Montini,1 Piergiovanni Messa,1 Pediatrics, Dialysis and Transplantation, Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milano, Italy; 1Nephrology, Dialysis and Transplantation, Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milano, Italy.

Background: Patients with chronic kidney disease have several dietary limitations that make their diet unappealing with detrimental consequences as adherence to prescriptions, malnutrition and overall poor quality of life. Cheese, an important component of the Western diet, has high phosphorus (P) content thus its consumption is generally restricted in patients on renal replacement therapy (RRT).

Methods: A special cheese was prepared by adding a fixed concentration of CaCO3 (5 g/L) to cow milk prior to production procedures. The cheese was then provided to a cohort of patients on chronic RRT with the working hypothesis that while eating the modified cheese patients would have benefited from the phosphorus-vacuum-binding effect of CaCO3. After a run-in period of 1 month, all patients were randomly assigned to receive standard cheese (SC) followed by modified cheese (FriP) or the opposite sequence in a double blind and cross-over fashion for 1 month for each product. The increase in inter-dialysis (48 hrs) P (DP) was regularly and repeatedly (n: 5) measured during each of the 2 periods. A washout period of 1 week was introduced between treatment periods.

Results: Twenty-one patients were enrolled and 16 successfully completed the 2 treatment periods. Drop outs were due to vaccination, COVID-19 infection or to documented non-adherence to the protocol. Observed mean (±DP) DP was as follows: Run-in: 2.8 (0.7) mg/dL, SC: 2.8 (0.85) mg/dL, FriP 2.4 (0.61) mg/dL with the latter being significantly lower compared with both other periods. Pre-dialysis P was also lower with FriP compared with SC: 5.00 (1.00) vs 4.66 (0.91) while Pre-dialysis Ca was not different: 9.24 (0.73) vs 9.24 (0.63) with SC and FriP, respectively. All patients appreciated both products equally and the mean amount consumed per week was not different: SC: 307 gr ± 9.24 (0.73) vs FriP: 283 gr (p: 0.56). All patients reported a significant gratification by reintroducing cheese consumption in their diet.

Conclusions: In conclusion, FriP cheese may reduce dietary limitations of patients on RRT mith significant benefits on: malnutrition, adherence to P binders prescription and ultimately to quality of life.

PO1067 Efficacy of Double-Dose Influenza Vaccine with a Booster Compared with Standard Dose in Hemodialysis Patients: Randomized Controlled Trial Ekapol Ritevareed,1 Kobporn Boonmak,2 Suree Yoowannakul,1 Blumibol Adulyadej Hospital, Bangkok, Thailand; 2Mahidol University Faculty of Tropical Medicine, Bangkok, Thailand.

Background: Patients on hemodialysis may be at higher risk of illness and death from infection of influenza virus. The efficacy of dose of influenza vaccine across dialysis patients is uncharacterized. We assessed the efficacy of double-dose and booster influenza vaccine versus standard-dose in hemodialysis patients.

Methods: A prospective, open-label, randomized study with 100 hemodialysis patients were enrolled. Double-dose and booster group(n=50) received two doses of IM inactivated seasonal quadrivalent influenza vaccine and one dose at the next 2 weeks while standard-dose group(n=50) received one dose of vaccine. Demographics and co-morbidity were collected at baseline. HAI titers were assessed prior to vaccination and at 14, 28 days post-vaccination.

Results: Hemodialysis patients had age of 61 years approximately and had similar baseline laboratory and co-morbidity. Double-dose with booster group had higher rate of seroprotection(100% vs 86%, p=0.006) and seroconversion(84% vs 60%, p=0.008) measured by using HAI against H3N2 were significantly different. Moreover, Double-dose with booster group had higher rate of sustained antibody level at 4 weeks after first vaccination measured by using HAI against H1N1(88% vs 52%, p=0.006) and H3N2(84% vs 72%, p=0.003) were significant differences. However, no differences in HAI against B strains were seen. At 4 weeks after first vaccination, HAI against H1N1, H3N2, B/Colorado and B/Yamagata are similar in both groups.

Conclusions: The double-dose with booster influenza vaccine can provide higher seroprotection and seroconversion rates of HAI against H3N2 but no different in other strains compared to standard-dose. This study is needed to explore the effect of double-dose with booster vaccine against all causes mortality or influenza related outcomes for adults undergoing hemodialysis compared to the standard-dose.

Funding: Private Foundation Support

PO1068 Temporal Trends in Clinical Phenotype, Bacterial Genotype, and Clinical Outcomes in Hemodialysis-Dependent Patients with Staphylococcus aureus Bacteremia Matthew R. Sinclair,1,2 Maria Souli,1 Felicia Rufina,1 Lawrence Park,3 Michael M. Dagher,1 Christina M. Wyatt,1 Vance Fowler,1,2 Duke University Hospital, Durham, NC; 1Duke Clinical Research Institute, Durham, NC; 2Duke Global Health Institute, Durham, NC.

Background: Staphylococcus (S.) aureus bacteremia (SAB) is a common and potentially lethal infection among hemodialysis-dependent (HD) patients. The determinants of clinical outcomes in HD patients with SAB are not completely understood. We evaluated temporal trends in SAB-attributable mortality, metastatic infections, and bacterial genotype in HD patients over a 20-year period.

Methods: Hospitalized, non-neutropenic HD and non-HD adults with monomicrobial SAB were prospectively enrolled from Jan 1, 1995 to Dec 31, 2015. Clinical characteristics, bacterial isolates, and outcome data were collected. Isolates were previously genotyped using spa typing. Differences between HD and non-HD patients were estimated using median/quantiles or counts/percentages with statistical significance evaluated with Mann-Whitney-U or Fisher’s Exact test. Proportions of patients experiencing each outcome were calculated overall and by calendar year. Secular trends in proportions were estimated with linear regression and associations between bacterial genotypes, clinical characteristics, and clinical outcomes were estimated using univariate and multivariate logistic regression.

Results: Among 2,347 unique participants, 495 (21.1%) were HD. Compared to the non-HD patients, HD patients were younger (median 57 years (y) vs 60 y, p=0.002) and more likely to be Black (74.6% vs 26% p<0.001), female (48.1% vs 42.1% p<0.019), and to have diabetes (56.2% vs 33.8% p<0.001). HD patients experienced significant increases in the annual prevalence of age- and diabetes-adjusted SAB-attributable mortality (0.49% per year p<0.05), metastatic infections (0.79% per year p=0.028), and infection with the highly virulent Methicillin resistant strain USA300 (0.97% per year, p=0.001). The increase in USA300 infections did not appear to explain the observed increases in metastatic infections (Odds Ratio [OR] 1.33, Confidence Interval [CI] 0.55-3.21) or SAB-attributable mortality (OR 0.57, CI 0.14-2.32).

Conclusions: Clinical characteristics differed significantly between HD and non-HD patients with SAB. Increases in mortality and metastatic infections over time were not explained by the rise in more virulent strains of S. aureus, but may be partially explained by changes in patients’ characteristics.

PO1069 Hemodialysis-Associated Increased Intraocular Pressure: A Vision-Threatening Complication Chad Y. Lewis,1 Nikhil Batra,2 Eric A. Steffen,2 Martha L. Graber,2 Dartmouth College Geisel School of Medicine, Hanover, NH; 2Dartmouth-Hitchcock Medical Center, Lebanon, NH.

Introduction: Elevation of intraocular pressure (IOP) is a potential complication of hemodialysis (HD). When patients with risk factors for angle closure undergo HD, aqueous humor volume may increase, thus elevating IOP.

Case Description: A 71-year-old female on ESRD secondary to type II diabetes and proliferative diabetic retinopathy reported one month of headache, left-sided eye pain and photophobia, and periocular redness occurring during dialysis. Ophthalmology diagnosed neovascular glaucoma occurring an elevated IOP of 36 mmHg in the left eye (normal < 22). Pre-dialysis IOP returned to normal with medical therapy. Dialysis modifications reduced the rate and magnitude of change in plasma osmolality (Table 1). However, elevated IOP and symptoms persisted and he underwent surgery on 5/6/2020 with full resolution of symptoms.

Discussion: Sitprija et al. (1964) first observed increased IOP during HD in 83 of 89 cases. Subsequent studies report that IOP may increase, decrease, or remain unchanged
during HD. One proposed mechanism for increased IOP is as plasma urea is reduced, the
hemoconcentration goes against the plasma. The choroid may also thicken, obstructing outflow.
We increased dialysate sodium and reduced HD time and dialysate flow. Other strategies include
infusing mannitol or hyperosmolar glucose, ultrafiltration to increase plasma onotic pressure, and more frequent or peritoneal
dialysis. Nephrologists should have heightened awareness for angle-closure glaucoma and
conditions predisposing to obstruction of aqueous outflow, including proliferative
diabetic retinopathy. Headache, ocular pain, or visual changes during dialysis warrant
urgent ophthalmic evaluation.

Table 1

<table>
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<th>Time (h)</th>
<th>Pre-HD IOP (mm Hg)</th>
<th>IOP 3 mins, 60 min, HD (mm Hg)</th>
<th>% No. in IOP (mm Hg)</th>
<th>% in IOP (mm Hg)</th>
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<td>5%</td>
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<td>5/25/20</td>
<td>114/78</td>
<td>131/100</td>
<td>2%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Discussion:
The role of decongestive therapy and guide the amount of ultrafiltration.

PO1070
Point-of-Care Ultrasonography to Assess Venous Congestion and Guide Ultrafiltration: Another String to Our Bow?
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Introduction:
Point of care ultrasound (POCUS) is rapidly evolving as a valuable adjunct to bedside clinical examination in internal medicine and subspecialties. However, there is no single accurate sonographic application to determine fluid volume status. While sonographic assessment of inferior vena cava (IVC) is popular among novice POCUS users, its isolated use to determine and monitor volume status is subject to numerous limitations. Similarly, lung ultrasound gives an idea of left sided filling pressures but does not
quantify venous congestion, which can have deleterious consequences in various
organ systems including kidney. Novel scoring systems like venous excess ultrasound
(VExUS) allow objective assessment of volume status using portal and hepatic
venous Doppler waveforms in addition to IVC measurements. Herein, we demonstrate
the natural history of these waveforms in a patient with advanced chronic kidney disease
(CKD) during the course of ultrafiltration.

Case Description:
A 39-year-old man with a history of CKD stage 5 presented with
generalized weakness, shortness of breath on exertion, worsening leg edema and weight
gain despite being compliant with prescribed diuretic therapy. He was admitted and
initiated on hemodialysis for refractory volume overload. POCUS showed mild pericardial
and pleural effusion as well as an enlarged IVC of ~5cm with <50% collapse. In addition,
Doppler ultrasound showed 100% pulsatility of portal vein (normal <30%) with systolic
flow reversal and hepatic vein with S wave reversal and only D wave below the baseline.

These findings constitute VExUS grade 3, suggestive of severe congestion. While IVC
continued to indicate high right atrial pressures, the Doppler waveforms showed parallel
improvement with ultrafiltration reaching VExUS grade 1 (mild congestion) at discharge
(Figure). No episodes of intradialytic hypotension occurred.

Discussion:
POCUS-derived venous waveforms aid in monitoring the effectiveness of
decongestive therapy and guide the amount of ultrafiltration.

PO1071
Can the Assessment of Ultrasound Lung Water in Hemodialysis Patients Be Simplified?
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Background:
Lung ultrasound (US) reliably estimates lung water and it is increasingly applied in clinical practice in dialysis patients. Lung water is measured by applying a semi-quantitative US score summing up the US-B lines detected in 28 lung intercostal spaces (LIS). A simplified assessment restricted to 8 LIS only has been proposed. However, the agreement among the scores has not been studied and their
prognostic value has never been compared.

Methods:
We included in the analysis 303 HD patients in which the pre-dialysis US-BL score was measured at baseline with both the semi-quantitative and the simplified method. The time needed for performing the 28-LIS and the 8-LIS score by six independent assessors with various experience on lung US assessment was accurately measured. Patients were divided into 4 categories, according to pre-established cut-offs specific for the two methods (28-LIS score: <5-15; 16–30; >30 US-BL; 8-LIS score: <10; 11-20; 21-50; >50 US-BL). The prediction power of these scores was assessed by the explained variance (R²).

Results:
The 28-LIS score and the 8-LIS score were highly inter-related (p=0.93; P<0.001). During a mean follow-up of 3 years, 112 patients died and 129 experienced a CV event. At univariate and multivariate analysis, both scores were associated to the study outcomes. R² of the 28-LIS score for death was 4.1% and that for CV events 4.6%. The corresponding R² of the 8-LIS score were 5.4% (death) and 4.7% (CV events), values close to those of the 28-LIS score. Accordingly, when the two scores were separately added to a clinical model including easily available clinical variables the
R² of the model including the 28-LIS score for death:31.1%; CV events:23.9% were again very similar to those of the 8-LIS score (30.7% and 23.1%, respectively). The median time needed to perform the examination was 3.05 min (IQR 2.22–5.00 min) for the 28 LIS score and 1.35 min (IQR 1:16–2:00 min) for the 8 LIS score.

Conclusions:
The simplified 8-LIS score is tightly related to the classical 28 LIS score and the two scores hold an almost identical predictive power. Even though the 28-LIS score demands less than 5 minutes, the 8-LIS score can be done in only about 90 sec. and it is therefore better suited for application in everyday clinical practice in hemodialysis units.

PO1072
Longitudinal Assessment of Random Variability in ICH-CAHPS Scores
Dena E. Cohen, Steven M. Brunelli, Francesca Tentori. Davita Clinical Research, Minneapolis, MN.

Background:
The Centers for Medicare & Medicaid Services mandates use of the
In-Center Hemodialysis Consumer Assessment of Healthcare Providers and Systems
(ICH-CAHPS) survey to assess dialysis patients’ experience of care. Survey responses,
collected twice annually and reported at the facility level, are intended to evaluate facility
performance over time and to compare across facilities at a given time. In order to be
useful for these purposes, the random variability in ICH-CAHPS scores must be relatively
low.

Methods:
ICH-CAHPS scores were analyzed among 2735 facilities managed by a
large dialysis organization that had at least one ICH-CAHPS score available between
2014 and 2018. The association between Center Global Rating score (1 of the 6 ICH-
CAHPS domains) and survey period was assessed using a mixed model with random
slopes and intercepts for each facility. Mean squared residuals were calculated for each
facility and categorized on the basis of the number of survey responses received at
the facility. Facilities with available scores in all 9 survey periods analyzed (N = 1074) were
assigned to quintiles based on their position within the distribution of scores in each
survey period, and movement across quintiles was assessed longitudinally.

Results:
The mean Center Global Rating score in the fall of 2018 was 64.9, with an
average increase of 0.2 points per period over the subsequent 8 survey periods. However,
random variation in scores was considerable and dependent on the number of survey
responses received. The root mean square error, a measure of random variation, ranged from 0.9 points for facilities with >27 responses to 9.2 points for facilities with 11 to 12 responses. Among facilities with survey responses available in all 9 periods, movement between quintiles was frequent, with 39.7% of facilities occupying 4 of the 5 possible quintiles at least once, and 11.5% occupying all 5 quintiles. **Conclusions:** Within facilities, there is substantial random variation in ICH-CAHPS scores over time. This diminishes the utility of ICH-CAHPS for its intended purposes. Improvements to ICH-CAHPS, or development of alternative measures of patient experience, are needed to enable accurate assessment of facility performance and to inform patient care.

**PO1073 Implication of Trends in Timing of Dialysis Initiation on Population Incidence of ESRD**

**Chi-yan Hsu,1 Rishi V. Parikh,2 Leonid Pravoverov,2 Siije Zheng,3 David Glidden,1 Thilda C. Tan,1 Alan S. Go,1,3,1 University of California San Francisco, San Francisco, CA; 1Kaiser Permanente, Oakland, CA.**

**Background:** In the past two decades, eGFR at start of chronic dialysis worldwide have changed notably. How changes over time in the likelihood of dialysis initiation at any given eGFR level impacts the population burden of ESRD has not been well-defined.

**Methods:** We analyzed data from 2001-2015 in successive 3-year intervals among adult members of a large, integrated health care delivery system in Northern California who had ≥1 outpatient serum creatinine in the prior year. One-year risk of initiating chronic dialysis was delineated stratified by starting eGFR levels per 3-year cohort. To assess multivariable-adjusted temporal trends, we evaluated the significance of a 3-year cohort term in a logistic regression model adjusting for age, gender, race, and diabetes mellitus status. We then estimated a potential reduction in dialysis initiation in 2013-2015 using the relative difference between the standardized 1-year risks (95% CI) in 2001-2003 and 2013-2015.

**Results:** Among those with eGFR 16-17 mL/min/1.73m² (N=2753), 14-15 mL/min/1.73m² (N=2074), and 10-13 mL/min/1.73m² (N=2655), the 1-year risk of initiating dialysis increased for every 3-year period by 11% (adjusted odds ratio [aOR] 1.11 [95% CI 1.03 to 1.21]), 11% (aOR 1.11 [1.03 to 1.20]) and 7% (aOR 1.07 [1.01 to 1.14]) respectively, adjusting for age, gender, race, and diabetes mellitus (Figure). We estimate that incidence of ESRD could have potentially been 16% (95% CI 13% to 18%) lower if there were no changes in system-level practice patterns or patient-related or other factors from 2001-2003 to 2013-2015.

**Conclusions:** Our data suggest that approximately two thirds of the target 25% relative reduction in new ESRD cases by 2030 called for in the White House AAKH Initiative could potentially be achieved by changes in the timing of initiation of chronic dialysis increased for every 3-year period by 11% (adjusted odds ratio [aOR] 1.11 [95% CI 1.03 to 1.21]). We estimate a potential reduction in dialysis initiation in 2013-2015 using the relative difference between the standardized 1-year risks (95% CI) in 2001-2003 and 2013-2015.

**PO1074 Investigation and Analysis of Post-Dialysis Fatigue in Maintenance Hemodialysis Patients**

**Jin-mei Liu,1 Jun Yan,2 1the Fifth Affiliated Hospital of Sun Yat sen University, Zhuhai, China; 2the Third Affiliated Hospital of Sun Yat Sen University, Guangzhou, China.**

**Background:** Post-dialysis fatigue is one of the concerns in recent years. The time of fatigue recovery can be used to predict the hospitalization rate and mortality rate. At the same time, there are few reports on the relationship between maintenance hemodialysis (MHD) and protein energy consumption (PEW). The purpose of this study is to investigate the status of fatigue in MHD patients, analyze the factors affecting fatigue and the feasibility of intervention with PEW and provide possible effective interventions.

**Methods:** 346 MHD patients in our blood purification center were selected. MHD patients were assessed with self-made general data questionnaire, international standard fatigue assessment scale (FAI) and subjective comprehensive nutrition assessment (SGA), and the basic routine and clinical results were obtained.

**Results:** More than half of patients claimed to experience post-dialysis fatigue. Time to recover from hemodialysis (TIRD) was different: the interquartile range time was 2.000.00, 3.000.00 hours. In the study, 30.1% patients reported no fatigue after hemodialysis. Recovery time in 30.5%/5% patients was more than 3 to 4 hours, 12.5% was 5 to 12 hours, 1.0% patients took longer time to recover from a dialysis session. According to the recovery time, these patients were divided into three groups. Among the three groups, SGA score, the ultrafiltration, the serum sodium and bicarbonate level after dialysis and PEW was significant different. It was showed by the unconditional logistic regression analysis that high SGA (OR=1.312,95%CI1.163-1.481), scoreultrafiltration (OR=2.15,95%CI1.24-3.41) and serum sodium (OR=0.83,95%CI 0.71-0.98) were associated of TIRD.

**Conclusions:** The incidence of post-dialysis fatigue in MHD patients is high. Medicine staff should pay attention to the nutritional status of MHD patients, control their weight growth, and maintain the stability of electrolyte and bicarbonate levels such as serum sodium.

**PO1075 Recurrent Episodes of Angioedema During Hemodialysis**

**Abhay Mishra,3,1 Cheryl C. Brown-Deacon,1 Praveena Koneru,3 2Milj J. Shah,1 Madhumita J. Mohanty,1,2 1John D.Dingell VAMC, Detroit, MI; 2Wayne State University, Detroit, MI.**

**Introduction:** Angioedema during hemodialysis (HD) is uncommon but can be potentially life-threatening. We report a patient with recurrent episodes of angioedema during HD who posed a diagnostic and therapeutic challenge.

**Case Description:** A 73-year old male with end stage renal disease was initiated on HD in 2012. He did well on HD till February 2018 when he developed angioedema along with richness two minutes after initiation of HD and required intubation for airway support. No medications, food ingestions, contact with any external agents or insect bites were identified which may have triggered the angioedema. His C4 was normal. C1 esterase inhibitor and C1Q binding assay were normal, radioallergosorbent test was negative to aeroallergens, food allergens and latex. As no specific cause for angioedema was identified, a dialyzer reaction was considered. He was being dialyzed via Optiflux F180NR dialyzer (electron beam sterilized polysulfone membrane) since initiation of HD in 2012. He was subsequently dialyzed with other dialyzers including Optiflux F180 NR (sterilized with ethylene oxide), Exeltra 190 (gamma radiation sterilized trifluorethane acetate membrane) and R sexy 155 (gamma radiation sterilized polysulfone membrane).

He developed angioedema with each of these dialyzers within a few months of using them and in spite of premedication with intravenous methylprednisolone, diphenhydramine and ranitidine and also rinsing the dialysis circuit with three liters of normal saline prior to HD initiation. These episodes of angioedema occurred within the first 30 minutes of HD initiation and required intubation on two occasions. At this point, a possible reaction to the dialysis blood tubing, which was ethylene oxide sterilized, was considered and the patient was switched to Streamline Express dialyzer (polyethersulfone membrane with pre-attached blood tubing, both sterilized with gamma radiation). The patient has had no further episodes of angioedema since this change was made five months back and has been off steroids for the last two months.

**Discussion:** In patients with unclear etiology of angioedema during HD, exposure to all components of the HD circuit, including the dialysis blood tubing, should be considered as a potential cause of angioedema and should be systematically ruled out.

**PO1076 The Impact of Serum Albumin Levels on Excess Hospital Spending**

**Linda Ficocello,1 Melissa M. Rosen,2 Claudey Mullon,1 Robert J. Kossmann,2 Michael S. Anger,1 Fresenius Medical Care Renal Therapies Group, Waltham, MA; 2Fresenius Medical Care North America, Waltham, MA.**

**Background:** National Kidney Foundation K/DOQI guidelines recommend that hemodialysis patients have serum albumin (sA) levels greater than or equal to 4 g/dL. Serum albumin lower than 4 g/dL has long been associated with an increased risk of morbidity and mortality in dialysis patients. Compared to both low and high flux dialyzers, a mean albumin loss of 3g per dialysis session has been observed with medium cut-off (MC) dialyzers (Kim et al., BMC 2020; Kirsch et al. NDT, 2017) which may decrease SA levels and increase the risk of hypoalbuminemia (serum albumin ≤3.5 g/dL). The aim of this analysis was to estimate the impact of SA levels on hospitalization and associated cost.

**Methods:** Prior research conducted by Rocco et al. (J. Am. Soc. Nephrol., 1996) identified SA level as a risk factor for hospitalization in ESKD patients receiving dialysis and estimated hospital utilization associated with SA levels. Data from this analysis was used to show that relative to patients with SA≤4 g/dL, on average each year, patients with SA of 3.5-3.99 g/dL, SA of 3.0-3.49 g/dL, and SA of 3.0 g/dL had 7.8, 15.8, and 34.5 more hospital days, respectively. Using an average cost per hospitalization for a dialysis patient of $15,907.18 and the average length of stay (11.3 days) from USRDS, and data from Rocco et al. (1996), we estimated the additional hospital spending associated with reducing albumin levels.

**Results:** Based on previous research demonstrating an association between SA levels < 4 g/dL and increased risk of hospitalization, we estimated the hospitalization costs...
associated with having reduced serum albumin. Relative to hemodialysis patients with a 4 g/dL, we calculated that having a lower average sA level may result in excess healthcare spending of $5,662 for sA of 3.5-3.9 g/dL, $10,769 for sA of 3.0-3.4 g/dL, and $10,980 for sA less than or equal to 3.0 g/dL.

**Conclusions:** Lower serum albumin levels are associated with increased hospital admissions, which is estimated to lead to excess hospital spending on average of $5,662, $10,769, and $10,980 per patient per year. Preventing albumin loss in dialysis patients may help to reduce the risk of hospitalization.

**Funding:** Commercial Support - Fresenius Medical Care Renal Therapies Group

**PO1077**

A Pilot Randomized Controlled Trial of an Energy Management Program for Adults on Chronic Hemodialysis with Fatigue: The Fatigue-HD Study

Janine F. Farragher,1 Pietro Ravani,1 Braden J. Manns,1 Meghan J. Elliott,1 Chandra M. Thomas,1 Maoliosa Donald,1 Brenda Hemmelslag.1 University of Calgary

**Background:** How to reduce fatigue and its impact on life participation is a top-ten unanswered research question among patients treated with chronic hemodialysis. We aimed to determine the feasibility of conducting a randomized controlled trial, to investigate an energy management education program for the chronic hemodialysis population.

**Methods:** We conducted a parallel-arm, 1:1, blinded pilot RCT at six hemodialysis units in Calgary, Canada. Patients who had moderate or severe fatigue on the Fatigue Severity Scale, and met other study eligibility criteria, were invited to participate. Consenting participants were randomized to general self-management education or the Personal Energy Planning (PEP) program, a tailored 7-9 week energy management program that guides participants in practicing efficient energy expenditure during valued life activities. We assessed study eligibility, recruitment and attrition rates. We then computed standardized intervention effects (Cohen’s D statistic) on self-reported fatigue and life participation measures, compared to control, at immediate post-intervention and 12 weeks post-intervention.

**Results:** Of 253 people on hemodialysis screened, 153 were eligible to be approached (clinically stable and English-speaking). 42 (26%) were interested and consented to participate, and 30 met all study eligibility criteria were enrolled (mean age 62.4, 60% male). 22 (73%) enrolled participants completed all study procedures. Medium intervention effects were observed compared to control on the global life participation scale, global life participation satisfaction scale, and COPM-Performance Scale at immediate post-intervention follow-up. At 12-week post-intervention, large and very large intervention effects were observed on the COPM Performance and Satisfaction Scales, respectively, compared to control. Minimal to no intervention effects were seen on other life participation or fatigue measures.

**Conclusions:** We have shown it is feasible to enroll and follow patients on hemodialysis with fatigue in a randomized controlled trial of an energy management intervention. Since the intervention led to improved life participation on some scales, we have justified the need for, and feasibility of, a larger trial.

**Funding:** Government Support - Non-U.S.

**PO1078**

Coffee and Headache in Hemodialysis Patients: The CoffeeHD Trial

Mabel Aoun,2,3 Najla Hilal,2 Chadia H. Beaini,3 Ghassan Sleelaty,1 Joseph Haji,1 Celine El boueri,2 Dania Chehala1 Saint-Joseph University, Beirud, Lebanon; Saint-George Hospital, Ajaltoun, Lebanon; ‘Université Saint-Esprit de Kaslik, Jounieh, Lebanon; ‘Bellevue Medical Center, Mansourieh, Lebanon.

**Background:** Headache occurs in 40 to 75 % of HD patients. Caffeine circulates unbound in the blood and passes the dialysis membrane. Some suggested that headache can result from caffeine withdrawal. This study aims to compare the incidence of headache and hypotension between patients taking or not coffee during dialysis.

**Methods:** This is a randomized double-blind multicenter trial. Patients of 3 HD units were included. 156 patients were randomized to two groups, group A was given coffee and group B decaffeinated coffee mid-session for 12 sessions. UF rate was fixed to <13 ml/h. Primary outcome was incidence of headache and secondary outcome incidence of hypotension. This clinical trial received the approval of the ethics committee and was registered on ClinicalTrials.Gov (NCT04057313).

**Results:** 139 patients completed the trial (6.4% vs 15.4 % of withdrawal in A and B respectively). Baseline characteristics are summarized in Table 1. Incidence of headache was not significantly different between A and B (54% vs 37% respectively, p=0.522), nor the incidence of hypotension (25% vs 26% respectively, p=0.539). In subgroup analysis, headache was lower in A (p=0.06) in two categories of patients: those with higher potassium dialysate (K⁺) and the non-hypertensive patients.

**Conclusions:** Headache occurred in 34% to 37% of dialysis sessions. There was no difference in headache or hypotensive episodes between patients in the coffee versus decaffeinated group.

**Baseline characteristics**

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.3±15.5</td>
<td>59.9±14.4</td>
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</tr>
<tr>
<td>Sex (M/F)</td>
<td>71.8/28.2%</td>
<td>70.9/29.1%</td>
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<tr>
<td>Dialysis Vintage (MD)</td>
<td>209.7±64.4</td>
<td>278.1±65.3</td>
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<tr>
<td>Smoking (N/Y)</td>
<td>43.4%/56.6%</td>
<td>51.9%/48.1%</td>
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<tr>
<td>Hypertension (N/Y)</td>
<td>139.9%/60.1%</td>
<td>149.4%/50.6%</td>
<td>0.221</td>
</tr>
<tr>
<td>Coffee daily</td>
<td>2.8±0.8</td>
<td>2.8±0.8</td>
<td>0.781</td>
</tr>
<tr>
<td>Coffee daily (N/Y)</td>
<td>46.2/53.8%</td>
<td>47.9/52.1%</td>
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</tr>
<tr>
<td>Diabetes (N/Y)</td>
<td>57.7/42.3%</td>
<td>48.2/51.8%</td>
<td>0.149</td>
</tr>
<tr>
<td>Fatigue level (N/Y)</td>
<td>12.1/87.9%</td>
<td>83.5/16.5%</td>
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<tr>
<td>CR</td>
<td>75.6±6.3</td>
<td>76.5±6.9</td>
<td>0.374</td>
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<tr>
<td>DA (1/10/2)</td>
<td>5.19±12.5/5.6%</td>
<td>7.2±15.9/5.9%</td>
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<tr>
<td>Pre-HD systolic BP</td>
<td>146.5±21.7</td>
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<tr>
<td>Pre-HD diastolic BP</td>
<td>78.7±12.8</td>
<td>72.6±9.1</td>
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<tr>
<td>Pre-HD hematocrit</td>
<td>37.0±6.0</td>
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</tbody>
</table>

**PO1079**

Physical Activity Levels in Hemodialysis Patients Measure Using a Commercially Available Activity Tracker

Priscila Pecchio,1 Maggie Han, Ohnmar Thwin, Leticia Tapia, Xia Tao, Mohamad I. Hakim, Amrish U. Patel, Lemuil Rivera Fuentes, Nadja Grobe, Jochen G. Raimann, Stephan Thijssen, Peter Kotanko. Renal Research Institute, New York, NY.

**Background:** Sedentary life is a major risk factor for all-cause mortality in the general population, more in those with cardiovascular (CV) diseases. Hemodialysis (HD) patients have an increased CV mortality and it has been shown that they are less active than their healthy piers. The use of physical activity (PA) tracking devices could provide an objective measurement of PA in HD patients’ everyday lives. We aimed to objectively quantify activity in a large HD population.

**Methods:** In our study, only a small number of patients exceeded the WHO recommendation of 10,000 steps/day. Overall, 83% of patients walked <10,000 steps/day. Further analysis is needed after completion of the study to assess the impact of a physical activity tracker device on physical activity levels. We hypothesized that the daily use of a tracker will positively impact activity levels and overall self-perceived health.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
PO1080
Feasibility and Acceptability of Symptom Monitoring with Feedback Trial (SWIFT) for Adults on Hemodialysis: A Pilot ANZDATA Registry-Based Cluster Randomized Trial

Rachael L. Morton,1 Kathryn Dansie,2 Paul N. Bennett,3 Emily Duncanson,2 Andrea K. Vicelli,2 Shilpa Jesudason,1 Karan K. Shah,1 Chris Brown,1 Suetonia Palmer,1 Fergus J. Caskey,3 Stephen P. McDonald,1,2 SWIFT NHMRC Clinical Trials Centre, Camperdown, NSW, Australia; 3Australia and New Zealand Dialysis and Transplant Registry, Adelaide, SA, Australia; 5Satellite Healthcare, San Jose, CA; 6University of Otago Christchurch, Christchurch, New Zealand; 7University of Bristol, Bristol, United Kingdom.

Background: We designed a registry-based randomized trial to test whether the collection and feedback of symptoms improves health-related quality of life (HR-QoL). The pilot study’s aim was to determine technical feasibility and patient-clinician acceptability of electronic tablet-based data capture and feedback integrated within the ANZDATA registry.

Methods: Hemodialysis units were cluster randomized to 3-monthly symptom monitoring using the Integrated Palliative Outcome Scale- Renal (IPOS-Renal) with feedback to clinicians plus 6-monthly HR-QoL using EQ-5D-5L questionnaire (intervention group); vs HR-QoL alone (control group). Feasibility and acceptability outcomes included, 1) individualized survey generation using QR codes linked to ANZDATA records; 2) patient completion rate and time; and 3) delivery of individualized symptom reports.

Results: Technical feasibility was demonstrated by successful development of a Qualtrics survey platform presented on tablet computers, use of QR reader codes to correctly identify patients from ANZDATA, and linkage to the relevant survey for the patient’s allocation and study timepoint. 226 patients (intervention =109; control =117), from 4 Australian units with median dialysis vintage of 1.6 years, mean age 62 years, 31% females, completed at least one symptom or HR-QoL measure, (72% of eligible patients, range 44-99%). Mean completion time was 6.5 minutes for IPOS-Renal (66% nurse assisted), 3.5 minutes for EQ-5D-5L. Consolidated symptom feedback reports and evidence-based symptom management guidelines for Nephrologists and dialysis nurses were delivered electronically within 2 weeks of measurement.

Conclusions: Electronic symptom monitoring in adults on hemodialysis with feedback to clinicians is feasible. These data support the commencement of the definitive trial in 3,072 patients.

Funding: Private Foundation Support, Government Support - Non-U.S.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

PO1081
Physiological Pre-Dialytic Changes Could Mediate the Effects of Extreme Heat Events on Hospital Admission Risk in Hemodialysis Patients

Richard V. Remigio,1 Rodman E. Turpin,1 Jochen G. Raimann,2 Peter Kotanko,3 Franklin W. Maddux,1 Len A. Usvyat,1 Xin He,1 Amir Sapatka,1 University of Maryland School of Public Health, College Park, MD; 2Renal Research Institute, New York, NY; 3Fresenius Medical Care AG and Co KGaA, Bad Homburg, Germany; 4Fresenius Medical Care North America, Waltham, MA.

Background: Thermoregulatory response to extreme heat events (EHE) includes reduced blood pressure and perspiration. EHE exposure increases the risk of hospitalizations among hemodialysis (HD) patients, though the underlying mechanism for this relationship is unclear. We employed traditional mediation analysis to decompose the total effect between EHE and hospital admissions using pre-HD systolic blood pressure (SBP) and interdialytic weight gain (IDWG) as mediators.

Methods: We assigned EHE exposure metric – calculated using calendar day and location-specific temperature thresholds – to HD patients treated at Fresenius Kidney Care clinics from 2003 to 2012. We used time-to-event methods using varying lag periods followed by VanderWeele’s difference method with bootstrapping to test mediators.

Results: EHE increased the hazard of hospital admission up to 17% after covariate adjustment (HR 1.16, 95% CI 1.06, 1.28, 95% CI 1.24-1.36), diastolic access via catheter (HR 1.63, 95% CI 1.51-1.76), congestive heart failure (HR 1.28, 95% CI 1.26-1.30), and diabetes mellitus (HR 1.14, 95% CI 1.12-1.16). Compared to white race, minority races had lower likelihood of developing a sepsis hospitalization (Black HR 0.89, 95% CI 0.87-0.90; Hispanic HR 0.82, 95% CI 0.80-0.84; Asian HR 0.79, 95% CI 0.76-0.82; Native American HR 0.80, 95% CI 0.75-0.86). Compared to no hospitalizations, ESKD patients had a twofold increase in mortality following a first non-sepsis hospitalization (HR 2.14, 95% CI 2.12 to 2.16), increasing to ninefold over baseline following a sepsis hospitalization (HR 9.00, 95% CI 8.79-9.13).

Conclusions: Sepsis hospitalizations are frequent and are associated with significant mortality in ESKD patients in the U.S. Further studies need to focus on modifiable risk factors of sepsis and explore optimal therapies for sepsis in ESKD subjects.

Funding: Clinical Revenue Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

PO1082
Frequency, Risks, and Outcomes of Sepsis Hospitalizations in the ESKD Population in the United States

Remigio V.,1 Vitcelli S.,1 Morton A.,1 Christiansson A.,1 Anthony L.,1 Karhikeyean M.,1 Kathleen H.,1 Samantha M.,1 Kazakhstan V. Thaker,1,2 Division of Nephrology, University of Cincinnati, Cincinnati, OH; 2Cincinnati VA Medical Center, Cincinnati, OH.

Background: Although a biologically plausible link between End Stage Kidney Disease (ESKD) and sepsis exists, little is known about frequency, risk factors, and outcomes of sepsis-related hospitalizations in ESKD patients.

Methods: Of a retrospective cohort of 1,123,731 incident ESKD patients on dialysis (2005 to 2014) from the United States Renal Data System (USRDS), we studied the 508,372 with linked Medicare claims at initiation of dialysis and complete demographic data. Hospitalization data were obtained from Medicare claims with a sepsis hospitalization being identified by previously validated ICD-9 codes. Using Cox proportional hazard models, we examined the risk factors associated with a sepsis hospitalization and effect of a sepsis hospitalization on mortality.

Results: The study cohort was 55% male, 62% white, and had an average age of 70 years. A sepsis hospitalization occurred in 20.8% of the cohort. The overall rate of sepsis hospitalizations was 15.4 per hundred patient years (PHPY), and the trend increased over time from 13.8 PHPY in 2005 to a peak of 16.7 PHPY in 2011. Factors associated with higher likelihood of a sepsis hospitalization included female sex (Hazard Ratio [HR] 1.05, 95% CI 1.03-1.06), age ≥80 (vs. age <60; HR 1.30, 95% CI 1.24-1.36), diabetes access via catheter (vs. fistula-graft; HR 1.61, 95% CI 1.58-1.63), congestive heart failure (HR 1.28, 95% CI 1.26-1.30), and diabetes mellitus (HR 1.14, 95% CI 1.12-1.16). Compared to white race, minority races had lower likelihood of developing a sepsis hospitalization (Black HR 0.89, 95% CI 0.87-0.90; Hispanic HR 0.82, 95% CI 0.80-0.84; Asian HR 0.79, 95% CI 0.76-0.82; Native American HR 0.80, 95% CI 0.75-0.86). Compared to no hospitalizations, ESKD patients had a twofold increase in mortality following a first non-sepsis hospitalization (HR 2.14; 95% CI 2.12 to 2.16), increasing to ninefold over baseline following a sepsis hospitalization (HR 9.00; 95% CI 8.79-9.13).

Conclusions: Sepsis hospitalizations are frequent and are associated with significant mortality in ESKD patients in the U.S. Further studies need to focus on modifiable risk factors of sepsis and explore optimal therapies for sepsis in ESKD subjects.

Funding: Other U.S. Government Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
intervention designed to rapidly diagnose and address recruitment issues in real-time. We report the root-causes of recruitment issues and how these were overcome using this novel methodology.

Methods: The QRI entailed monthly scrutiny of pre-randomisation screening data, interviews with nephrologists/nurses (n=27) and audio-recorded consultations between clinicians/patients (n=33). Data were triangulated, informing strategies to address recruitment issues.

Results: Recruitment was hampered by logistical issues that varied, requiring bespoke solutions by centre. More challenging to address were the underlying complex issues entwined with routine clinical practice, manifesting as reluctance to approach all eligible patients, and issues with conveying equipoise. Clinicians often only approached patients whom they felt could not decide between dialysis or conservative care, assuming other patients’ treatment intentions were fixed. Audio-recorded consultations indicated patients were not necessarily committed to treatments, and preferences were often complicated by misconceptions. Recordings also revealed recruiters’ tendencies to unknowingly undermine dialysis, and hesitancy in exploring preferences. The trial team iteratively produced guides/training to support equipoise communication and used presentations/clinical vignettes to challenge assumptions that patients have fixed treatment plans. As of May 2020, 246 patients have been randomised (48% of target of 512).

Conclusions: Factors hindering recruitment to this challenging RCT were complex, but amenable to change once well-understood. Novel methodologies, like the QRI, can unlock the potential to deliver seemingly impossible- but vitally important- RCTs to improve renal practice.

Funding: Government Support - Non-U.S.

PO1084

Time Course of Tissue Sodium Flux in Maintenance Hemodialysis (MHD) Patients

Hsin-Yu Fang,1 Luis M. Perez,2 Ryan J. Larsen,2 Deepa H. Shankar,3 Talat Alp Ikizler,4 Kenneth R. Wilund.5 1University of Illinois at Urbana-Champaign, Urbana, IL; 2Vanderbilt University Medical Center, Nashville, TN.

Background: Recent 2Na-MRI studies show that sodium can accumulate in tissues. MHD patients have higher tissue sodium concentration ([Na+]) than healthy counterparts, while tissue [Na+] can be partially reduced during hemodialysis (HD). This study aimed to evaluate the magnitude of tissue [Na+] removed during HD and the time-course for its recalibration.

Methods: Seven HD patients (57% male; 60±12 yr; BMI: 36±10 kg/m²; spCr/V: 1.4±3.2; dialysate [Na+]: 136±190 meq/l; UFR: 7.2±1.4 mL/hr; thrice-weekly HD) had sequential 2Na-MRI scans (3T system) over 3 consecutive days, including 2 HD days and the non-HD day in between, at 4 time points: pre-first HD (T1), post-first HD (T2), 24 hours post-first HD (T3), and pre-second HD (T4). [Na+] of the medial (MG) and lateral (LG) gastrocnemius, soleus (Sol), tibialis anterior (TA), and the whole lower leg (WL) were quantified from MRI images. Plasma [Na+] was also assessed at T1, T2, and T4 by colorimetric enzymatic assays (Piccolo). Repeated measures ANOVA and the nonparametric Friedman test were used to test the differences in tissue and plasma [Na+] over time.

Results: Tissue [Na+] was reduced at the end of HD (T2) compared to baseline (T1) in the WL (P=0.06), MG (P=0.04), LG (P=0.006), Sol (P=0.029), and TA (P=0.006), (Figure 1A-E). For the WL and all 4 examined muscles, tissue [Na+] at both T3 and T4 did not differ from baseline (all P>0.05), indicating that tissue [Na+] returned to the baseline within 24 hours after last HD. In contrast, plasma [Na+] did not change over time (P=0.067; Figure 1F).

Conclusions: We found that tissue [Na+] was reduced by HD but returned to baseline levels within 24 hours that remained stable until next pre-HD. More studies are needed to determine the mechanisms for these shifts, and whether lifestyle or pharmacological interventions can inhibit tissue [Na+] accumulation or enhance its removal.

Funding: Private Foundation Support

PO1085

Association Between Dialysate Sodium Concentration and Interdialytic Weight Gain in Patients Undergoing Twice Weekly Haemodialysis


Background: Chronic kidney disease is highly prevalent in the world with more than two million people worldwide requiring renal replacement therapy. Interdialytic weight gain is the change in body weight between two sessions of haemodialysis. Higher interdialytic weight gain has been associated with increased mortality and adverse cardiovascular outcomes. It has long been questioned whether using a lower dialysate sodium concentration during dialysis would reduce the interdialytic weight gain and prevent these adverse outcomes.

Methods: This was a single blind cross-over study of adult patients undergoing twice weekly haemodialysis conducted over two six week periods. Patients were divided into two groups – the first underwent dialysis with dialysate sodium concentration of 137meq/l, the other underwent dialysis with a sodium concentration of 140meq/l. These groups switched over after a six-week period without a washout period. Interdialytic weight gain, pre and post dialysis blood pressures were measured at each dialysis session.

Results: 41 patients were included in the primary analysis after meeting inclusion criteria. Mean age was 61.37 years, and 73% were males. Mean duration for dialysis was 2.53 years. 13% were aneure, 56% were oliguric, and 31% were non-oliguric. 59% of patients had diabetes mellitus and 80% had hypertension. The interdialytic weight gain was not significantly different among the two groups (2.14 for the low NaD (137meq/l) group and 2.35 for the high NaD (140meq/l) group, p = 0.97). Mean blood pressures were as follows. Pre-dialysis: DNa 137meq/l: systolic 152±19, diastolic 78±12.20, DNa 140meq/l: systolic 156.95 ± 26.45, diastolic 79.75 ±11.25 (p = 0.379, 0.629 respectively). Post-dialysis: DNa 137meq/l: systolic 147.29 ± 22.22, diastolic 77.85 ± 12.82 DNa 140meq/l: systolic 151.48 ± 25.65, diastolic 79.66 ± 15.78 (p = 0.369, 0.621 respectively).

Conclusions: There was no significant difference in the interdialytic weight gain as well as pre dialysis and post dialysis systolic and diastolic blood pressures between the low dialysate sodium concentration and high dialysate sodium concentration. Therefore using a lower dialysate sodium concentration does not appear useful in altering the interdialytic weight gain although further studies with a larger sample size are warranted.

PO1086

Low Sodium Dialysate for Hemodialysis Is Associated with Lower Blood Pressure and Interdialytic Weight Gain, but Not a Lower Pre-Dialysis Serum Sodium

Huyen Nguyen, Andrew I. Chin. University of California Davis, Sacramento, CA.

Background: The use of high dialysate sodium (NaD) concentrations for hemodialysis (HD) is associated with greater interdialytic fluid gain (IDWG). The association with higher blood pressure has not been found routinely. Conversely, use of a lower NaD may improve on these parameters, but may lead to a lower pre-dialysis serum sodium concentration, which may have adverse consequences in this population. We aimed to examine IDWG, blood pressure, calculated serum osmolality and serum Na in HD patients on a high NaD (145) who transitioned to a low NaD (137-138)

Methods: In this retrospective, single-center study of 3-times weekly HD patients without residual kidney function, we queried long-term HD patients who were prescribed NaD of 145 and were then switched to a NaD of 137 or 138, based on change in standard clinic dialysate sodium. Parameters investigated included: pre-dialysis serum Na and albumin, calculated pre-HD serum osmolality, pre and post-HD weights, and pre and post-HD blood pressures. Paired T-test was used for comparison of each parameter between dialysate time periods.

Results: We identified 136 patients who were started on HD with NaD of 145 for at least 1 year, subsequently changed to a NaD of 137-138 for at least 1 additional year. See Figure comparison of parameters.

Conclusions: In patients on 3-times a week HD, long-term use of a high NaD of 145, compared to a low NaD of 137-138, was associated with a higher IDWG, similar to what is found in other studies. A lower NaD was associated with lower pre and post-HD systolic and diastolic blood pressures, but we found no difference in pre-HD serum Na or calculated serum osmolality. The degree of drop in blood pressure during HD on the low NaD caused hypotensive events in some patients. There are some clinical parameter benefits to a lower NaD and serum Na does not appear to suffer.

Funding: Clinical Revenue Support
Table 1. Paired T-test comparison of averaged parameters during low and high dialysate sodium HD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low NaD</th>
<th>High NaD</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Serum Sodium</td>
<td>138.3 ± 2.6</td>
<td>138.7 ± 3.0</td>
<td>0.69</td>
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<tr>
<td>Serum Albumin</td>
<td>3.8 ± 0.4</td>
<td>3.8 ± 0.4</td>
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<td>Post HD wt (kg)</td>
<td>71.5 ± 25.2</td>
<td>72.2 ± 25.1</td>
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<td>Inter-HD wt gain (kg)</td>
<td>2.7 ± 1.1</td>
<td>3.8 ± 1.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Calculated Serum osmol</td>
<td>300 ± 8</td>
<td>302 ± 8</td>
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<tr>
<td>PreHt DBP</td>
<td>151 ± 21</td>
<td>157 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PostHt DBP</td>
<td>138 ± 16</td>
<td>144 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PreHt MAP</td>
<td>74 ± 11</td>
<td>79 ± 9</td>
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<tr>
<td>PostHt MAP</td>
<td>104 ± 14</td>
<td>109 ± 13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP</td>
<td>95 ± 11</td>
<td>100 ± 10</td>
<td>&lt;0.001</td>
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PO1087
Medicare Reliance After Implementation of Medicare Payment Reform and the Affordable Care Act Marketplace
Virginia Wang,1,2 Abby Hoffman,1,3 Bradley G. Hammill,1 Caroline E. Sloan,1,2 Matthew L. Maciejewski,1,2 Duke Univ, Durham, NC; 2Durham VAHCS, Durham, NC; 3UNC-Chapel Hill, Chapel Hill, NC.

Background: Medicare finances health care for most US patients with ESKD, regardless of age. The 2011 Medicare bundled payment for dialysis reduced Medicare reimbursement for hemodialysis, increasing the difference between Medicare and private insurance that commonly reimburses dialysis providers at higher rates. Passage of the 2014 Affordable Care Act also increased patient access to new private insurance options. These policies may have influenced providers to adjust their payer mix, as dialysis facilities have reported increasing rates of patients not enrolled in Medicare since 2011. This study describes trends in Medicare enrollment among new ESKD patients in 2006-2016.

Methods: From the US Renal Data System, we identified a cohort of incident ESKD patients between 2006 and 2016. We identified each patient’s insurance status (Medicare, pending Medicare, non-Medicare) at dialysis initiation and observed changes over time. We report trends for the overall incident population, for patients aged 18-64, and by race.

Results: The proportion of new ESKD patients enrolled in Medicare remained stable between 2006 (65%) and 2016 (67%). There was an increase in non-Medicare coverage (13.2% in 2006, 19% in 2016) and a reduction in pending Medicare applications (21% in 2006, 14% in 2016). These trends were more pronounced among patients aged 18-64 (i.e., not already in Medicare due to age) and among aged 18-64 non-Whites (Figure). Multivariable regression results are pending.

Conclusions: There was a modest shift in payer mix among new patients with ESKD after bundled payment reform in 2011 and private insurance expansion in 2014, with fewer patients applying for or enrolled in Medicare over time. To address concerns among policymakers about facilities encouraging private insurance coverage, future work should examine the implications of these trends on outcomes for patients.

Funding: NIDDK Support

PO1088
The Correlated Case of Dialysis Facility and Hospital Star Ratings
Eric D. Weinhard,1,2 David T. Gilbertson,1 James B. Wetmore,1,3 Kirsten L. Johansen,2,4 Chronic Disease Research Group, Minneapolis, MN; 2University of Minnesota, Minneapolis, MN; 3Hennepin County Medical Center, Minneapolis, MN.

Background: The Centers for Medicaid and Medicaid Services (CMS) periodically releases star ratings for several types of health care facilities, including acute care hospitals and outpatient dialysis facilities. Because respective rating systems utilize disparate quality measures, star ratings of dialysis facilities and nearby hospitals may be weakly correlated. However, hospital quality could influence dialysis patient outcomes. Furthermore, confounding by unmeasured economic, environmental, and social factors could induce correlation. We used public use files to assess whether star ratings of dialysis facilities and hospitals within the same region are correlated.

Methods: We ascertained dialysis facility star ratings from Dialysis Facility Compare and hospital star ratings from Hospital Compare (source: data.medicare.gov). Star ratings were based on quality measures that were accumulated in 2015-2018. We categorized each health care facility into 306 Hospital Referral Regions (HRRs), according to ZIP code. In each HRR, we estimated the mean star rating of all dialysis facilities and the mean star rating of all hospitals. Using loess regression, we estimated the correlation between these HRR-specific means.

Results: The analysis included 6667 dialysis facilities and 3565 hospitals, or approximately 22 dialysis facilities and 12 hospitals per HRR. The mean star rating in dialysis facilities was 3.7 (standard deviation, 1.0) and 3.2 (1.1) in hospitals. As displayed, HRR-specific mean star ratings of dialysis facilities and hospitals were positively and nearly linearly correlated. The correlation coefficient of these HRR-specific means was 0.4.

Conclusions: CMS star ratings of dialysis facilities and hospitals within the same region are positively correlated. Future studies should identify the sources of this correlation.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO1089
The Budgetary Impact of Point-of-Care Hemoglobin Testing for Hemodialysis Patients
Linda Ficociello,1 Melissa M. Rosen,2 Claudio Mullon,3 Robert J. Kossmann,2 Mark Costanzo,4 Fresenius Medical Care Renal Therapies Group, Waltham, MA; 2Fresenius Medical Care North America, Waltham, MA.

Background: Point of care (POC) testing in dialysis clinics can improve the quality of care provided to end-stage renal disease (ESRD) patients. The objective of this study was to estimate the budgetary impact of transitioning from weekly lab-based analysis of hemoglobin from each dialysis session to POC testing.

Methods: A budget impact model with a 1-year time horizon was developed. Our model included costs of POC testing in real-time in dialysis clinics compared to requiring the shipment of 3 blood samples per month to a lab for analysis. A non-invasive monitoring technology, the Crit-Line monitor® (CLM) measures hematocrit. Hemoglobin levels can be calculated from the measured hematocrit value. CLM is already used for fluid management in dialysis clinics and can also be used for POC testing. The model took the perspective of a healthcare organization responsible for providing dialysis treatments. The 2020 Medicare reimbursement value for a hematocrit test was used as a proxy value for lab testing costs. Our model also included costs associated with shipping, blood collection tubes, and erythropoiesis-stimulating agent (ESA) which is indicated for the treatment of anemia. Labor costs were excluded as they were considered fixed costs and would not change if POC testing was implemented.

Results: By replacing three blood draws per month, the use of a Crit-Line monitor® to assess hemoglobin levels could save $16.82 USD per patient per month.

Conclusions: The use of Crit-Line monitor® technology for point of care assessment of hemoglobin levels can result in decreased resource use and costs savings of $16.82 USD per patient per month compared to lab-based testing. Point of care testing may also have environmental benefits by reducing emissions associated with shipping samples and decreasing packaging needed to ship samples to a lab for analysis.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO1090
Physician Action on Medication Therapy Management (MTM) Recommendations Within 14 Days Associated with Lower 30-Day Readmission in Dialysis Patients
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Background: We previously reported lower 30-day readmission rates associated with MTM (vs. no intervention) in maintenance dialysis patients. After aggressive implementation of MTM, we now compare 30-day readmission risk in a more recent

Conclusions: CMS star ratings of dialysis facilities and hospitals within the same region are positively correlated. Future studies should identify the sources of this correlation.
Use of Predictive Analytics to Inform Integrated Care Programs to Reduce Hospitalizations Among Hemodialysis Patients

Katherine L. McKeon,1 Adam G. Walker,7 Jiaqiong Luo,1 Scott Sibbel,2 Meredith L. Zywno,2 Bryan N. Becker,2,7 Tiffany L. Bray,2,7 Juliana Stebbins,3 Nick Lefeber,2 David A. Roer,2 Steven M. Brunelli.1 Davita Clinical Research, Minneapolis, MN; Davita Inc, Denver, CO; Davita Integrated Kidney Care, Denver, CO.

Background: Integrated care for dialysis patients could benefit from identification of those who are at high risk for poor outcomes in order to efficiently deploy clinical resources. We recently developed a hospitalization risk stratification model to target intervention in high-risk patients of Davita hemodialysis (HD) patients for clinician contact and assessment within an integrated care clinical program (ICCP). In this analysis, we compared hospitalization rates before and after model implementation for patients enrolled in an ICCP and control patients who were not.

Methods: All patients received our standard level of care consistent with industry best practices and regulations. ICCP patients predicted to be medium and high risk received additional services proportional to predicted risk level. Relative differences in annualized hospitalization rates for HD patients enrolled in an ICCP were compared to controls who were not by calculating relative rate ratios (RRR) and 95% confidence intervals (CI) in the baseline (Feb 2017-April 2018) and postmodel implementation (Jan-Aug 2019) eras. Comparisons were stratified by predicted risk level.

Results: The baseline hospitalization rate was 3.0 admissions/patient-year (pt-yr) for all high-risk patients. Post implementation, hospitalization rates decreased to a greater extent among ICCP patients (-0.4 admissions/pt-yr) versus controls (-0.2 admissions/pt-yr): RRR (95% CI) = 0.94 (0.90, 0.97). The baseline hospitalization rate was 1.7 admissions/pt-yr for all medium-risk patients. Post implementation, hospitalization rates decreased to a greater extent among ICCP patients (-0.2 admissions/pt-yr) versus controls (-0.1 admissions/pt-yr): RRR (95% CI) = 0.95 (0.90, 1.00). No differences were observed among low-risk ICCP patients and low-risk control patients.

Conclusions: These results support the potential utility of predictive analytics to support programs aimed at improving clinical outcomes among HD patients.

Intradialytic Online Multicomponent Total Removed Solute Monitoring in Spent Dialysate by a Novel Miniaturized Optical Sensor

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Background: Urea is the most commonly exploited marker of dialysis adequacy, but also provides representation of solute transport in FXD patients. Commonly, the uramic solutes are divided into three physicochemical types with the representative markers urea, uric acid (UA); indoxyl sulfate (IS); and β2-microglobulin (B2M). Instead of total dialysate collection for quantification of the amount of uramic solutes removed during dialysis, an optical on-line monitoring has been proposed. The aim of this study was to evaluate intradialytically on-line multicomponent total removed solute (TRS) monitoring in the spent dialysate by a novel miniaturized optical sensor during hemodialysis (HD) and hemodiafiltration (HDF) with different settings.

Methods: Ten ESKD patients (6 M, 4 F; 60.2 ± 756 μL/min, Qd ≥ 300 mL/min, Qd ≥ 300 mL/min) were enrolled into the study. For each patient 5 midweek dialysis sessions (240 min) HD: N = 1, Qd = 200 mL/min, Qf = 300 mL/min, 1.5 μm; HD: N = 4, Qs 300 mL/min, Qd 500 mL/min, V dial 15 L, 1.8 μm, and 1 μm) were included. Spent dialysate from the drain was monitored on-line using a miniaturized sensor prototype (Optothul Technologies OÜ, Estonia). For the reference, samples from the spent dialysate drain tube of the HD machine were taken, 60, 120, 180 and 240 min after the start of the dialysis session. Concentrations of urea and B2M in the dialysate were determined in the clinical laboratory. Concentrations of IS and UA were determined utilizing the HPLC. TRS values were calculated using the tank weight and the lab or optical tank solute concentrations. t-test was used to determine significant differences between the methods (P<0.05).

Results: The laboratory and optical TRS values were 489±112 μmol/L and 512±87 μmol/L for urea (R2 = 0.928, P<0.001); 423±127 μmol/L and 421±756 μmol/L for UA (R2 = 0.930, P<0.001); 203±90 and 231±40 μmol/L for B2M (R2 = 0.951, 600±339 μmol/L and 616±321 μmol/L for IS (R2<0.951), being not statistically different for any uramic solutes. The reason for higher correlation for UA and IS is direct measurements of UA and IS by the optical sensor whereas urea and B2M are estimated indirectly.

Conclusions: There was a high proportion (>90%) of Controller-UF recommendations that were accepted by the nurses. Of the few cases where nurses overrode the recommendation, the majority (>40%) were due to “staff preference”, this is likely owed to the fact that the nurses exclusively attended one patient at a time for the entire HD session.

Funding: Commercial Support - Fresenius Medical Care North America
Conclusions: Novel miniaturized optical sensor successfully carried out intradialytic on-line multicomponent TRS monitoring for the uremic solutes urea, UA, B2M and IS in the spent dialysis effluents.

POI094
Patient Safety in a Large Multinational Renal Services Provider Network

Background: Patient safety is considered of paramount importance under any qualified provision of care, but results from routine tracking of incidents have scarcely been reported, even when that may negatively impact survival. Objectives: To analyze all types of incidents in a multinational renal service provider network during 2019.

Methods: For the last 10 years, our institution has tracked all incidents under a structured process program, as well as, educated our staff in the importance of proactively reporting and analyzing incidents in a quarterly basis at the clinic, by country and globally. Incidents are categorized in 4 different types: A-Patient related, B-Staff and visitors, C-Products and D-Equipment. Different incident codes are assigned to each type (up to 54). Communication to Health Authorities applies in accordance with local country regulations. “Serious incidents” are immediately notified to the Corporate Office and to each Country Medical lead.

Results: A total of 92,923 incidents (2.7 incidents/patient/year) have been reported during 2019 (higher than in 2018: 2.2). This means an increase of 20% in the total number of reported incidents. Total incidents/1000 treatments was 17.2 (12.2 patient-related incidents). Reporting follows a heterogeneous pattern among countries, being lowest in Argentina and highest in the UK. Top 5 reported incidents were as follows: Codes A15 (voluntarily shortened treatment) and A14 (Patient did not show up), both related to patient adherence to treatment, accounted for 36% of total incidents, vascular access (VA) complications (A4) for 10.2%, change of dialyzer and/or blood lines due to clotting (A2) for 8.5% and recurrent minor monitor malfunction (D1) for 7.6% of incidents. Codes related with unexpected death or cardiorespiratory arrest are not present among the total global top 10 incidents.

Conclusions: Detailed tracking of incidents and comparison between countries have potential to increase quality of care and patients outcomes. Room for improvement recently made the Corporate Medical Office to launch new strategies on VA management, anticoagulation and patient compliance, among others. This large series may help other institutions to better monitor and standardize patient safety on dialysis.

POI095
Incidence of Intradialytic Hypotension Throughout a Hemodialysis Session: Does the Time of Onset Matter?
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Background: Intradialytic hypotension (IDH) is a common complication of hemodialysis (HD). Probability of IDH would be expected to increase during HD in the absence of ultrafiltration (UF) volumes increase. We aimed to describe the incidence of IDH throughout HD and associations of the time of IDH with clinical parameters and with survival.

Methods: We studied routinely collected data from 21 US dialysis clinics. IDH was defined as: 1) systolic blood pressure (SBP) < 90 mmHg; and 2) SBP < 90 mmHg and a reduction in SBP > 30 mmHg. Only the first IDH incident per session was included. Time of IDH occurred in 13% and 7% of treatments with a range of 2.6-3.3 and 0.9-2.7 episodes per 100 session-intervals at risk, respectively. IDH incidence was not associated with time into HD using definition 1; a positive association was observed using definition 2. Adjusted IDH rates and lower BMI and SBP.

Conclusions: Early-onset IDH is not uncommon. More consideration of the nature and time of IDH onset, in the context of how it is defined, could help to minimize IDH.

POI096
Endothelin 1 and Parameters of Systolic Blood Pressure in Hemodialysis Patients
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Background: Blood pressure (BP) fluctuates widely during intermittent hemodialysis (HD), with greater variability associated with adverse cardiovascular outcomes. As endothelin-1 (ET-1) is a potent vasoconstrictor, we hypothesized that higher concentrations of ET-1 is associated with higher pre-HD systolic BP (SBP).

Methods: ET-1 concentrations were measured at baseline from the DaVita Biorepository (N=784), a longitudinal prospective cohort study with quarterly collection of clinical data and biospecimens. Unadjusted and adjusted linear mixed effects regression models were fit to determine associations of log-transformed ET-1 with SBP at dialysis (pre-HD, nadir intra-HD, post-HD, drop (pre- minus nadir-HD) and delta (pre- minus post-HD). Multivariable models were adjusted for age, sex, race, access, diabetes, heart failure, cardiovascular disease, peripheral vascular disease and pre-HD SBP.

Results: Mean age was 58 years, 59% were males, 40% black. Mean pre-HD SBP was 152 (± 28) mmHg and mean ET-1 concentration was 2.3 (±1.1) ng/mL. Subjects in higher quartiles of baseline ET-1 tended to be younger, diabetic, have higher SBP and lower serum albumin. In fully adjusted models, each unit increase in SD of log-transformed ET-1 was associated with a 3.0 (95% CI 1.8 to 4.2) mmHg higher pre-HD SBP, 1.2 (95%CI 0.5 to 1.9) mmHg higher nadir-SBP; 1.6 (95% CI 0.6 to 2.5) mmHg higher post-SBP; 1.2 (95%CI 0.2 to 1.5) mmHg lower SBP drop and 1.6 mmHg (95% CI 0.6 to 1.0) lower delta SBP. In categorical analyses a monotonic increase in pre-SBP was noted in higher quartiles of ET-1 (Q4: 7.8 mmHg increase (95% CI 4.5 to 11.2; P<0.0001) compared with Q1. Similar patterns were noted for the other variables of interest.

Conclusions: Higher ET-1 is independently associated with higher SBP in maintenance HD patients. These results suggest a role for studying ET-1 antagonism in HD patients with resistant hypertension.
Kidney Transplant Access Among Children and Young Adults on Dialysis in the United States

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Background: Only 20% of children and young adults with advanced CKD receive preemptive kidney transplant (KT). This study aimed to investigate secular trends in KT access among incident US dialysis patients who were ≥12 years old.

Methods: In a cohort of incident dialysis patients ≥12 years of age who initiated dialysis between 1995-2014 from the USRDS database, we examined secular trends in the likelihood of receiving KT, using a Cox proportional hazards regression.

Results: Among 24,860 patients, the median (IQR) age at dialysis initiation was 17 (11–20) years of age, among whom 56% were <18 years old. A total of 16,912 (68%) patients underwent a KT during a median (IQR) follow-up of 2.0 (0.9–4.3) years (total follow-up: 82,244 patient-years). The 1-, 2-, and 3-year probabilities of receiving a KT were 23%, 43%, and 55%, respectively. The likelihood of receiving KT slightly improved but decreased after 2005 among patients <18 years old; a decreasing trend was remarkable among patients ≥18 years old (Figure A). While increasing among patients <18 years old, the likelihood of receiving a deceased donor transplant declined among those ≥18 years old. For a living donor transplant, there were decreasing trends in both age groups (Figure B).

Conclusions: While the likelihood of receiving pediatric KT declined over two decades, there was an increase in deceased donor transplantation among those ≥18 years old. Since biological factors determine unmet need for KT in pediatric or young adult populations having short waiting time, an old kidney allocation system (KAS), which achieved the goal by transplanting patients with the longest waiting time, may not improve transplant access and outcomes. A new KAS commenced in December 2014, and living donor transplant may provide different trends or improve pediatric KT access, although further long-term studies are needed.

Figure: Time-to-event outcomes for receiving a kidney transplant among pediatric (<18 years old) and young adults (18 years old) between 1995 and 2014. A. Unadjusted and case-mixed adjusted models B: Stratified into living and deceased donor renal transplantations
**PO1100**

Predictors of Extracorporeal Circuit Clotting in Patients Requiring Continuous Renal Replacement Therapy

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**Background:** Extracorporeal circuit (ECC) clotting frequently occurs during continuous renal replacement therapy (CRRT) resulting in treatment interruption, blood loss and increased resource use. The purpose of this study was to evaluate risk factors for ECC clotting in patients receiving CRRT.

**Methods:** A retrospective chart review was conducted to identify adult patients who received CRRT at Methodist Le Bonheur Healthcare for a minimum of 24 hours during January 2015 to October 2019. The primary outcome was the occurrence of ECC clotting which was defined as documentation of a thrombotic event in the ECC. Demographic and laboratory data, anticoagulant medications, and CRRT parameters were evaluated for a maximum of 7 days to determine potential risk factors for clotting. Multivariable logistic regression was used to identify predictors of clotting.

**Results:** A total of 200 patients were included: [108 (54%) male; mean age 56 ± 13 years; mean sequential organ failure assessment score 12 ± 4; 52 (26%) with past medical history of liver disease; 143 (72%) with acute kidney injury; mean duration of CRRT 3.6 ± 2.0 days; 97% receiving continuous venovenous hemodiagnosis]. Overall, 131 (66%) patients experienced an ECC clot with a mean time to first ECC clot of 1.3 ± 1.3 days. Patients receiving an unfractionated heparin (UFH) infusion (n=25) had a lower probability of an ECC clot occurring compared to those receiving no anticoagulation (n=86) (40% and 70%, respectively, p=0.01) and those receiving prophylactic UFH (n=70) (40% and 64%, respectively; p=0.04). Factors associated with an increased odds of clotting in patients not receiving an anticoagulant were non-African American race (odds ratio (OR) 4.0; 95% confidence interval (CI) 1.1-14.6), lower blood flow rates (OR 1.01; 95% CI 1.0-1.03), internal jugular catheters (OR 3.32;95% CI 1.1-9.9), and no history of hypertension (OR 4.79; 95% CI 1.4-16).

**Conclusions:** This study suggests a high risk of ECC clotting, particularly in patients not receiving anticoagulation. Eligible patients on CRRT should receive an UFH infusion in preference to no anticoagulation or prophylactic UFH.

**PO1101**

Gram-Negative Bacteremias in Haemodialysis Patients: Pathogen and Source Identification

Anna Naito, Fatima Malik, Christopher M. Cregg, Lisa Bradwell, David Makanjuola. Epsom and Saint Helier University Hospitals NHS Trust, Carshalton, United Kingdom.

**Background:** Gram-negative bacteremia (GNB) in haemodialysis (HD) patients is associated with significant morbidity and mortality. Efforts to reduce rates of bacteremias caused by Methicillin Resistant Staphylococcus Aureus have been hugely successful. Epidemiological studies now show the re-emergence of gram-negative pathogens, particularly *Escherichia Coli* (*E.Coli*) in causing bloodstream infections. We aimed to determine the source and pathogens responsible for GNB in our HD cohort.

**Methods:** Data on all confirmed bacteremias in HD patients between 2007 and 2018 were collected from clinical and electronic records from the hospital’s renal and microbiology databases. Results: 283 episodes of GNB occurred in 1361 patients over the 12-year period. 58.7% were male. The median age was 71 years (range 26-95). 31.8% had arteriovenous fistulae or grafts, the remainder had dialysis lines, of which 21.2% had dual access. The organisms isolated are shown in table 1. *E.Coli* and *Klebsiella Pneumoniae* were the dominant pathogens, accounting for 40.6% and 15.9% of bacteremias isolated respectively. The most common sources of infection were HD access related in 31.4% (n=89), urinary tract 18.4% (n=52), hepato-biliary 7.8% (n=22), chest 7.8% (n=22), gastrointestinal 6.0% (n=17), skin/soft tissue in 4.9% (n=14), other in 4.6% (n=13), no information on 4 patients (1.5%) and unknown source in 50 (17.7%).

**Conclusions:** *E.Coli* bacteremias remain a major cause of GNB in our HD population. Dialysis lines are a significant risk factor for bacteremia, lending further weight to the importance of establishing early definitive vascular access. Resistance trends of gram-negative organisms are of particular and increasing concern. We have noticed changing sensitivity patterns of isolates and it is not clear whether local empiric antibiotic policy is contributing to selection pressures and antimicrobial resistance.

<table>
<thead>
<tr>
<th>Source</th>
<th>Frequency</th>
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</thead>
<tbody>
<tr>
<td>HD Access</td>
<td>31.4%</td>
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<tr>
<td>Urinary Tract</td>
<td>18.4%</td>
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<tr>
<td>Hepato-Biliary</td>
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<tr>
<td>Gastrointestinal</td>
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<tr>
<td>Skin/Soft Tissue</td>
<td>4.9%</td>
</tr>
<tr>
<td>Other</td>
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Table 1: Gram negative isolates from blood cultures

**PO1102**

Five-Year Outcome of a Retrospective Cohort Study of Patients with Two Hemodialysis Sessions per Week

Aurora E. Hernandez, L. M. Perez-Navarro, Gloria G. Garcia Villalobos, Elba O. Medina, Rafael Valdez-Ortiz. Hospital General de Mexico Dr Eduardo Liceaga, Ciudad de Mexico, Mexico.

**Background:** The indication of two hemodialysis (HD) sessions per week is a common strategy in patients with chronic kidney disease without social security. Some studies reveal that the indication of fewer HD sessions per week has been shown to be associated with adequate clinical results. **Objective:** To describe the clinical and biochemical status of patients in HD program twice a week in the last five years.

**Methods:** Retrospective cohort study of patients with two HD sessions per week. Their clinical, nutritional status was evaluated by vectors of impendimient and quality of life KDQOL-SF 36. The statistical package SPSS V 22.0 was used for data analysis.

**Results:** Forty-one patients with a mean age of 37.9 ± 12.6 years, 56% women, were analyzed. The mean time with renal replacement therapy was 5.1 years; Average session time was 180 minutes; average ultrafiltration of 2726.8 ± 755.96 ml / session and an average Kt / V single pool of 1.54 ± 0.38. In 59% of patients the cause of CKD was undetermined. 46% of the patients had an arteriovenous fistula. Laboratory tests with Urea Pre-dialysis 164.5 ± 38.9 mg / dl; hemoglobin 10.32 ± 1.9 g / dl; albumin 3.99 ± 0.4 g / dl; phosphorus 5.3 mg / dl; calcium 8.05 ± 0.9 mg / dl; parathyroid hormone 886 ± 747 pg / dl. Body composition BMI 23.6 kg / m2; R (Q2) 622.3; X (Q4) 48.4; and phase angle 4.3°. 44% of the patients had mild malnutrition according to the Score Malnutrition Inflammation classification. The generic dimensions of the KDQOL-SF 36 revealed scores greater than 60 for CKD symptoms and effects, with an SF-12 Physical Health Composite 36.3 and SF-12 Mental Health Composite 56.3.

**Conclusions:** The costs of hemodialysis (HD) treatment are usually a huge financial burden for health systems and patients. HD sessions twice a week are common practice in many countries in patients without social security. Our results show that this therapy should not be categorized as a suboptimal therapy but as an option for patients with certain clinical characteristics.

**PO1103**

Feasibility of and Adherence to Using a Wrist-Based Activity Tracker in Hemodialysis Patients

Maggie Han,1 Priscila Preciado,1 Ohnmar Thwin,1 Xia Tao,1 Mirell Tapia,1 Lemuel Rivera Fuentes,1 Mohammad I. Hakim,2 Amrish U. Patel,1 Nadja Grobe,1 Stephan Thijssen,2 Peter Kotanko,2,3* Renal Research Institute, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY.

**Background:** Wearables allow insights into patient’s status outside the clinical setting. We aim to quantify how long patients will use a wearable device before requiring an intervention to improve adherence.

**Methods:** Hemodialysis (HD) patients were enrolled from 4 clinics in New York City from May 2018 and followed for up to 1 year. Patients ≥18 years, on HD ≥3 months, able to walk, owning a smartphone, mobile tablet or PC were enrolled, provided with a Fitbit Charge 2, and instructed on how to use the device and sync data. If a patient failed to sync data for 7 consecutive days, a SMS or email reminder was sent. Time to first intervention (TFI) was evaluated using Kaplan Meier time-to-event analysis. Predictors of TFI, including gender, age, living situation, and education level, was assessed via uni/ multivariate Cox Regression. Patients were censored at the end of the observation period.

**Results:** 125 patients were enrolled into our study and 7 failed screening. At enrollment, patients were 54±12 years old with a dialysis vintage of 5.6±5.8 years; 37% lived alone, 56% were single, 59% unemployed, 64% were African American, and 42% had an education level of some college or higher. 82% of the patients required a text message reminder. Mean and median TFI were 101 days (95% CI 80 to 123) and 50 days (95% CI 35 to 70 days), respectively. The probability of no intervention is shown in Figure 1. None of the a priori defined parameters were significant predictors of TFI.

**Conclusions:** Majority of patients studied required at least some intervention to maintain the use of a wrist-based wearable device. While most patients require an intervention before 2 months, the patients who maintain use independently after that point are unlikely to require intervention.

**Funding:** Commercial Support - Fresenius Medical Care

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
POI104
 Routinely Measured Cardiac Troponin I and NT-ProBNP as Predictors of Mortality in Japanese Hemodialysis Patients: The Dialysis Outcomes and Practice Patterns Study

Masahiro Irie,1 Kazuhiro Tsutsuya,1 Marcelo Lopez,2 Brian Bieber,2 Keith McCullough,2 Roberto Pecorini-Filho,2 Bruce M. Robinson,2 Ronald L. Pisoni,3 Eiichiro Kanda,1 Kunitoshi Iseki,1 Hideki Hirokata,4 1Nara Medical University, Kashihara, Japan; 2Arbor Health Care Co, Extendicare Health Services Inc, Milwaukee, WI; 3Kawasaki Medical School, Kurashiki, Japan; 4Nakamura Clinic, Urayoe, Japan; 5Fukuoka renal clinic, Fukuoka, Japan.

Background: Due to the interplay of chronic kidney disease and the heart, it is common for myocardial damage and strain to be present in hemodialysis (HD) patients. The cardiac troponin I (cTnI) and NT-proBNP are widely used as cardiac biomarkers to evaluate the patients at high risk for cardiovascular disease (CVD). However, international The Dialysis Outcomes and Practice Patterns Study (DOPPS) data indicate that these cardiac biomarkers are measured in fewer than 2% of HD patients in real-world practice.

Methods: Pre-dialysis levels of cTnI and NT-proBNP at study enrollment were measured in 1176 prevalent Japanese HD patients (DOPPS phase 5). Cox regression was used to test the association of the cardiac biomarkers with all-cause mortality, adjusting for potential confounders. Subgroup analyses were performed to assess potential effect modification of clinical characteristics: age, systolic blood pressure, HD vintage, diabetes mellitus, CVD, and heart failure.

Results: Median [IQR] cTnI (99th percentile; 0.04 ng/mL) and NT-proBNP levels were 0.018 [0.005, 0.04] ng/mL and 3452 [1580, 8017] pg/mL, respectively. There were 175 deaths during a median [IQR] follow-up of 2.8 [2.3, 2.9] years. Higher levels of both biomarkers were incrementally associated with mortality after adjustment for potential confounders. Even after adjustment for the alternative cardiac biomarker, the HRs of death for cTnI >0.04 and NT-proBNP >8000 pg/mL was 2.05 (95% CI 1.04-1.57, P = 0.022), all cardiac diseases (HR 1.33, 95%CI 1.04-1.69, n=354, P=0.023), and CHD and its complications (HR 1.57, 95% CI 1.08-2.27, n=117, P=0.019).

Conclusions: All three tested POI1 polymorphisms correlate with atherogenic dyslipidemia in HD patients. Associations of POI1 with dyslipidemia, ICS, and cardiovascular mortality provide arguments for the consideration of POI1 as a therapeutic target in the prevention of atherosclerosis and its complications in uremic subjects.

POI106
 Plasma and Erythrocytes Lipidomic Analysis of Adverse Cardio-Cerebrovascular Outcome in Maintenance Hemodialysis Patients

Yui Inan, Ke Zheng, Xiemei Li. Peking Union Medical College Hospital, Dongcheng-q, China.

Background: Cardio-cerebrovascular diseases are prevalent and devastating in maintenance hemodialysis patients. Lipid metabolism is vital for cardiovascular diseases in non-dialysis populations. The disorder of lipid metabolism in dialysis patients is prominent, but the relation of lipids to cardiovascular diseases in dialysis patients is still controversial. Traditional lipid makers failed to identify hemodialysis patients with cardiovascular events. Using high-throughput targeted lipidomic analysis, this study aimed to evaluate the potential of lipids to assess risk of future cardio-cerebrovascular events in hemodialysis patients.

Methods: From July 2013 to August 2019, we followed up the dialysis patients in our dialysis center for stroke and myocardial infarction events, and these patients' plasma and hemocerebrovascular events were stored at the baseline. Lipidomic analyses were performed on an Exion LC-system coupled with a QTRAP 6500 PLUS system (Sciex). Principal component analysis and orthogonal project to late structures discriminant analysis, and heatmaps were used to analyze the differences between patients in with/without adverse cardio-cerebrovascular outcome groups.

Results: A total of 45 plasma samples and 117 hemocerebrovascular events were collected. 9 plasma samples and 28 hemocerebrovascular events were from patients with cardiovascular events. 53% of kind of metabolites were detected in plasma, 23% of lipid were detected in erythrocytes. Compared with the patients without cardio-cerebrovascular events, the patients with events presented higher level of plasma PS 34:2 and TAG 44:1 (16:1), lower level of plasma TAG 52:6 (16:2), TAG 58:9 (22:5), LPS 18:0, and lower level of erythrocytes Cer d18:1/20:0, Cer d18:1/18:0 and cer d18:1/21:0 (Fold change >1.5 or <1/1.5, P value <0.05).

Conclusions: These findings revealed novel plasma and erythrocytes lipidic predictors for cardio-cerebrovascular diseases in hemodialysis patients.

Funding: Clinical Revenue Support, Government Support - Non-U.S.

POI107
 β-Blocker Dialyzability and Adverse Cardiovascular Outcomes in Hemodialysis Patients: A Meta-Analysis

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Background: β-blockers (BB) are one of the most common medications among hemodialysis (HD) patients. There are several BB with different pharmacokinetic properties. Particularly relevant for HD patients is BB dialyzability. In non-dialysis patients, abrupt withdrawal of BB has been associated with adverse cardiovascular events (CVE). HD patients receiving dialysis therapy may also be increased risk of β-blockers. This systematic review aims to determine in HD patients if highly dialyzable BB (HDBB) (metoprolol, atenolol, and acebutolol) compared to poorly dialyzable BB (PDBB) (carvedilol, labetalol, bisoprolol, and propranolol) alters CVE and mortality.

Methods: We searched MEDLINE from 1990 through February 2020 for studies of all forms. All cause mortality (ACM) and CVE were our primary outcomes. Random effects models were used to calculate pooled risk ratios (RR).

Results: An initial search identified 1,066 articles. Exclusion criteria eliminated articles that did not include HD participants or did not compare at least two BB. Ultimately, three cohort studies comparing HDBB and PDBB were identified. All studies were retrospective cohort studies of large HD datasets of patients in the U.S. and Canada. The combined population size of the analyzed studies was 38,580 patients: 24,596 on HDBB and 13,984 on PDBB. There was significant heterogeneity between studies, with two suggesting harm associated with HDBB and one suggesting a reduction in mortality. The risk ratio derived from pooled data across these studies was 1.03 (95% CI: 0.88–1.22) for ACM and 0.94 (95% CI: 0.80–1.11) for CVE. Significant heterogeneity was seen with F2 values of 86% and 84% for ACM and CVE respectively.

Conclusions: All three tested POI1 polymorphisms correlate with atherogenic dyslipidemia in HD patients. Associations of POI1 with dyslipidemia, ICS, and cardiovascular mortality provide arguments for the consideration of POI1 as a therapeutic target in the prevention of atherosclerosis and its complications in uremic subjects.
Conclusions: After a comprehensive search, only three cohort studies were identified comparing BB of different dialyzabilities. No randomized control trials were identified. The three cohort studies had varying results with two favoring HDBB and one favoring PDBB. Pooled results suggested a greater incidence of CVE in patients on PDBB compared to those on HDBB, while ACM is lower for PDBB than for HDBB. Given the heterogeneity of results it is unclear what type of BB should be used in HD patients. A randomized controlled trial comparing BB of different dialyzabilities is warranted.

Funding: Veterans Affairs Support

PO1108

Pre-Dialysis Transition Predictors of Vascular Access Type in 73,928 Veterans Who Started Hemodialysis Therapy Between 2007-2015

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Background: Studies showed dialysis patients with central venous catheter (CVC) had worse outcomes compared to arterio-venous fistula/graft (AVF/AVG) patients. It is hypothesized that a CVC may be a surrogate for sicker patients. From the US Veteran transition of care (TC-CRD) cohort, we sought to characterize factors associated with initiating dialysis with CVC vs. AVF/AVG access type within a year prior to dialysis transition.

Methods: Among US veterans who transitioned to end-stage renal disease (ESRD) from 2007 to 2015, we examined predictors of access type using adjusted logistic regression. An adjusted reverse cox model was used to examine predictors at time of dialysis initiation to identify time to access placement surgery prior to transition.

Results: Logistic regression showed patients with higher Charlson comorbidity index, multiple preexisting comorbidities, and higher hospital and primary care visit before access surgery, had a higher odds of receiving CVC versus AVF or AVG. Among a subset of 28,759 patients, those who were older, female, black, had dementia, and had higher serum phosphorus, white blood cells, and eGFR were more likely to have CVC. Patients who were married, had higher serum albumin, calcium, sodium, hemoglobin, had slower 1 year eGFR decline, and higher nephrology visits, were less likely to have CVC. Fully adjusted reverse cox regression showed patients with higher serum alkaline phosphatase and blood urea nitrogen were more likely to have AVF/AVG placed closer to time of transition. Among 44,558 patients who had at least 1 VA primary care visit in the year prior to dialysis, patients with 2 nephrology visits were more likely to have a AVF/AVG placement surgery in the year prior to transition (figure).

Conclusions: We found that starting dialysis with CVC is a surrogate of adverse outcomes and faster CKD progression, while frequent nephrology visits in a year prior to transition is associated to higher likelihood of AVF/AVG placement.

PO1110

Comparison of Mortality Risk Among Deciles of Cystatin C and Creatinine Among US Veterans

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Background: While both creatinine and Cystatin C (CysC) are markers of renal function, a low serum creatinine level can be related to less muscle mass and hence associated with worse outcomes. Prior studies among elderly persons found that higher serum CysC and creatinine levels were predictors of mortality. However, this relationship has not been examined in contemporary cohorts of US veterans. We sought to examine the relationship of creatinine and CysC with mortality risk in US veterans.

Methods: We examined a historical cohort consisting of 7,849 Veterans with baseline CysC and creatinine data between 10/01/2004-09/30/2015. Veterans were divided into deciles of serum creatinine and CysC levels separately. We examined the association of deciles with all-cause mortality using Cox proportional hazards regression adjusted for demographics, comorbidities, and other lab variables using decile 5 as the reference.

Results: The mean age in the cohort was 69±12. 4% were female, 77% were white, 15% were African American. The median (IQR interquartile range)) for CysC was 1.28 (0.99,1.71) mg/L, for creatinine 1.24 (0.92,1.68) mg/dl. There were 1872/7849(24%) deaths during follow-up. Cox proportional hazards model showing the relationship between deciles of creatinine and cystatin C with all-cause mortality (Reference:5th decile). Model adjustments include demographics and comorbidities and lab variables.

Conclusions: Among US veterans, there is a linear relationship between CysC and mortality risk while the relationship between creatinine and mortality risk is U-shaped. These clinical results indicate that CysC may be a better marker of risk for adverse outcomes than creatinine, as previously shown in epidemiological studies.

Figure: Time for dialysis transition back to AVF/AVG placement surgery prior to transition.

PO1109

Effect of Treatment According to Intervention Modality with Central Venous Catheters

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Background: A general cause of hemodialysis vascular access failure, a primary cause of morbidity patients undergoing hemodialysis, is central venous occlusion or stenosis. There are several interventions to resolve problem; however whether method is best for dialysis patients. The purpose of this study is to compare which method is best choice to hemodialysis patients.

Methods: We searched Outcomes included the rate of primary patency, assisted primary patency, secondary patency, re-intervention subjects, re-intervention rate regarding balloon angioplasty, nondrug metal stent, drug-eluting balloon, or drug-eluting stent in PubMed, Embase, CENTRAL, Ovid and other relevant websites. We selected and assessed the trials that met the inclusion criteria and conducted a network meta-analysis using the R software.

Results: A total of eighteen studies were included in the network meta-analysis among treatment of intervention group. Overall, 967 patients were reviewed and analyzed for primary and secondary patency rates at 6, 12 months and 24 months post-treatment. Compared with nondrug metal stent, drug-eluting stent group showed a significantly lower secondary patency rates (odds ratio 0.67 [95% credible interval, 0.46–0.92]) at 12 month. However, primary patency and assisted primary patency rates showed no differences among the intervention during observational period. In rank probability, Percutaneous transluminal angioplasty was second in secondary patency rates. However, there is not statistically significant difference in rankgram.

Conclusions: We anticipate that the data of this study will assist physicians in making informed decisions when selecting intervention, such as drug-eluting stent, as a treatment option for central vein stenosis in hemodialysis patients.
POI111
Comparative Mortality of ESKD from Nephrolithiasis or Urolithiasis in the United States
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Background: Patient with nephro-ureolithiasis (NL/UL), when compared with patients without kidney stone disease, experience higher rates of adverse health outcomes, including increased mortality, cardiovascular morbidity, and progressive kidney disease. Little is known about the epidemiology and outcomes of patients who reach end-stage kidney disease (ESKD) secondary to NL/UL.

Methods: From the USRDS, we identified all patients with incident ESKD who initiated dialysis, 1995-2016, from the Medical Evidence Report (CMS-2728). We ascertained the kidney disease causing ESKD as reported by the patient’s nephrologist. Categories included: NL/UL; diabetes; hypertension; gluceroluricnephatis, polycystic kidney disease (PKD); other uroligic; and other/missing/unknown. We also noted patients’ age, sex, race, Hispanic ethnicity, Medicaid coverage. Up to 11 comorbid conditions and health behaviors were also abstracted from form CMS-2728. Patients were followed from first dialysis to all-cause mortality, censoring at kidney transplant and end of database (12/2017). Cox proportional hazards regression models, stratified by year, estimated hazard ratios (HR) and corresponding 95% confidence intervals (CI).

Results: We studied 1,979,430 new ESKD patients, of whom 4190 (0.21%) patients had NL/UL as the reported cause of ESKD. Patients with NL/UL had similar age and sex distributions, but more were White (82 vs 66%) and fewer Black (11 vs 28%) or Hispanic (9 vs 13%) than among other causes of ESKD. All-cause mortality during median follow-up of 2.6 years was 173 per 1000 person-years among NL/UL patients. HR and 95% CIs comparing different causes of ESKD with NL/UL, at varying levels of model adjustment, are shown in Table.

Conclusions: Compared to patients whose ESKD was attributed to NL/UL, mortality was significantly higher among patients with DM, HTN, and other/unknown/missing cause of ESKD, but lower among patients with GN or PKD as cause of ESKD.

Mortality of Causes of ESKD vs. Nephro-Urolithiasis [HR (95% CI)]

POI1112
Sleep Patterns and Mortality Risk in a Prospective Hemodialysis Cohort
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Background: While sleep disorders are common in hemodialysis (HD) patients, the association of sleep patterns and mortality. Patients underwent protocolized self-reported sleep questionnaires over 3/2014-6/2019. We examined the association between sleep patterns and mortality. Patients underwent protocolized self-reported sleep questionnaires over 3/2014-6/2019. We examined associations of baseline sleep patterns with all-cause mortality using Cox regression adjusted for expanded case-mix covariates.

Methods: Among 452 HD patients from the prospective Malnutrition, Diet, and Racial Disparities in Kidney Disease study, we examined the association between sleep patterns and mortality. Patients underwent protocolized self-reported sleep questionnaires over 3/2014-6/2019. We examined associations of baseline sleep patterns with all-cause mortality using Cox regression adjusted for expanded case-mix covariates.

Results: In the overall cohort, the median (IQR) sleep duration was 6.0 (4.5, 8.0) hours on dialysis vs. 7.0 (5.0, 8.0) hours on non-dialysis days, respectively. In analyses examining the association of sleep duration (defined as median) with all-cause mortality using Cox regression adjusted for expanded case-mix covariates.

Conclusions: In HD patients, shorter sleep duration, frequent sleeping difficulties, and moderate to frequent use of sleeping pills were associated with higher mortality risk. Future studies are needed to determine if interventions that improve sleep patterns increase survival in this population.

Funding: NIDDK Support

POI1113
Self-Reported Sleep Patterns in a Prospective Hemodialysis Cohort

Background: Growing evidence suggests that altered sleep patterns are prevalent in the general population, and are associated with worse health outcomes (obesity, hypertension, cardiovascular disease). However, there has been sparse examination of habitual sleep patterns in chronic kidney disease (CKD) patients, including those receiving dialysis. We thus examined self-reported sleep patterns in a well-defined prospective hemodialysis (HD) cohort.

Methods: Among 452 HD patients from the prospective Malnutrition, Diet, and Racial Disparities in Kidney Disease cohort recruited across 16 dialysis clinics, we administered protocolized sleep surveys during routine dialysis treatments over 10/2011-3/2015. Using self-reported questionnaires, patients were queried with respect to their habitual sleep patterns, including survey items related to 1) sleep duration, 2) sleep quality and disturbances, and 3) mental/emotional and physical symptoms potentially linked with sleep alterations.

Results: The means ±SD age of the study population was 55±14 years, among whom 54% were male, 28% were Black, 51% were Hispanic, and 55% had diabetes. In the overall cohort, the median (IQR) sleep duration was 6.0 (4.0, 8.0) and 7.0 (5.0, 8.0) hours on dialysis vs. non-dialysis days, respectively. Over two-thirds to three-quarters of the cohort reported sleeping during dialysis (76%), having difficulties sleeping at night (68%), and having insufficient sleep (72%); sleeping pill use was reported in 21% of patients. Half of the cohort reported stress/anxiety during dialysis, and 87% vs. 64% described feeling tired/exhausted on dialysis vs. non-dialysis days, respectively.

Conclusions: Our findings uncovered a high prevalence of altered sleep patterns in a well-defined prospective HD cohort. Further studies are needed to identify the modifiable and non-modifiable determinants of sleep alterations, as well as their downstream sequelae in dialysis patients.

Funding: NIDDK Support

POI1114
Self-Reported Sleep Apnea-Related Symptoms in a Prospective Hemodialysis Cohort

Background: Obstructive sleep apnea (OSA) is the most prevalent sleep-related breathing disorder in the general population. While growing data suggests that OSA is more common in hemodialysis (HD) patients, there remains under-diagnosis of this disorder in end-stage renal disease (ESRD) due to symptom overlap with uremia. We thus sought to examine clinical features associated with OSA in a well-defined prospective cohort of HD patients.

Methods: Among 452 HD patients from the prospective Malnutrition, Diet, and Racial Disparities in Kidney Disease cohort recruited across 16 outpatient dialysis centers, we administered protocolized questionnaires querying clinical features of OSA over 10/2011-3/2015. Using self-reported surveys, information was collected regarding OSA-related symptoms including presence and frequency of snoring and apneic events.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: The mean ± SD age of the study population was 55 ± 14 years, among whom 54% were male, 28% were Black, 51% were Hispanic, and 55% had diabetes. In the overall cohort, 68% of patients reported snoring, among whom 62% reported having frequent (i.e., sometimes, frequent, or always) symptoms. Approximately 17% of patients reported apnea symptoms, among whom 24% reported having frequent events. While over two-thirds of the cohort reported an OSA-related symptom (e.g., snoring, apnea), only 18% were diagnosed with a sleep disorder and 3% had received treatment.

Conclusions: Our findings suggest that clinical features of OSA are common in HD patients, although only a fraction are diagnosed with this disorder and/or undergo treatment for symptoms. Further studies are needed to identify effective OSA screening tools specific to the ESRD population, as well as the impact of OSA interventions in this population.

Funding: NIDDK Support

POI115

High-Frequency Oscillations of Intradialytic Arterial Oxygen Saturation in Hemodialysis Patients

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Background: High-frequency oscillation of arterial oxygen saturation (SaO2) presenting as repetitive “sawtooth” patterns was observed in sleep apnea patients, but it has never been reported during treatment in hemodialysis (HD) patients. In this study, we explored the prevalence of intradialytic “sawtooth” patterns and their clinical correlates in HD patients.

Methods: We prospectively studied chronic HD patients who didn’t use breathing devices, cardiac pacemaker, nasal oxygen, alpha blockers, short-acting nitrates, or have a history of sickle cell anemia and non-sinus cardiac arrhythmia. During two visits per subject, we used the Crit-Line® Monitor to record SaO2 at a frequency of 1 Hz, and video recording to capture periods of wakefulness for the entire treatment. SaO2 data were analyzed for occurrence of “sawtooth” patterns (100% increase in standard deviation lasting ≥10s) and oxygen desaturation episodes (ODE, 3% drop from baseline lasting for ≥10s).

Results: 16 subjects studied were 54±11 years old, 63% males, 69% African Americans. SaO2 was 94.3±2.1%. “Sawtooth” patterns covered 19.1% of the recorded treatment time, whereas ODE made up only 0.3%. 9 of 11 subjects who displayed “sawtooth” patterns, showed them in both visits. “Sawtooth” patterns were more likely to occur during the time when subjects were not awake than during wakefulness (25.3% vs. 17.0% of time in each status). Although ODE were rarely seen, 70% were observed during times when “sawtooth” patterns were also present. Figure 1 shows typical SaO2 “sawtooth” patterns recorded.

Conclusions: Sleep-related breathing disorders are both highly prevalent and underdiagnosed in HD patients and may be underlying the high-frequency oscillations of intradialytic arterial SaO2 observed in this study. These observations might be useful in identifying sleep-related respiratory abnormalities in HD patients that may warrant diagnostic workup. Further studies are needed to identify sleep-related SaO2 oscillations and their relationship to clinical outcomes.

Funding: Commercial Support - Renal Research Institute, LLC

POI116

CKD and Concomitant Sleep-Disordered Breathing Is Associated with Increased Overall Mortality: A Meta-Analysis

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Background: Sleep-disordered breathing (SDB) is common in advanced chronic kidney disease (CKD) patients. However, the association between CKD and SDB is not well studied and SDB overall mortality remains inconclusive. As it has been established that SDB and CKD individually contribute to overall mortality and that a large proportion of CKD patients have concomitant SDB, there comes a question if their morbid effects are compounded together.

Methods: We identified OVID, EMBASE, and the Cochrane Library were searched for eligible publications, including non-transplant CKD patients older than 18 years-old with CKD. Studies were included if they compared prevalence of SDB, and their association with overall mortality. Two reviewers independently assessed the studies for inclusion and disagreement was resolved by consensus. We performed a meta-analysis for overall mortality and pooled odds ratio for overall mortality.

Results: A total of 7 observational studies (n = 186,686) were included in the meta-analyses for patients with 94.2% of patients had end-stage kidney disease (ESKD) requiring hemodialysis (HD), 5.0% had ESKD requiring peritoneal dialysis (PD), and 0.8% had non-dialysis CKD. The mean patient age was 76.8 ± 2.2 years. Most patients were male (53.4%) and caucasian (76.8%). Up to 39.3% of patients had diabetes. The mean body mass index was 28.0 ± 6.6 kg/m². Upon analysis, patients with advanced CKD and SDB demonstrated a pooled estimated odds ratios for overall mortality and cardiovascular events were 2.092 (95% CI, 1.594-2.744) and 1.020 (95% CI, 0.929-1.119), respectively compared to patients with CKD alone. No potential publication bias was detected. There were no significant differences in odds ratios for overall mortality, based on subgroup analyses.

Conclusions: Co-existence between advanced CKD and SDB is associated with significantly increased overall mortality, but not cardiovascular (CV) events when compared with CKD alone. The analysis of CV events requires additional studies to corroborate these findings. Moreover, these results suggest clinical interventions should be aimed to prevent the progression of SDB and CKD to mitigate the mortality associated in patients with both diseases.

POI117

A Randomized, Double-Blind, Phase 2a Study to Evaluate the Tolerability, Feasibility, and Efficacy of AKST1210 in Patients on Hemodialysis with ESRD and Cognitive Impairment


Background: Studies show that elevated levels of beta-2-microglobulin (b2M) negatively impact cognition. In patients on hemodialysis (HD) for end stage renal disease (ESRD), b2M levels are up to 60-fold higher than in those with normal kidney function; these patients also have a higher prevalence of cognitive impairment. AKST1210 is a device that removes b2M from plasma. To test if removal of b2M could improve cognition, we administered pooled human HD plasma with and without b2M to mice. Mice that received HD plasma with b2M showed a reduction in neurogenesis, neuronal activity, and synaptic markers, while few detrimental effects were seen in mice that received AKST1210 treated HD plasma, suggesting b2M removal is beneficial. Based on robust preclinical data, a clinical study was initiated to assess safety, tolerability, and feasibility of using AKST1210 during HD in subjects with ESRD and cognitive impairment (ESRD-CI).

Methods: In this study, subjects 40 years or older with ESRD-CI are randomly assigned to receive AKST1210 or control during HD sessions for 3 months. Approximately 26 subjects will be recruited and undergo a screening visit, run-in period, treatment visits, and end of study visit. Safety and tolerability will be assessed at every visit. Cognitive assessments will be administered periodically and b2M and proteomics samples collected at specific timepoints.

Results: Primary endpoints are the safety and tolerability of using AKST1210 in subjects with ESRD-CI undergoing HD. Safety is measured by the incidence of treatment-emergent adverse events and serious adverse events. Tolerability is measured by subject retention and compliance with visit completion. Secondary endpoints assess the change from baseline in cognitive assessments and the feasibility of conducting expanded
PO1118
Selection of the Best Equation for Serum Osmolality Calculation in Hemodialysis Patients
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Background: Although the serum osmolality (SOsm) is determined by circulating solutes including sodium, potassium, glucose and urea, calculated serum osmolality formula without potassium (2[Na, in mmol/L] + [Glucose, in mg/dL] / 18 + [BUN in mg/dL] / 2.8) is commonly used. Several different equations have been previously described to estimate SOsm. Although in hemodialysis patients it is important to monitor homeostasis by means of estimating SOsm, few studies have examined the accuracy of these equations.

Methods: We identified 20 patients who transitioned to hemodialysis therapy and had repeated SOsm data along with, pre-dialysis sodium, potassium, glucose, and blood urea nitrogen (BUN) on the same day. We compared estimated SOsm by the 13 equations used in the previous literature and measured SOsm.

Results: The patients were 52% male, 33% non-white, and the mean age was 60 ± 17 (mean±SD) years. There were 65 measured SOsm and the mean ± SD was 310.8 ± 12.0 mOsm/Kg. The following equation provided the best fit between measured and calculated SOsm: 2[Na, in mmol/L] + [K, in mmol/L] + [Glucose, in mg/dL] / 18 + [BUN in mg/dL] / 2.8 (mean difference, -0.7 mOsm/Kg; 95% confidence interval, -2.12-0.71; P=0.32).

Conclusions: Our result suggests that the equation for estimating serum osmolality in hemodialysis patients should include serum potassium in addition to other components usually used to estimate serum osmolality in non-hemodialysis patient.

PO1119
Effect of Dialyse Potassium on Interleukin 6 During Hemodialysis in Patients with ESRD
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Background: Chronic inflammation is associated with poor outcomes in end stage renal disease (ESRD). Pro-inflammatory markers including interleukin-6 (IL-6) increase during hemodialysis. Efforts of intracellular potassium in cell cultures result in activation of inflammasome and release of inflammatory markers. We studied the effect of potassium efflux during hemodialysis on serum IL-6.

Methods: 15 patients with ESRD on chronic maintenance hemodialysis at Hunter Holmes McGuire VAMC were enrolled. Each subject participated in both interventions separated by at least two weeks. Intervention A involved 2K dialysate for the 1st hour followed by 4K for the second hour. Intervention B involved 4K for the 1st hour followed by 2K for the second hour. After first two hours, dialysate potassium was switched to the prescribed concentration for the remaining time Blood was drawn at 0, 30, 60, 90, 120, 180, and 240 minutes after start of dialysis. Serum IL-6 was measured using ELISA. Data were analyzed using Mixed linear model with p<0.05 considered significant.

Results: IL-6 was detectable at baseline and increased during dialysis. However, mean levels of IL-6 were parallel between the 2 interventions (Figure 1.), implying no change in the rate of IL-6 production over time between the 2 interventions (Table 1.)

Conclusions: IL-6 increases during hemodialysis but rate of increase is not affected by dialysate potassium.

Funding: Veterans Affairs Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

Table 1. Linear Mixed Model Serum IL-6

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Figure 1. Serum IL-6 at different timepoints between 2 Interventions(Mean±SE)

PO1120
Racial Differences in Physician Trust Among ESRD Patients in Upstate New York
Spencer Dahl, Basil S. Kazi, Fahad Saeed. University of Rochester Medical Center, Rochester, NY.

Background: Black patients have worse health outcomes in comparison to White patients, including 2.8 times higher incidence of End Stage Renal Disease, and a significantly higher age stratified risk of death on dialysis. Historically, low levels of physician trust in the healthcare system have been postulated as one of the mediators of health care disparities. Previous literature has suggested that black patients are less likely to trust their physicians, however there is a paucity of such data in the dialysis population.

Methods: We surveyed 223/380 (response rate 58%) of hospitalized patients receiving maintenance dialysis in Upstate New York, including 91 white and 82 black patients. We assessed physician trust using the Primary Care Assessment Survey (PCAS). This scale has been previously validated in adult and older adult populations.

Results: We found no difference in the level of trust between black and white patients (3.01 vs 2.95 respectively), assessed on the PCAS scale.

Conclusions: We found no difference in physician trust between black and white patients in our sample. Addressing healthcare disparities is a priority issue for maintenance dialysis patients. Future research to investigate issues related to access to the health care system, health literacy, and socioeconomic status may shed further light into health disparities.

PO1121
Mobile Health (mHealth) Readiness Among Dialysis Patients
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Background: Mobile health (mHealth) is the healthcare use of mobile devices such as mobile phones. mHealth has demonstrated improvement in patient-reported outcome measures, resource efficiencies and cost savings. The aim of this study was to examine the status and correlates of mHealth readiness among individuals on dialysis.

Methods: Cross-sectional 30-item questionnaire, adapted from Bonner’s mHealth instrument guided by Khutun’s mHealth readiness model, was distributed to people on dialysis from 13 in-center hemodialysis (HD) facilities and 14 home dialysis centers. Proficiency was determined by reported use of applications of increasing level of complexity. We used regression analysis to investigate the relationship between demographic and social factors with proficiency.

Results: 949 patients (632 HD and 317 home dialysis) completed the survey (56% response rate), 38% were female. 73% of respondents reported using the internet: 90% of
them requiring no assistance. 81% of respondents owned smartphones or other internet-capable devices. 70% had intermediate or advanced mHealth proficiency. Main reasons for using mHealth were appointments (56%), communication with healthcare personnel (56%), laboratory results (55%) and obtaining kidney care information (50%). The main reported concerns with mHealth were privacy & security (18%), and cost (6%). mHealth proficiency was lower in older patients: compared to the 45-65 years (yrs) group, respondents in age groups < 45 yrs, 61-70 yrs, and > 70 yrs had adjusted odds ratio (aOR) of 5.04 (95% Confidence Interval: 2.23-11.38), 0.39 (0.24-0.62), and 0.22 (0.14-0.35) respectively. Compared to those with college education, the aOR associated with higher home dialysis school only were 0.89 (0.03-0.16) and 0.26 (0.18-0.39) respectively. Hispanic ethnicity (aOR 0.49 [0.31-0.75]) was compared with non-Hispanic was associated with lower mHealth proficiency, while employment was associated with higher proficiency (aOR 2.26 [1.18-4.32]). Although home dialysis was associated with higher proficiency in the univariate model, we did not observe this in the fully adjusted model.

Conclusions: The majority of dialysis patients surveyed were ready to use, and proficient in, mHealth. These results are encouraging for the nephrology community to increase endorsement of mHealth technologies in patient care.

POI1122
Clinician Perspectives on Access to Kidney Replacement Therapy in Rural Communities
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Background: Patients with chronic kidney disease (CKD) requiring kidney replacement therapy in rural communities are at higher risk of mortality compared with patients in urban areas, and encounter many barriers in accessing care. We aimed to describe clinicians’ perspectives of patient access to dialysis and kidney transplantation in rural communities.

Methods: We conducted 28 semi-structured interviews with clinicians (nephrologists, nurses, transplant coordinators and social workers) from Australia. Transcripts were thematically analyzed.

Results: We identified five major themes: the tyranny of distance (overwhelming burden of travel, minimizing relocation distress, scarcity of transportation options, concerns for patient safety), supporting navigating of health systems (reliance on local champions, negotiating variability of literacy, providing flexible pathways, frustrating presence of gatekeepers), disrupted care and lacking services (without continuity of care, scarcity of specialist services, fluctuating capacity for dialysis), pervasive financial distress (coping with out-of-pocket expenditure, widespread socio-economic disadvantages), and awareness of rurality (lacking availability of safe and sustainable resources for dialysis, sensitivity to local needs, dependence on social support, limited options available). Selected quotations are provided in Table 1.

Conclusions: Clinicians felt hampered and frustrated for patients living in rural communities who had limited access to quality care because of geography, financial burden, and complexity and rigidity of the health system. Increased use of telehealth, increased specialist outreach clinics in rural locations and improving flexibility of pathways were suggested to improve access.

Funding: Government Support - Non-U.S.

Table 1. Selected illustrative quotations

POI1123
Estimation and Prediction of Prevalence of Patients Receiving Dialysis in China Based on Claims Data
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Background: The national prevalence of end-stage kidney disease in China has not been well studied. We aimed to estimate the prevalence of patients receiving dialysis to predict the trend using claims data in order to provide evidence for developing prevention strategies.

Methods: Medical claims data from Jan 1, 2013 to Dec 31, 2017 were extracted from a large claims database, which used a two-stage sampling design to obtain a national sample of insured population. Patients receiving maintenance dialysis, including hemodialysis (HD) and peritoneal dialysis (PD), were identified according to medical billings and ICD-10 codes. The age-adjusted prevalence and number of dialysis patients were calculated stratified by year and gender. The Verhulst model was used to predict the short-term prevalence from 2018 to 2025.

Results: From 2013 to 2017, the age-adjusted prevalence of dialysis patients increased from 252.46 per million population (PMP) to 419.23 PMP. In 2017, the age-adjusted prevalence of HD and PD was 384.32 PMP and 34.91 PMP, respectively, and the total number of dialysis patients in China was estimated to be 581,055. The overall trend in the predicted prevalence of dialysis patients was increasing. The predicted prevalence was 533.61 PMP in 2020 and 623.49 PMP in 2025, and the corresponding number of patients was 743,304 and 865,704, respectively.

Conclusions: We have firstly made an attempt to assess the prevalence of dialysis patients in China and establish a national surveillance system based on claims data. It is urgent to formulate prevention and control strategies to reduce the escalating burden of kidney diseases.

Funding: Government Support - Non-U.S.

POI1124
Low Socioeconomic Status Increases Risk of Mortality and Hospitalization in Korean Maintenance Hemodialysis Patients
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Background: The number of hemodialysis (HD) patients and medical expenses are growing rapidly in Korea owing to aging society and accompanying diseases such as diabetes. Whether low socioeconomic status (SES) affects poorer HD outcome is controversial. Therefore, this study was performed to evaluate the effect of SES upon mortality and hospitalization in Korean maintenance HD patients.

Methods: We used HD quality assessment data from the year of 2013 and 2015 for collecting demographic and clinical data. The mortality data was collected until Dec 2017. We used insurance status as a proxy indicator of SES in which the subjects were classified into low SES (Medical Aid recipients) and high SES (National Health Insurance beneficiaries). We analyzed mortality and hospitalization risk based on SES using Cox proportional hazard model.

Results: A total of 21,786 HD patients from 2013 survey and 35,454 HD patients from 2015 survey were included in the analysis. The ratio between high and low SES group was 76.7% versus 23.3%. The low SES group was younger and showed higher proportion of male, and lower proportion of diabetes, hypertension, and cerebrovascular accidents compared to the high SES group. The crude mortality rate was 93/1,000 person-year in 2013 and 106/1,000 person-year in 2015. After adjusting for age, gender, comorbidity and laboratory parameters, the low SES group showed significantly higher mortality risk compared to the high SES group (hazard ratio 1.151 [95% confidence interval (CI) 1.082-1.225], P < 0.0001 in 2013 survey and hazard ratio 1.073 [95% CI 1.009-1.14], P = 0.0254 in 2015 survey). The low SES group was also an independent risk factor for hospitalization after adjusting for age, gender, comorbidity and parameters (hazard ratio 1.129 [95% CI 1.09-1.17], P = 0.0001 in 2013 survey and hazard ratio 1.142 [95% CI 1.108-1.178], P < 0.0001 in 2015 survey).

Conclusions: Low SES independently increases risk of patient mortality and hospitalization in Korean maintenance HD patients.

Funding: Government Support - Non-U.S.

POI1125
Iron Overload in ESRD Treated with Doferoxamine for Chelation
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Introduction: The patient is a 23-year-old female with a history of sickle cell disease, uncontrolled hypertension, and ESRD on HD 3x week for the past 4 years, requiring transfusions to control hemolysis. Due to the patient’s uncontrolled hypertension epoetin alfa was withheld for a few months. The patient presented to Loyola with severe symptomatic anemia, and concerns for iron overload.
Case Description: The patient presented to the hospital with severe anemia and decreased mental status. Labs revealed a Hgb of 5.8g/dL, SBP of 177mmHg, and platelets of 40,000/mL. Hematology was consulted for further evaluation of anemia and thrombocytopenia. Her reticulocyte index was calculated at only 0.10, LDH 206, haptoglobin < 15, with peripheral smear showing no schistocytes or sickle cells. Iron was 13mg/dL, transferrin 100, ferritin 4284mg/ml, and iron saturation 98%. Bone marrow biopsy was obtained showing normal cellular marrow for her age and iron laden macrophages. Hgb electrophoresis showed HgbS 3.3% indicating that most of the patient’s blood was transfused blood volume. Epoetin alfa was restarted and chelation therapy was recommended by hematology for iron overload. The patient was started on deferoxamine 50 mg/kg three times per week following hemodialysis. Most recent labs obtained show a ferritin level decreased to 2378ng/ml after receiving several doses of deferoxamine for over a month.

Discussion: This represents a unique case of iron overload from sickle cell disease along with ESRD leading to transfusion dependence. The treatment of iron overload was from the chelating agent deferoxamine. Initial repeat ferritin levels indicate favorable treatment response without adverse events to date. There are only a few case reports along with ESRD leading to transfusion dependence. The treatment of iron overload was most of these cases per literature review with ESRD. Most recent labs obtained show the patient receiving chelation therapy during her hospital admission.

PO1126
Role of Hemodialysis in Severe Ethanol Poisoning
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Introduction: The treatment for acute ethanol intoxication remains largely supportive. About 1% of patients presenting with ethanol intoxication require the utilization of critical care support. We present a case of a 19-year-old with altered mental status and a serum ethanol level above assay who required hemodialysis for rapid ethanol elimination and made a full recovery.

Case Description: A 19-year-old male with no past medical history presented with unresponsive alter a night of heavy ethanol use. His serum ethanol level was above assay at >550mg/dL. Methanol and ethylene glycol levels were undetectable. He had normal kidney and liver blood tests, without metabolic acidosis. His osmolar gap was attributed purely to ethanol. Given a Glasgow Coma Scale of 3, he was intubated for airway protection. He then developed atroventricular dissociation and required atropine, and hypotension requiring vasopressor support. A repeat serum ethanol level at 9 hours remained above assay at >550mg/dL and he remained unresponsive at 14 hours. Decision was made to initiate patient on hemodialysis. Two hours into his hemodialysis session, he became conscious and was successfully extubated at a serum ethanol level of 260mg/dL. His neurologic status returned to baseline and he was discharged from the hospital within 24 hours.

Discussion: The patient’s ethanol metabolism elimination rate without hemodialysis was calculated to be at 15mg/dL/hour. Using this elimination rate, his initial serum ethanol level was predicted to be about 63mg/dL. Without hemodialysis, it would take roughly 41 hours for complete elimination. While on dialysis, the patient’s rate of elimination increased by a factor of four from 15mg/dL/hr to 56mg/dL/hr. Complications of prolonged intubation in acute and neurologic toxicity from severe ethanol poisoning in this young patient include life-threatening arrhythmias, and possible permanent neurologic damage which was avoided using hemodialysis to expedite ethanol elimination. This case demonstrates the role and benefit of hemodialysis for a critically ill patient who is experiencing organ toxicity and exposes a need for updated recommendations in this specific set of patients.

PO1127
A Polysulfonamide Membrane with a Direct Thrombin Inhibitor to Decrease Local Thrombus Formation
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Background: Extracorporeal circulation, such as hemodialysis, is required systemic anticoagulation to avoid thrombus formation. However, conventional anticoagulation methods may induce hemorrhage complications, especially those patients who have bleeding disorders. As dialysis is the main site of thrombosis, anticoagulant modification of the dialysis membrane may decrease local clotting of the dialyzer membrane, and doesn’t increase the bleeding risk of dialysis patients.

Methods: We chose argatroban (AG), a direct thrombin inhibitor, to modify a polysulfonamide (PES) membrane. Fourier transform infrared spectroscopy (FTIR) was used to confirm that AG was grafted to the PES successfully. Scanning electron microscopy (SEM) was used to observe the characteristic morphology of the membranes. Activated partial thromboplastin time, prothrombin time, and thrombin time were determined to evaluate the antithrombotic property of the modified membrane.

Results: FTIR indicated that argatroban modified PES membranes (PES-AG) were successfully prepared. Compared with the PES membrane, the clotting time value of the PES-AG membrane was significantly prolonged, and the difference was statistically significant, which initially indicated that the PES-AG membrane had a better anticoagulant effect. SEM showed that the PES-AG membrane could decrease local thrombus formation.

Conclusion: Preparation of the argatroban modified PES membrane is feasible, and the anticoagulant performance is superior to the unmodified PES membrane.

Funding: Government Support - Non-U.S.

PO1128
Filter Operation Mode Affects the In Vivo Performance of a Synthetic Plasma Fractionation Membrane
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Background: The mode a dialyzer or fractionator is operated may affect the fouling processes of the filter membrane and, hence, may determine its potency and performance. Purpose of the present study was to assess such effects in vivo. To avoid the often varying treatment conditions in humans, a large animal model was used.

Methods: In a prospective, randomized, controlled, crossover trial, four sheep were subjected to double filtration plasmapheresis with a polysulfonamide plasma fractionation membrane intended for lipid apheresis (FractioPES® 200; 3M, Germany). Five different operation modes were tested in each animal: Low (30 mL/min), medium (36 mL/min) and high (42 mL/min) plasma flow rates as well as high flow rate at increased plasma temperature (38.5 °C; thermodialfiltration) and reversed plasma filtration flow direction (outside-in), respectively. The totally treated plasma volume was 1500 mL. Reduction ratios (RR) and sieving coefficients (Sc) were determined for LDL cholesterol (2.500–3.000 kDa), HDL cholesterol (175–360 kDa), fibrinogen (305–385 kDa), immunoglobulin IgG (150 kDa) and albumin (67 kDa).

Results: Compared to the other operation modes, outside-in filtration and, less pronounced, also high plasma flow rates increase the permeability of a synthetic fractionation membrane for larger proteins. The differences in Sc did not translate into different reduction ratios.

Funding: Commercial Support - 3M Deutschland GmbH
PO1129

Abstract Withdrawn

PO1130

Online High-Volume Hemodiafiltration Reduces Pre-Dialysis Levels of Indoxyl Sulfate Compared with High-Flux Hemodialysis: Results from the HDFit Multicentric Randomized Controlled Trial Jordana D. de Lima,1 Murilo H. Guedes,2 Silvia D. Rodrigues,3 Ana Clara S. Almeida,4 Ana Beatriz L. Barra,5 Maria Eugenia F. Canziani,6 Americo L. Cuvello neto,7 Carlos E. Poli de Figueiredo,8 Roberto Pecocis-Filho,9 Lia S. Nakao.1 1Universidade Federal do Parana, Curitiba, Brazil; 2Pontificia Universidade Catolica do Parana, Curitiba, Brazil; 3Fresenius Medical Care, Rio de Janeiro, Brazil; 4Universidade Federal de Sao Paulo, Universidade Federal de Sao Paulo, Sao Paulo, Brazil; 5Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; 6Pontificia Universidade Catolica do Rio Grande do Sul, Porto Alegre, Brazil.

Background: Although HDF improves the clearance of smaller uremic toxins, recently, it was observed that HDF impacts pre-dialysis plasma levels of the PBUTs indoxyl sulfate (Ixs), p-creSy1ulfate (pCS) and indole-3-acetic acid (IAA) compared to HD.

Methods: This is post hoc analysis of the multicentric randomized controlled trial studying the impact of HDF versus hf-HD on measured physical activity (HDFit - clinicalTrials.gov: NCT02787161), which included clinically stable HD patients with a vintage >3 to <24 months. Total plasma levels of Ixs, pCS and IAA were determined by high performance liquid chromatography with fluorescence detection at baseline, 3 and 6 months. Mean difference in pre-dialysis PBUTs between HDF and hf-HD during the 6 months was estimated by linear mixed effect models.

Results: One hundred ninety-three patients (mean age 53 years old, 70% males and 60% white) were analyzed. There were no differences between HD and HDF groups regarding clinical and biochemical characteristics at the baseline. In the HDF group, 99% of patients achieved a convective volume higher than 22 L. The mean differences (95% CI) in concentrations over time for PBUTs among HDF and HD groups are shown in the Figure.

Conclusions: In this post-hoc analysis of the HDFit trial, high-volume HDF consistently reduced pre-dialysis concentration of Ixs compared to hf-HD. These results demonstrate the sustained effect of mixed-diffuse convective methods in the removal of PBUTs compared to predominantly diffusive techniques.

Figure. Mean differences between groups in the change from baseline along with 95% confidence intervals (CI). Results shown Ixs favored by HDF compared to HD.

PO1131

Use of Cytokine Adsorbing Membranes in Patients with Acute Renal Failure in Intensive Care Units Eva Jakopin, Martin Hren, Tina Stropnik Galuf, Masa Knehtl, Tadej Zorman, Nina Vodosek Hojs, Robert Ekart, Radovan Hojs, Sebastian Beve. Univerzitetni Klinični Center Maribor, Maribor, Slovenia.

Background: Use of cytokine adsorbents has been proposed as a novel therapeutic approach in sepsis management. Our aim was to evaluate laboratory markers, clinical parameters and SOFA (Sequential Organ Failure Assessment) score in patients who were treated with cytokine adsorbing membrane (CytoSorb®, CytoSorbents Corp. New Jersey, USA) and Compare to the usual standard haemodialysis.

Methods: We included adult patients with septic shock and acute renal failure. We retrospectively collected laboratory results (leukocytes, thrombocytes, C-reactive protein, procalcitonin, lactate, urea, creatinine, bilirubin, PaO2), clinical parameters (mean arterial pressure (MAP), heart rate, HR, sodium, serum creatine, blood gas, residual diuresis), SOFA score and vasopressor use at the beginning and at the end of the procedure.

Results: We included 69 patients, 51 men, aged 56.6 ± 15 years. 51 patients had 1 procedure, 14 patients had 2 procedures, 3 patients had 3 procedures and 1 patient had 4 procedures. Median time from admission to initiation of procedure was 47 hours, median treatment time was 23.6 hours. We discovered significant improvement in procalcitonin (35.36 ± 37.33 ng/mL vs. 24.25 ± 31.18 ng/mL; p<0.001), creatinine (345.06 ± 174.65 μmol/L vs. 233.11 ± 108.82 μmol/L; p<0.0001), SOFA score (14.20 ± 2.64 vs. 12.69 ± 3.52; p<0.001) and FiO2 (48.17 ± 21.7% vs. 44.63 ± 21.45 %; p<0.020). Patients with more than 1 procedure showed statistically significant reduction in lactate (15.50 ± 4.74 mmol/L vs. 2.46 ± 1.74 mmol/L; p<0.010) and vasopressin dose (1.26 ± 1.61 vs. 0.88 ± 3.21 L/h; p<0.022).

Conclusions: We observed potential beneficial effect of adsorptive membrane use in septic patients. According to our results two or more procedures were associated with improved laboratory markers and lower vasopressor requirement.
Association Between Nrf2 and CDKN2A Expression in Patients with ESRD: A Pilot Study

Keichi Sumida, Zhongji Han, Ankur A. Dashputre, Praveen Kumar Potukuchi, Chi-Yang Chiu, Csaba P. Kovetsy, The University of Tennessee Health Science Center, Memphis, TN.

Background: Patients with ESRD display phenotypic features of premature biological aging, characterized by disproportionately high morbidity and mortality at a younger age. Nuclear factor erythroid 2-related factor 2 (Nrf2) activity, a master regulator of antioxidative responses, declines with age and is implicated in the pathogenesis of age-related disorders; however, little is known about the association between Nrf2 and premature biological aging in ESRD patients.

Methods: In a cross-sectional pilot cohort of 34 ESRD patients receiving maintenance hemodialysis, we measured the expression of Nrf2 and cyclin-dependent kinase inhibitor 2A (CDKN2A, or p16INK4a, a biomarker of biological aging) genes in whole blood and examined the association of Nrf2 with CDKN2A expression and with chronological age, using Spearman’s rank correlation and multivariable linear regression models with adjustment for chronological age, gender, race, and diabetes status.

Results: The mean (SD) age was 62.6 (9.8) years old; 52.9% of patients were male; 70.6% were African American; and 70.6% were diabetic. There was a significant negative correlation between Nrf2 and CDKN2A expression (rho=-0.51, P=0.002; Figure); while no significant correlation was found between Nrf2 expression and chronological age (rho≈-0.02, P≈0.91). While multivariable adjustment, Nrf2 expression was significantly and negatively associated with CDKN2A expression (β coefficient=-0.0151, P=0.01).

Conclusions: Lower Nrf2 expression levels were significantly and negatively associated with higher CDKN2A expression levels in whole blood of patients with ESRD, independent of chronological age. Our findings suggest a potential contribution of Nrf2 dysfunction to the development of premature biological aging and its related morbidities in ESRD patients.

PO1135

Do Dialysis Facilities Improve Quality After Receiving a Penalty Under the ESRD Quality Incentive Program

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Background: We examined whether quality measures improve at dialysis facilities penalized under the Centers for Medicare and Medicaid (CMS) End-Stage Renal Disease Quality Incentive Program (ESRD QIP) after receipt of a penalty.

Methods: Using data from CMS public use files from payment years (PY) 2014-2017, Medicare claims, and CROWNWeb, we used a difference-in-differences analysis to compare patient level measures of dialysis quality at facilities that did and did not receive penalties before and after the performance period. We also used a regression discontinuity design to compare patient quality measures two years after the performance period at facilities just above and just below ESRD QIP’s performance score penalty threshold.

Results: Patients at penalized facilities had improved dialysis adequacy after the performance periods associated with PY2014-2017 and improved vascular access after the performance period associated with PY2014, compared to patients at nonpenalized facilities. Changes in vascular access after the PY2015 – PY2017 performance periods were not statistically significant. In the 5 years after the performance period associated with PY2014, the percent of patient-months with a fistula use in the percent of patient-months meeting adult HD Kt/V standard (HD Kt/V ≥1.2) increased by 2.2 percentage points (95% CI 0.9 to 3.4) and 2.9 percentage points (95% CI 1.4 to 4.4), respectively, while the percent of patient-months with a catheter in use decreased by 2.6 percentage points (95% CI -3.7 to -1.5) at penalized facilities compared to nonpenalized facilities. Compared to those at nonpenalized facilities with relatively similar quality scores, patients at penalized facilities had lower catheter use two years after the PY2014 performance period and higher fistula use two years after the PY2016 performance period. However, these estimates are sensitive to specification changes. Other estimates were not statistically significant.

Conclusions: Receiving an ESRD QIP penalty is associated with subsequent improvements in some measures of dialysis quality, though results differ across payment years and analytic method.

Funding: Other U.S. Government Support

PO1136

Predicting Dialysis Facilities at Risk of Low ICH-CAHPS Quality of Center Scores

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Background: Medicare administers biannual ICH-CAHPS surveys to capture patients’ perceived experience of outpatient hemodialysis (HD) care. Recent operations efforts at a national dialysis provider aimed to develop prediction models to identify HD facilities at risk of low ICH-CAHPS rating in the subsequent survey period.

Methods: We used retrospective data from HD facilities at a national dialysis provider during 2018-2019. Two models were built to predict HD facilities that continued to have (Model 1) or decreased below (Model 2) a ≥60% top box ICH-CAHPS rating on the dialysis center staff, care, and operations subdomain in the spring 2019 survey period. Facility variables in 2018 included were: fall and spring ICH-CAHPS ratings; patient/employee net promoter (NPS) scores; employee retention rate; center quality Five Star rating; years of certification; facility size; composite clinical quality score; and % of HD non-adherence. Predictor variable importance was evaluated, and the performance of various modeling methods was assessed using several machine learning algorithms. We randomly selected derivation (70%) and validation (30%) datasets.

Results: We found the highest performance using GLM and GAM methods for both Models (Figure 1). The assessment of performance via the area under curve (AUC) showed use of GLM modeling correctly predicted true/false positives in 73% of facilities that continued to have (Model 1) and 70% of facilities that decreased below (Model 2) a ≥60% top box ICH-CAHPS rating.

Conclusions: The developed prediction models may be used as a tool in identifying HD facilities at risk of low patient ICH-CAHPS ratings. Prospective use in quality improvement efforts appears warranted.

Funding: Commercial Support - Fresenius Medical Care
PO1137

Variability and Trends over Time and Across Centers in Hemodialysis Weekly Duration in Australia and New Zealand

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Background: Hemodialysis treatment prescription varies widely around the world. This study explored patient- and center-level characteristics associated with weekly haemodialysis durations.

Methods: Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry data was analyzed. Characteristics associated with weekly duration were evaluated using mixed-effects linear regression models with patient- and center-level covariates as fixed effects, and dialysis center and state as random effects using the 2017 prevalent in-centre hemodialysis (ICHHD) and home hemodialysis (HHD) cohorts. Evaluation of patterns of weekly duration over time analyzed the 2000 to 2017 incident ICHHD and HHD cohorts.

Results: Overall, 12,494 ICHHD and 1,493 HHD prevalent patients in 2017 were included. Median weekly treatment duration was 13.5 (interquartile range (IQR) 12-15) hours for ICHHD and 16 (IQR 15-20) hours for HHD. Male sex, younger age, higher body mass index, arteriovenous fistula/graft use, Aboriginal and Torres Strait Islander ethnicity and longer dialysis vintage were associated with longer weekly duration for both ICHHD and HHD. No center characteristics were associated with weekly duration. Variability in duration across centers was very limited in ICHHD compared to HHD, with variation in and dialysis-facility level clinical quality measures and survival between dual-eligible and Medicare-only incident dialysis patients.

Conclusions: This study in the Australian and New Zealand hemodialysis population showed that weekly treatment duration was primarily associated with patient characteristics. No center effect was demonstrated. Practice patterns seemed to differ across states/countries, with more variability in HHD than in ICHHD.

Funding: Government Support - Non-U.S.

PO1138

Clinical Outcomes Among Dual-Eligible Medicare and Medicaid Dialysis Patients in the United States

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Background: Dual Medicare-Medicaid eligible beneficiaries generally live in poverty and account for approximately 28% of the US end-stage kidney disease (ESKD) population, yet their clinical outcomes are largely unknown. We compared individual- and dialysis-facility level clinical quality measures and survival between dual-eligible and Medicare-only incident dialysis patients.

Methods: In this retrospective cohort study using the United States Renal Data System, we identified 52,863 patients who had Medicare as the primary payer, initiated on dialysis from January 1, 2016 through December 31, 2016, and followed until June 1, 2018. We incorporated data from the Consolidated Renal Operations in a Web-Enabled Network (CROWNWeb) and the Centers for Medicare & Medicaid Services (CMS) Dialysis Facility Compare files. We excluded those who were <18 years, transplanted or died within 90 days of dialysis initiation. We conducted multivariable Cox regression with death as the outcome, adjusted for demographic and clinical factors.

Results: The Medicare-primary cohort consisted of 19,819 (37.5%) dual eligible and 33,044 (62.5%) Medicare-only beneficiaries, with median follow-up of 1.8 years. Dual eligibles were more likely to be female, Black, Hispanic and younger than their Medicare-only counterparts (59 ± 15 vs. 66 ± 14 years, p<0.001). At 12 months after dialysis initiation, individual-level quality measures such as hemodialysis treatment time, KT/V, hemoglobin, albumin, calcium, and phosphorus were similar between the 2 groups. However, a slightly greater proportion of dual eligibles were dialyzed via catheter at 12 months compared with Medicare-only patients (47.2% vs. 43.0%, p<0.001). At a facility level, mortality rates, hospitalization rates, standardized infection ratios for bloodstream infection, and total performance scores were similar between the 2 groups. Adjusted analyses demonstrated higher risk of death in dual eligibles compared to Medicare-only patients (hazard ratio 1.29 (95% CI 1.23-1.34, p<0.001).

Conclusions: The Medicare-Medicaid dual eligibility status, as an indicator of poverty, was independently associated with higher mortality, despite similar individual- and facility-level performance measures. Further studies to delineate factors associated with death in this large segment of the ESKD population are needed.

PO1139

The Implementation of a Clinical Pharmacist in a Hemodialysis Center

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Background: Hemodialysis (HD) patients have complicated disease states placing them at a higher risk for drug related problems (DRPs), medication discrepancies, and non-adherence. The objective of the study is to evaluate the impact of a clinical pharmacist in a HD center by assessing the efficacy of medication reconciliation (MR) in HD patients and evaluating the potential impact on the health system.

Methods: This is a retrospective study conducted in Greenfield Health Systems, a division of Henry Ford Health System that operates 14 dialysis centers throughout southeast Michigan. West Pavilion outpatient dialysis clinic, one of the centers in Detroit, Michigan consisting of an interprofessional team. Patients included in the study had at least four visits from the clinical pharmacist or pharmacy interns from August 2017 to October 2018. Study aim was to evaluate the impact of a clinical pharmacist in a HD center by assessing the efficacy of MR in HD patients and evaluating the potential impact on the health system. Descriptive statistics were used to collect DRPs and classified based on the modified Hepler-Strand approach.

Results: A total of 1403 DRPs with an average of 8.94 DRPs per patient were found with an average number of 7 visits per patient. Adherence was the most common DRP (31%). The most common drug class the pharmacist made interventions on was for medications used to treat blood pressure (37%) followed by vitamin D analogs/calcinimetics (29%). A projected total of $447,355 was saved.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
POI1140
Dietary Potassium Intake and All-Cause Mortality in Adults Undergoing Hemodialysis: The DIET-HD Cohort Study
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Background: Dietary modification to reduce the risk of hyperkalemia in people undergoing maintenance hemodialysis is standard practice and is commonly recommended in guidelines despite a lack of evidence. A low potassium diet may impair quality of life and nutritional status. We aimed to assess the association between dietary potassium intake and all-cause mortality and whether hyperkalemia mediates this association.

Methods: 9690 adults undergoing maintenance hemodialysis in Europe and South America were recruited in the DIET-HD study, of which 1647 were excluded for lack of data-linkage identifier or incomplete or implausible dietary assessment. We measured baseline potassium intake from the GA2LEN food frequency questionnaire and performed time-to-event and mediation analyses.

Results: The median dietary potassium intake at baseline was 3.5 g/day (IQR 2.5 to 5.0). During a median follow-up of 3.97 years (25,890 person-years), we observed 2921 (36%) deaths including 1316 (45%) from cardiovascular causes. After adjusting for baseline characteristics including presence of cardiac disease and food groups, dietary potassium intake was not associated with all-cause mortality (hazard ratio [HR] 1.00 95% confidence interval [CI] 0.95 to 1.05). A mediation analysis showed no association of potassium intake with mortality either through or independent of serum potassium (HR 0.999, 95% CI 0.996 to 1.002 and 1.000, 95% CI 0.999 to 1.002, respectively).

Higher dietary intake of potassium is not associated with hyperkalemia or death in patients treated with maintenance hemodialysis.

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POI1141
Serum-to-Dialysate Calcium Gradient and Its Association with Mortality in Incident Hemodialysis Patients
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Background: A high serum-to-dialysate calcium gradient at start of hemodialysis leads to rapid lowering of serum calcium and was associated with higher risk of witnessed cardiac arrests. However, the association of serum-to-dialysate calcium gradient with mortality remains unclear. The objective of this study was to evaluate the serum-to-dialysate calcium gradient associated with a greater risk of adverse events in incident hemodialysis patients.

Methods: We retrospectively examined 96,339 in-center hemodialysis patients who initiated dialysis treatment between January 1, 2007, and December 31, 2011 in a large United States dialysis organization. Cox proportional hazards model was used to assess the multivariable association between serum-to-dialysate calcium gradient and patient survival.

Results: Higher serum-to-dialysate calcium gradient was associated with older age, higher proportion of hypertension, lower blood pressure in post dialysis, and worse nutritional indices. Adjusting for patients differences, there was a dose-response relationship between higher serum-to-dialysate calcium gradient and greater risk of all-cause mortality [adjusted hazard ratios: 1.00 (95% confidence interval [CI]: 0.96 – 1.04), 1.02 (95% CI: 0.97 – 1.06), and 1.09 (95% CI: 1.05 – 1.15) for subjects in the second, third, and fourth quartiles (reference: first quartile group)]. Similar trends were observed for cardiovascular and sudden cardiac mortalities.

Conclusions: Higher serum-to-dialysate calcium gradient is independently associated with greater risk of all-cause, cardiovascular, and sudden cardiac mortalities in hemodialysis patients.

POI1142
Pharmacokinetics, Pharmacodynamics (PK-PD), and Exposure-Efficacy Evaluation from CalLIPSO, a Phase 2B Study to Assess the Effect of SNF472 on Progression of Cardiovascular Calcification in Patients on Hemodialysis
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Background: Cardiovascular calcification (CVC) is a major contributor to increased morbidity and mortality in end stage kidney disease (ESKD) patients on dialysis. SNF472, a selective calcification inhibitor that interferes in the formation and growth of ectopic hydroxypatite (HAP), has showed a significant reduction in CVC progression in CalLIPSO, a randomized, double-blind, placebo-controlled phase 2b trial. The drug is also currently in Phase 3 trial for the treatment of calciphylaxis. Our aim was to perform PK-PD and exposure-response analyses from the CalLIPSO trial

Methods: PK and PD were assessed at weeks 1, 10, 22 and 52, following intravenous administration thrice weekly over 52 weeks. Efficacy was assessed as % change in coronary artery calcification score by volume (CACv) over 52 weeks. The relationship between PK (Cmin) - PD (ex-vivo inhibition of HAP crystallization in plasma), PK- efficacy and PD-efficacy was evaluated using linear and Emax models.

Results: The analyses included data from 56 patients. Cmin values and PD responses per group were similar over the 52 weeks of treatment, indicating no accumulation of SNF472. Mean plasma Cmax mean PD effect and % change in CACvs over 52 weeks per group are shown in the table. An Emax model described well the relationship between PK-PD (Emax=-8.8%, Emax=-75.9%, EC50=-7.5 μM); and PK-efficacy (E50=-16.9%, Emax=-14.5%, EC50=-12.2 μM). The PD-efficacy relationship was better described by a linear model.

Conclusions: SNF472’s PK showed no accumulation and PD remained constant over 52 weeks of treatment. Emax models showed a robust relationship between SNF472’s Cmax and both the ex-vivo inhibition of HAP crystallization and clinical efficacy measured by % change in CACv over 52 weeks. Higher SNF472 exposure and inhibition of HAP crystallization correlated with a reduction in CVC progression in ESKD patients on dialysis.

Funding: Commercial Support - Sanifit Therapeutics

POI1143
Associations of Dialysis Facility Clinical Performance with Patient Outcomes in the Medicare ESRD Quality Incentive Program (QIP)
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Background: In CY2017, CMS implemented the Meaningful Measures Initiative, which aimed to reduce data reporting burden and costs for health care providers and to focus improvement efforts on the most meaningful outcomes for patients. To assure the ESRD QIP is aligned with this initiative and is achieving CMS goals, we assessed whether facility clinical measure performance is associated with improved patient outcomes.

Methods: Patient outcomes at the facility level were evaluated using the CY17 standardized mortality ratio (SMR) and standardized hospitalization ratio (SHR) from Dialysis Facility Compare, and the ESRD QIP CY17 In-Center Hemodialysis Consumer Assessments of Healthcare Providers and Systems (ICH-CAHPS) scores. Facility-level performance in CY17 on ESRD QIP measures for hypercalcemia, fistula, long-term catheter, comprehensive K/V, NHSN bloodstream infection (BSI) standardized infection ratio (SIR), and standardized transfusion ratio (STIR) was assessed using tertiles. Associations between facility measure performance and outcomes were tested using Poison models for SMR and SHR and Analysis of Variance (ANOVA) models for ICH-CAHPS scores.

CACv: Coronary artery calcification score by volume

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PO1144

**Types of Incidents (Patient Safety) Managed at Two Different Medical Levels in a Large Multinational Renal Services Provider Network**


**Background:** Patient safety programs need a well-structured organization to facilitate proactive and fair reporting, prompt evaluation analysis and timely feedback followed by measure implementation and auditing. **Objectives** To analyze all types of incidents in our network during 2019 by two different levels (Corporate and Country) of medical management alert.

**Methods:** Our institution has tracked all incidents under a structured process program for the last 10 years, according to 4 incident types (Patient related, Staff-visitors, Products and Equipment) and 54 subcodes. Incidents are considered as serious when they may be life-threatening or result in death, impaired body function/structure and/or are deemed serious based on appropriate medical judgment. Communication to Health Authorities applies in accordance with local country regulations. “Serious incidents” are immediately notified to the Corporate Office and to each Country Medical lead, whilst different codes may generate alerts into Corporate or Country.

**Results:** 92,923 incidents (2.7 incident/patient/year) were reported during 2019. Total incidents/1000 treatments were 17.2 (12.2 were patients related incidents). Causes for alerts at Corporate level (n=81) were cardiorespiratory arrest (26%); unexpected death (19%); re-conversion (9%); wrong disposable/dialyzer (9%); hemolysis (7%); severe hypertension (5%) and different mix codes (25%). Reported incidents at country level (n=831) were more than half ascribed to equipment [water supply, power failure and flooding (53%), medication errors (35%), venous needle dislodgment (20%) and staff-visitors injuries (4%)].

**Conclusions:** Tracking of incidents have potential to increase quality of care and patients outcomes. Despite continuous efforts to get better results, there is room for improvement on better staff compliance with our standard operating procedures especially regarding medications and venous needle dislodgment risk assessment.

PO1145

**Roxadustat in Treating Anemia in Dialysis Patients (ROAD): Short-Term Impact on Serum Iron Markers**

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**Background:** Diaverum has been shown effective in lowering serum cholesterol in treating patients with anemia due to chronic kidney disease. However, its effect on serum triglyceride (TG), especially in dialysis patients that have high prevalence of hypertriglyceridemia remains unknown. This analysis is to provide clinical data of Roxadustat on serum TG in a real-world prospective observational cohort.

**Methods:** This is a multicenter, prospective, longitudinal observational cohort study assessing if Roxadustat improves triglyceride in at least 250 dialysis patients with renal anemia. Primary outcomes will be major cardiovascular events. The current analysis was done in the enrolled 144 patients to compare the changes of iron markers from baseline to present.

**Results:** Till May 20, 2020. 144 dialysis participants (76 male, mean age 52±15 years) were enrolled from 11 sites of the study with a follow up of 8 (0–12) weeks. The primary disease of kidney failure was predominantly primary glomerulonephritis (67 cases, 46.5 %) and diabetes (28 cases, 19.4%). The serum TG at baseline and at the last follow up was 2.06±1.58 mmol/L (range from 0.14 to 12.04 mmol/L) and 1.90±1.09mmol/L respectively (p=0.162). In patients with TG greater than 1.7mmol/L, serum TG decreased significantly (n=53, 2.59±1.06 vs. 3.09±1.75 mmol/L, p=0.028) after Roxadustat treatment with -0.50mmol/L (95%CI: -0.05, 0.95mmol/L).

**Conclusions:** Hypertriglyceridemia is prevalent in ROAD cohort. Roxadustat could alter serum TG, especially lowering its level in dialysis anemia patients with hypertriglyceridemia which should be confirmed in future studies.

PO1146

**Roxadustat in Treating Anemia in Dialysis Patients (ROAD): Short-Term Impact on Serum Iron Markers**

Daqing Hong,† Guangyi Zheng,† Yang Zou,† Yanrong Cai,† Jingdong He,† Hen Xue,† Qiang He,† Guisen Li.† 1Department of Nephrology, Sichuan Academy of Medical Sciences & Sichuan Provincial People’s Hospital, Chengdu, China; 2Department of Nephrology, Sichuan Academy of Medical Sciences & Sichuan Provincial People’s Hospital, Chengdu, China; 3Gao Xin Boli Hospital, Chengdu, China; 4The Second Affiliated Hospital of Chengdu Medical College, Chengdu, China; 5Department of Nephrology, Ya’an People’s Hospital, Leshan, China.

**Background:** Diaverum has been shown effective in lowering serum cholesterol in treating patients with anemia due to chronic kidney disease. However, its effect on serum triglyceride (TG), especially in dialysis patients that have high prevalence of hypertriglyceridemia remains unknown. This analysis is to provide clinical data of Roxadustat on serum TG in a real-world prospective observational cohort.

**Methods:** This is a multicenter, prospective, longitudinal observational cohort study assessing if Roxadustat improves iron markers in at least 250 dialysis patients with renal anemia. Primary outcomes will be major cardiovascular events. The current analysis was done in the enrolled 144 patients to compare the changes of iron markers from baseline to present.

**Results:** Till May 20, 2020. 144 dialysis participants (76 male, mean age 52±15 years) were enrolled from 11 sites of the study with a follow up of 8 (0–12) weeks. Hemoglobin increased by 8.5G/L (95%CI:+6.1 to 10.8 G/L, p<0.001) significantly from baseline to last follow up. The serum ferritin at baseline and at the last follow up was 639.13±530.18 pg/ml and 473.52±520.34 pg/ml respectively (p<0.001). TSAT remained stable from baseline to last follow up (36.8%±20.5% vs. 36.7%±22.7%, p=0.93). In patients with ferritin greater than 400 pg/ml, serum ferritin were 245 pg/ml (95%CI: 117.62 to 373.46, p<0.001) and 362.01 pg/ml (95%CI: 99.34 to 580.30, p<0.008). In patients with low responsiveness to ESA, according to ESA dosage (greater than 300U/kg/Week, 199.41pg/ml, 95%CI: 37.69 to 316.12, p=0.019) or by investigators’ judgement (143.83pg/ml, 95%CI:55.99 to 231.67 pg/ml, p=0.002), the results were similar and significant. TSAT did not change significantly among the whole cohort and in the subgroup analysis.

**Conclusions:** Roxadustat could increase hemoglobin in dialysis patients in ROAD cohort. It could decrease serum ferritin in dialysis patients, regardless of the high ferritin or responsiveness of ESA treatment and maintains stable TSAT. These might indicate that Roxadustat partially increase hemoglobin by alter iron status even in patients have low responsiveness to ESA treatment.

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Hemodialysis and Frequent Dialysis - 3

PO1147

Relationship Between Fluid Overload (FO) and Hemoglobin Concentration (Hgb) in Hemodialysis (HD) Patients (Pts)

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Background: FO is common in HD pts and the BCM (Fresenius Medical Care, Germany) allows the assessment of fluid volumes and FO. We studied the association between FO and Hgb concentration in a cross-sectional study in four urban US dialysis clinics and tested the effects of inflammation and erythropoiesis-stimulating agents (ESA).

Methods: We conducted BCM measurements in participating HD pts, and obtained Hgb, neutrophil-to-lymphocyte ratio (NLR) and ESA usage from the EMR. The association between FO (stratified into tertiles) and Hgb and NLR, resp., was tested using ANOVA and that between FO and ESA usage using Chi-Square Test. We further employed linear regression, stratified by ESA usage (yes/no), to test associations of FO with Hgb and NLR.

Results: We studied 170 pts (40% female, 52.9% black, 28.2% Hispanic, 61.3±14.4 years, FO 2.2±2.4 L, Hgb 10.9±1.3 g/dL, NLR 3.5±1.9). Greater FO associated with higher NLR (Figure 1a) and lower Hgb (Figure 1b) and also with ESA use (P<0.001). Hgb inversely correlated with NLR (r=0.1, P=0.10) and FO (r=0.3, P<0.01). The association between Hgb and FO remained after adjustment for NLR (Beta -0.17, P<0.01). When the same association was tested separately for pts on ESA and those not on ESA, Hgb was inversely correlated with FO only in patients not on ESA (Beta -0.22, P<0.01), whereas its inverse relationship with NLR remained significant in both subgroups.

Conclusions: FO and inflammation inversely associates to Hgb and deserves consideration in anemia management. BIA can help the clinician assess whether FO may be contributing to low Hgb values. As such, it is a valuable diagnostic tool that should find its way into routine care for US HD pts.

PO1148

Automated Early Detection of Hyponatremia in Hemodialysis Patients Derived from Online Conductivity Measurement

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Background: Hyponatremia in dialysis patients is a strong indicator of poor outcome that requires early detection to facilitate clinical workup and management. However, plasma sodium concentration as determined by lab methods (Na-Lab) is measured at the best monthly in clinical practice. Recently, online monitoring of predialytic plasma Na (pPlNa) as estimated from dialysate conductivity using an electrolyte model has become available at every hemodialysis session, thus providing an unprecedented close and almost continuous monitoring of this crucial indicator. This could be used as diagnostic tool to earlier alert the physician of underlying clinical illnesses.

Methods: In a monocentric retrospective clinical study in 114 patients on maintenance hemodialysis (>90% online postdilution HDF) for whom online pPlNa was available for a period of at least 12 months at least once a week, kinetics of pPlNa were analyzed. For 11 patients with hyponatremic episodes as manifested in pPlNa, the agreement between time course of pPlNa and Na-Lab and the correlation to the manifestation of clinical findings was explored.

Results: Time course of pPlNa and Na-Lab showed very good agreement. In addition, in each case the onset of hyponatremia was linked to a subacute illness development (i.e., sepsis, congestive heart failure, …) undriven by various degrees of fluid overload. Correction of the underlying pathology and fluid overload by dry weight adjustment permitted to improve clinical outcome.

Conclusions: The clinical examples show that due to the good agreement of the time course of pPlNa and Na-Lab, pPlNa can be used as adjuvant diagnostic tool for the early detection of onset and progression of morbid events. This online tool will support physicians in decision making for improving dialysis patient management and likely outcome. Further studies are deserved to confirm the clinical value of this tool.

Funding: Commercial Support - Fresenius Medical Care Deutschland GmbH

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Figure 1a Ferritin changes from ROAD cohort.

A. patients with hyperresponsiveness to ESA

B. patients with baseline ferritin greater than 500 pg/ml.
Prevalence of Fluid Overload in a US Dialysis Population

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Background: Hypervolemia remains one of the main reasons for increased cardiovascular (CV) morbidity and mortality in chronic hemodialysis (HD) patients. Quantification of fluid status using bioimpedance spectroscopy (BIS) has become routine in many countries outside the United States (US). Due to previous unavailability of FDA-cleared BIS devices, no cross-sectional appraisal of fluid status in HD patients has yet been done in the US. The aim of this study was to perform the first assessment of fluid status in a US dialysis population using a BIS device.

Methods: Fluid overload (FO) was measured in 170 chronic HD patients from four clinics in New York City using the BCM Body Composition Monitor (Fresenius Medical Care) which provides the amount of excess extracellular water (ECW) in liters. Measurements were performed before dialysis; post-dialysis fluid status was estimated by subtracting the removed fluid from pre-dialysis FO.

Results: Pre- and post-dialysis FO were found to be 2.2L ± 2.4 L and -0.2 ± 2.7 L (mean ± SD), respectively. Before the start of HD, 42.9% of patients were fluid overloaded (criterion: FO/ECW > 15% in males, and >13% in females), 53.5% were normally hydrated, and 3.5% were fluid depleted (FO/ECW <7%).

Conclusions: The prevalence of pre-HD fluid overload was significantly higher in this US population (42.9%) than in a previously published large European cohort (29.6%). This suggests the need for more adequate assessment of fluid status to support the clinicians in identifying and treating fluid overload in HD patients.

Funding: Private Foundation Support

Assessment of Estimated Dry Weight in Dialysis Patients Undertaking Kidney Transplantation by Evaluating Post-Transplant Weight: The Kidney Knows Best

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Background: The consequences of volume overload include recurrent hospitalizations and increased mortality in dialysis patients. Dry weight (EDW) is estimated in dialysis patients to provide a target for ultrafiltration and to prevent the consequences of volume overload. New kidney transplant recipients with good allograft function provide a unique opportunity to evaluate the accuracy of EDW. With the assumption that a good functioning kidney allograft would return the patient to their optimal dry weight (ODW), we compared the differences between EDW and ODW in a cohort at our center.

Methods: We retrospectively reviewed 138 adult kidney transplant recipients at Baystate Medical Center between June 2015 and October 2019. Patients were excluded on the basis of not achieving a serum creatinine of ≤1.5 mg/dL at 2 weeks post-transplant. ODW was defined as the weight at 2 weeks in a patient with good allograft function. Patients with EDW in the range +3% and -1% of ODW were considered to be euvolemic pre-transplant. Patients with EDW below and above that range were considered hypovolemic and hypervolemic, respectively. 35 patients met criteria and were included in the analysis.

Results: The mean (SD) age was 54.3 (12.7) years with 52% male. 31.4% of patients had live donors. Based on pre-transplant EDW values, 23% were above (hypervolemia), 17% within, and 60% below (hypovolemia) the range of euvolemia (Figure 1).

Conclusions: We conclude that many dialysis patients (83%) may not be at their ODW. This illustrates the importance of finding novel tools to help achieve accurate dry weight patient undertaking dialysis in order to reduce hospitalizations and improve mortality.

The Use of Loop Diuretics in Newly Initiated Hemodialysis Patients: The Clinician’s Perspective

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Background: ESRD patients newly initiated on HD have varying levels of residual renal function (RRF). The loss of RRF is associated with increased cardiovascular and all-cause mortality and decreased quality of life (QOL). There are no studies reported to date that have explored in detail the physicians’ clinical opinion and approach to the use of diuretics after the initiation of HD.

Methods: A one-time anonymous electronic survey was created to explore the clinicians’ opinion and practice pattern of diuretic use in new-start HD patients. 50 nephrologists associated with the Mount Sinai Health System were included.

Results: 23 (46%) completed the survey and 8 (35%) have practiced nephrology for >15 years. 16 (70%) assess RRF monthly. The level of urine output per day (UOP/d) considered adequate for diuretic use was 200-250 mL by 7 (30%) and 400-500 mL by 12 (52%). While 20 (87%) and 18 (78%) of the physicians felt that diuretics are effective in HD patients and improve quality of life (QOL), respectively, only 5 (22%) always continue diuretics and 13 (57%) sometimes start diuretics after initiation of HD (Fig 1).

Physicians with >15 years in practice were more likely to continue diuretics than physicians with less experience (50% vs. 7%, P=0.03). Volume status (70%) and the ineffectiveness of diuretics (64%) were considered more important factors in the decision to use diuretics. Only 5 (26%) routinely use furosemide > 240 mg/day, but only 10 (43%) were influenced by ototoxicity.

Conclusions: While a majority of physicians believe that diuretics are effective and improve patient QOL, few consistently continued diuretics and only half started diuretics “sometimes”. The factors that were considered more important in decisions to continue or start diuretics were volume status and the opinion that diuretics can be ineffective in HD patients.

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PO1152

Novel Ultrafiltration Rate Feedback Controller for Attainment of Relative Blood Volume Targets During Hemodialysis

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Background: Preciado et al. have identified half-hourly relative blood volume (RBV) targets during a hemodialysis (HD) session that are associated with significantly improved patient survival. Attainment of these RBV targets would require incessant empiric adjustments to the ultrafiltration rate (UFR) by the dialysis nurse. We developed a novel proportional-integral-controller that takes RBV data from the commercially available CLiC® device as an input and provides UFR suggestions to guide the RBV curve into the desired targets. The clinician specifies the desired UF goal with the maximum allowed upward/downward deviation from this goal, and the UFR Feedback Controller then optimizes the RBV trajectory within the limits of the prescription. The present study aimed to characterize the behavior of this feedback controller.

Methods: We conducted a single-arm, prospective, interventionai pilot study in subjects on chronic HD at 3 dialysis centers in NYC. RBV was measured with the CLiC® device. CLiC® and HD machine data were fed into a research laptop running the UFR Feedback Controller software. The UFR recommendations (generated every 10 min) were evaluated by dialysis nurses who then either implemented or disregarded them as they deemed clinically appropriate.

Results: 15 subjects (58.9 ± 15.3 years, 53% black, weight gain 2.6 ± 0.8 L, HD time 22.2 ± 28 min) were studied (63 study visits, 4.2 ± 1.9 visits/subject). Of 300 analyzed RBV target points, 63% had RBVs within the desired target range, 33% of the RBVs were above and 4% were below target. Stratified by timepoint, the on-target percentage increased from 37% at 30 min to 73% at 3h into HD. The rate of intradialytic morbidity events did not appear to be increased. In subjects with at least 4 complete study visits (N=8), on average 71.8% of subjects were within the desired RBV target at 3h into HD.

Conclusions: The UFR Feedback Controller behaved as expected, steering the patients’ RBV curves toward the predefined target ranges while strictly observing the prescribed UF goal. Preciado et al. had reported a third of patients within the favorable RBV target range at 3h into conventional HD. In contrast, with the use of this novel UFR Feedback Controller, approx. 72% of subjects were within the desired RBV target range at 3h.

Funding: Private Foundation Support

PO1154

Peak Oxygen Capacity in Patients on Dialysis: The Role of Fluid Overload

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Background: Exercise capacity is predictive of cardiovascular disease and mortality in patients with chronic kidney disease on dialysis. Fluid overload, a common feature in these patients, may play a role in this pathophysiology.

Methods: The Duke Activity Status Index (DASI) questionnaires was administered to 27 patients on peritoneal dialysis (PD) and 82 patients on hemodialysis (HD). Results were expressed as peak oxygen uptake (VO2peak, ml/kg/min). Electrical bioimpedance was applied to assess body composition. Fluid overload was assessed as the ratio of extracellular water/total body water (ECW/TBW).

Results: The patients on HD and PD have no difference in age (44 ± 15 vs. 49 ± 18 years, p=0.224) and body mass index (25.0 ± 4.9 vs. 26.3 ± 4.9kg/m², p=0.245), with similar gender distribution (p=0.870), prevalence of diabetes (p=0.404) and smoking habit (p=0.223). VO2peak was lower among patients on PD than HD (21.4 ± 7.5 vs. 25.3 ± 7.6ml/kg/min, respectively, p=0.023). VO2peak correlated with ECW/TBW (r=0.436, p=0.0001) and age (r=-0.483, p=0.0001) in both groups and within each group. VO2peak correlated with intradialytic weight gain in patients on HD (r=-0.236, p=0.031).

Conclusions: Patients on dialysis present reduced exercise capacity, which is even more pronounced for patients on PD. Volume overload seems to be involved in this reduction and might be a target for interventional therapies.

PO1155

Simplifying the 28-Zone Lung Ultrasound Protocol

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Background: Lung ultrasound (LUS) using a 28-zone quantitative B-line score (BLS) is a reliable marker of fluid overload (FO) among patients with end-stage kidney disease (ESKD) on hemodialysis (HD), outperforming physical exam and correlating well with cardiovascular outcomes. A trial comparing BLS-guided dry weight probing to usual care showed improved blood pressure and echocardiographic parameters. However, 28-zone BLS study is criticized as impractical for clinical practice. Using a machine learning algorithm we determined whether accurate assessment of FO can be determined using just 4, 6, and 8 scanning zones.

Results: Sensitivities, specificities, and Youden’s indices (=sensitivity+specificity−1) for 1-15 treatments and across the different rates of positive RBV curves are shown. We found a sensitivity of 92%, specificity of 80%, and Youden’s index of 73% when >=50% of 10 preceding treatments were positive.

Conclusions: Our algorithm requires only a small number of RBV readings to identify presumably fluid overloaded patients with a clinically acceptable sensitivity and specificity. It would be of interest to compare the performance of this algorithm with volume status as determined by bioimpedance; however, bioimpedance has not yet been approved for use in HD patients in the U.S.
were performed on Endexo™ SMM and the dialyzer, based on ISO 10993 guidelines. We applied line discriminant analysis to study whether we could predict FO severity (low: BLS <15, moderate: BLS =15 to 23, high: BLS >23) based on existing 4, 6, and 8-zone scans. We tested whether we could achieve better diagnostic performance with subs of scan zones that had not previously been reported. Final outcome measures were reported as correlation coefficients and Cohen’s kappa.

Results: We found that the BLS of the 4, 6, and 8-zone scan correlated strongly and linearly with the BLS of the full 28-zone scan with Pearson correlations of 0.95, 0.92, and 0.92, respectively. In determining FO severity based on the limited scanning zones, the model predicted resultant Cohen’s Kappa values of 0.74, 0.76, and 0.71 for the 4, 6, and 8-zone scan respectively. We identified an underscored 4-zone scan that yielded a Kappa of 0.82. We found that equal linear weighting of all zones gave the best accuracy.

Conclusions: We found that 4, 6, and 8 zone BLS scores perform similarly to the 28-zone BLS. We identified a subset of 4 zones that gave better accuracy than existing 4, 6, or 8 zones scans. These findings support that a limited number of scanning zones can be used to reliably determine FO. Further work is needed on a larger dataset to validate these findings and to explore the physiological mechanism to support the novel 4-zone scan.

POI1156
Incidence and Outcomes of Gram-Negative Bacteraeas in Haemodialysis Patients: 12-Year Single-Centre Experience
Fatima Malik, Anna Naito, Lisa Bradwell, Christopher M. Cregg, David Makanjula. Epsom and Saint Helier University Hospitals NHS Trust, Carshalton, United Kingdom.

Background: Patients on haemodialysis (HD) are at increased risk of contracting infections. Gram-negative bacteraeas in HD patients is associated with early mortality. In our HD population, we looked at the incidence and clinical outcomes of gram-negative bacteraeas over 12 years.

Methods: Data were collected from clinical records and the hospital’s microbiology database of all confirmed bacteraeas in HD patients between 2007 and 2018.

Results: 283 episodes of gram-negative bacteraeas occurred in 1361 patients over the study period (166 (58.7%) were male. The median age was 71 years (range 26-95). The proportion of gram-negative bacteraeas fell significantly between 2007 and 2010 and has plateaued since then. 90 (31.8%) had arteriovenous fistulae (AVF) or grafts, the remainder had dialysis lines, of which 41 (21.2%) had dual access (AVF or graft + line), with AVF/graft not yet in use. The bacteraeas were deemed to be access related in 89 events (31.4%). Of these, 73 (82.0%) were related to dialysis lines, 16 (18.0%) were related to AVF/graft. 190 (67.1%) were from other sources including urinary tract 18.4% (n=52), hepatobiliary 7.8% (n=22), chest 7.8% (n=22), gastro-intestinal 6.0% (n=17) and skin/soft tissue in 4.9% (n=14). There was no information on 4 patients (1.5%). Complications of the bacteraeas included: discitis (6, 2.1%); osteomyelitis (5, 1.8%); endocarditis (2, 0.7%); septic arthritis (2, 0.7%); and death (34, 12.0%).

Conclusions: The incidence of gram-negative bacteraeas in our cohort appears to have plateaued, with bacteraeas originating from other sources such as the urinary tract and intra-abdominal accounting for a greater proportion of gram-negative bacteraeas in our cohort - a trend reflected in other similar observational studies in HD populations. Dialysis lines remain a significant risk factor for bacteraeas, lending further weight to the imperative of establishing early definitive vascular access. The increased incidence of pathogens from non-access related sources however, highlights that HD populations are exposed to both community and healthcare associated infections, and ongoing surveillance and strategies to reduce the burden of infections in this at-risk cohort remains imperative not just in dialysis centres, but also in the community.

POI1157
New Polymeric Dialysis Membrane with Endexo™ Surface Modifying Macromolecule
Chih-Hu He, Colleen M. Fisher, Claudiy Mullon. Fresenius Medical Care North America Ogden, Ogden, UT.

Background: Surface-modifying macromolecules (SMM) may improve the hemocompatibility of hemodialyzers. We report our center for a total of 2808 scored LUS clips. Using linear correlation and discriminant analysis, we fit models that allowed us to approximate the 28-zone BLS based on 4, 6, or 8 zone protocols. We next applied linear discriminant analysis to study whether we could predict FO severity (low: BLS <15, moderate: BLS =15 to 23, high: BLS >23) based on existing 4, 6, and 8-zone scans. We tested whether we could achieve better diagnostic performance with subs of scan zones that had not previously been reported. Final outcome measures were reported as correlation coefficients and Cohen’s kappa.

Results: We found that the BLS of the 4, 6, and 8-zone scan correlated strongly and linearly with the BLS of the full 28-zone scan with Pearson correlations of 0.95, 0.92, and 0.92, respectively. In determining FO severity based on the limited scanning zones, the model predicted resultant Cohen’s Kappa values of 0.74, 0.76, and 0.71 for the 4, 6, and 8-zone scan respectively. We identified an underscored 4-zone scan that yielded a Kappa of 0.82. We found that equal linear weighting of all zones gave the best accuracy.

Conclusions: We found that 4, 6, and 8 zone BLS scores perform similarly to the 28-zone BLS. We identified a subset of 4 zones that gave better accuracy than existing 4, 6, or 8 zones scans. These findings support that a limited number of scanning zones can be used to reliably determine FO. Further work is needed on a larger dataset to validate these findings and to explore the physiological mechanism to support the novel 4-zone scan.

POI1158
Prolactin Is a Biomarker for Inflammation in Outpatient Hemodialysis Patients
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Background: Prolactin is a widely used test to distinguish bacterial infections from viral infections, but its level is influenced by kidney function. The normal range of prolactin in end-stage renal disease (ESRD) patients on hemodialysis (HD) is not well established. In this study, we evaluated the relationship between Prolactin and inflammatory markers and outcomes in ESRD patients on HD.

Methods: We recruited 71 ESRD outpatients on HD from October 1st 2019 to December 15th 2019 and measured their prolactin levels prior to dialysis. We evaluated whether prolactin levels were associated with clinical characteristics, laboratory parameters, and future hospitalizations and infections.

Results: In this cohort, the median prolactin level was 0.38 ng/mL with an interquartile range of 0.23 ng/mL and 0.54 ng/mL. The distribution of prolactin values are found in Fig. 1A. African Americans had a significantly higher prolactin level than non-African Americans (P<0.02, Wilcoxon rank sum test). ESRD outpatients with hypertension, diabetes mellitus, or HIV did not have significantly higher prolactin levels than those who did not (P<0.05). Prolactin levels were positively correlated with CRP (r=0.57, P=0.001) (Fig. 1B) and negatively correlated with albumin (r=-0.28, P=0.02) (Fig. 1C). Prolactin levels were not correlated with Kt/V, white blood cell count, ferritin levels (P>0.05). ESRD outpatients who developed infections or who were hospitalized did not have significantly higher initial prolactin levels than those who did not (P=0.05).

Conclusions: Prolactin levels are correlated with inflammatory markers such as CRP and albumin, suggesting potential use to identify ESRD on HD at high risk for complications, especially in the era of COVID-19.

Funding: Private Foundation Support

POI1159
Prolactin and Inflammatory Cytokines in Hemodialysis Patients: A Cross-Sectional Study
Marcelio M. Dourado, Fabricio Souto, Amaury Cantilino, Lucio Vilar, Frederico C. Cavalcanti. Universidade Federal de Pernambuco, Recife, Brazil.

Background: Cardiovascular disease (CVD) is the main cause of mortality in patients with chronic kidney disease. Non-traditional CV risk factors such as hyperphosphatemia, inflammation and microalbuminuria are important in these patients. Among these, hyperprolactinemia emerges as a potential non-traditional risk factor because it
accumulates with loss of renal function and is associated with increased mortality. Initially described as a lactation hormone, today it is known that prolactin (PRL) has several actions, from pro-inflammatory effects to accelerated atherosclerosis. The aim of our study was to correlate serum levels of inflammatory cytokines in hemodialysis (HD) patients with normal and elevated PRL.

Methods: Single-center cross-sectional study evaluating all patients regularly enrolled in HD program in September 2019. Patients over the age of 18, on HD for at least 6 months, using an arteriovenous fistula for dialysis access were included. Those with active viral or bacterial infections, active cancer, inadequate Kt/V, use of medication or disease known to elevate PRL (hyperthyroidism, chronic liver disease, macroaomena), pregnant women and using immunosuppressants were excluded. Clinical, biochemicals and inflammatory cytokines [interleukin (IL)-2,-4,-6,-10,-17A, TNF-α and gamma interferon] were evaluated and compared between HD patients with elevated and normal PRL.

Results: Of the 360 regular HD patients, 249 were excluded: 110 temporary access, 87 active infection (viral or bacterial), 23 on drugs, 12 on immunosuppression, 5 cirrhosis, 4 inadequate Kt/V, 4 cancer, 3 less than 6 months on HD, 1 macroaomena. Comparing data between patients with high(61) and normal(50) PRL, no statistical difference was seen in terms of age, BMI, etiology, time on HD, cholesterol, albumin, calcium, phosphorus, PTH, glycated hemoglobin, IL-2, IL-4, IL-17A, TNF-α, and GFN. There was a positive PRL correlation with serum levels of IL-6(p<0.0001,R=0.44); between PRL and IL-10, the correlation was negative and also statistically significant(R=-0.046,R=-0.2).

Conclusions: HD patients with elevated PRL have been shown to have higher levels of IL-6 and lower levels of IL-10.

Funding: Commercial Support - Siemens Healthcare Diagnostica Ltda, Private Foundation Support

Laboratory parameters of patients with high and normal Prolactin

<table>
<thead>
<tr>
<th>Variable</th>
<th>Elevated Prolactin</th>
<th>Normal Prolactin</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Interleukins-2</td>
<td>5.85±0.79 [2.22-5.44]</td>
<td>3.32±0.96 [2.08-4.68]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interleukins-10</td>
<td>14.15±5.40 [12.66]</td>
<td>27.8±18.61 [6.13-43]</td>
<td>0.001</td>
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POI166

Biphasic Dynamics of Inflammatory Biomarkers Following Dialysis Initiation: Results from the MONDO Initiative

Xiaoling Ye,1 Dalia E. Youssi,2 Len A. Usyvat,2 Stefano Stuard,3 Adrian M. Guinsburg,4 Jeroen Guinsburg,4, Jeroen van der Sande,5 Peter Kotanko,5 1Renal Research Institute, New York, NY; 2Fresenius Medical Care AG und Co KGaA, Waltham, MA; 3Department of Medicine, Faculty of Medicine, Tampere, Finland; 4Department of Internal Medicine, University Medical Center, Utrecht, Netherlands; 5Department of Internal Medicine, University Medical Center, Maastricht, Netherlands.

Background: Inflammation is highly prevalent among patients (pts) with end stage kidney disease and is associated with adverse outcomes. We aimed to investigate in a large diverse international cohort of incident hemodialysis (HD) pts firstly the dynamics of inflammatory markers, namely white blood cells (WBC), neutrophil-to-lymphocyte ratio (NLR), serum albumin (lab) and C-reactive protein (CRP), following initiation of HD. Secondly their predictive power over all-cause of death.

Methods: We included all incident in-center adult HD pts treated 01/2000 to 12/2012 with a 1 neutrophils, lymphocytes, WBC, and CRP values within the study periods. Following HD initiation, pts were stratified into 7 subgroups: 6 semi-annual groups according to the dialysis vintage at the time of the pts’ death (0 to 6; 7 to 12; 13 to 18; 19 to 24; 25 to 30; 31 to 36 months) and a survivor group (pts who survived ≥37 months). Cubic smoothing spline functions were applied to study the trends of each marker. Receiver Operating Characteristic Curve (ROC) Analyses were performed to evaluate the predictive power of each of the markers with 1st year as the baseline and the following 1 year as the follow-up.

Results: In total, 18,276 incident pts who were treated in 25 countries were included. WBC, NLR (Figure 1), and CRP declined sharply after HD initiation and increased before death, while started & remained low in the survivors. In general, WBC, NLR, and CRP were highest at HD initiation and prior to death in non-survivors. Alb levels increased after HD initiation and remained high in the survivor cohort. In contrast, lab levels dropped significantly before death. Alb (AUC: 0.66), CRP (AUC: 0.64), and NLR (AUC: 0.62) all show stronger predictive power than WBC (AUC: 0.55) (Figure 2).

Conclusions: In non-survivors, NLR, WBC, and CRP showed a similar trend after HD initiation and before death. As CRP is not a routinely used marker in many regions of the world and NLR has not comparable predictive power, this marker could be used as an alternative indicator of inflammation in resource-limited areas.

POI167

The Accumulation of Various Uremic Retention Solutes Is Associated with Early Mortality After Starting Hemodialysis

Yohji Ara1,2,3 Shingo Shioji,3 Hiroyuki Tanaka,3 Haruka Noguchi,2 Mira Chinen,2 Suzuki Mikako,2 Isao Kondo,2 Emi Sakamoto,2 Takahito Niikura,2 Minami Suzuki,2 Daisuke Katagiri,2 Fumihiko Hiroshita,1 1Department of Nephrology, Graduate School of Medicine, Tokyo Medical and Dental University, Bunkyo-ku, Japan; 2Department of Nephrology, National Center for Global Health and Medicine, Shinjuku-ku, Japan; 3Department of Nephrology, Yokosuka Koyoai Hospital, Yokosuka, Japan.

Background: Uremic retention solutes (URS) generally accumulate in patients with end-stage renal disease (ESRD). Many of these URS have been shown to exert unfavorable biological activity resulting in poor prognosis. Although some kinds of URS before starting hemodialysis (HD) has been proven to be a risk factor for early mortality after starting HD, it remains unknown whether excess accumulation of various URS is associated with further worse prognosis after starting HD according to the degree.

Methods: We conducted a retrospective cohort study to investigate the association between the accumulation of various URS and early mortality after starting HD. The cohort consisted of adult patients who started HD for ESRD at the National Center for Global Health and Medicine from 2010 to 2019. To evaluate the accumulation of various URS, the uremic score was specifically defined as a total number of measurable variables related with uremia in clinical practice; blood urea nitrogen (BUN) >100 mg/dl, change in anion gap corrected for albumin (AANCGA) >5 mmol/l and [2-microglobulin (Z2MG) >20 mg/l before starting HD. The primary outcome was death within a year of the start of HD. The hazard ratio for one score increase in the uremic score was calculated using Cox proportional hazard models with adjustments for baseline characteristics. Moreover, we investigated underlying characteristics related with these variables using logistic regression.

Results: We enrolled 206 patients (males, 76%). During a mean follow-up of 344 days, the primary outcome was observed in 16 patients. The uremic score was significantly associated with the primary outcome (hazard ratio: 1.97, 95% confidence interval 1.19-3.27; adjusted hazard ratio: 4.82, 95% confidence interval 1.97-11.7). Patients with high

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
BUN had a lower frequency of cardiovascular disease. High AAG and B2MG were associated with hypobulinemia respectively. Moreover, patients with high AAG were relatively young and had a lower frequency of diabetes.

**Conclusions:** The accumulation of various URS is associated with early mortality after starting HD.

**PO1163**

**Routinely Measured Cardiac Troponin I and NT-ProBNP as Predictors of Mortality in Japanese Hemodialysis Patients: The Dialysis Outcomes and Practice Patterns Study**

Marcelo Lopes,1 Masahiro Eriguchi,2 Kazuhiko Tsuruya,2 Brian Bieber,4 Roberto Pecots-Filho,1 Ronald L. Pisoni,1 Keith McCullough,1 Bruce M. Robinson,1 Eiihiro Kanda,3 Kunishio Iseki,4 Hideki Hirakata,1 1Arbor Research Collaborative for Health, Ann Arbor, MI; 2Nara Daigaku, Nara, Japan; 3Kawasaki Ika Daigaku, Kurashiki, Japan; 4Nakamura Naika Inn, Kumamoto, Japan; 5Fukuoka Renal Clinic, Fukuoka, Japan.

**Background:** Due to the interplay of chronic kidney disease and the heart, it is common for myocardial damage and strain to be present in hemodialysis (HD) patients. The cardiac troponin I (cTnI) and NT-proBNP are widely used as cardiac biomarkers to evaluate the patients at high risk for cardiovascular disease (CVD). However international The Dialysis Outcomes and Practice Patterns Study (DOPPS) data indicate that these cardiac biomarkers are measured in fewer than 2% of HD patients in real-world practice.

**Methods:** Pre-dialysis levels of cTnI and NT-proBNP at study enrollment were measured in 1176 prevalent Japanese HD patients (DOPPS phase 5). Cox regression was used to test the association of the cardiac biomarkers with all-cause mortality, adjusting for potential confounders. Subgroup analyses were performed to assess potential effect modification of clinical characteristics: age, systolic blood pressure, HD vintage, diabetes mellitus, CVD, and heart failure.

**Results:** Median [IQR] cTnI (99th percentile; 0.04 ng/mL) and NT-proBNP levels were 0.018 [0.005, 0.04] ng/mL and 3442 [1580, 8017] pg/mL, respectively. There were 175 deaths during a median [IQR] follow-up of 2.8 [2.3, 2.9] years. Higher levels of both cardiac biomarkers were incrementally associated with mortality after adjustment for potential confounders. Subgroup analyses were performed to assess potential effect modification of clinical characteristics: age, systolic blood pressure, HD vintage, diabetes mellitus, CVD, and heart failure.

**Conclusions:** Routinely measured NT-proBNP and cTnI are strongly associated with mortality among prevalent Japanese HD patients. These associations were still significant even after adjustment for the alternative biomarker, suggesting that cTnI and NT-proBNP may reflect different pathologic aspects for cardiac abnormalities.

**PO1164**

**Efficacy of Double Filtration Plasmapheresis Therapy on Patients with Lipoprotein Glomerulopathy**

Wening Fan, Yongchun Ge, Jianhua Dong. Nanjing General Hospital of Nanjing Military Command Research Institute of Nephrology, Nanjing, China.

**Background:** To Retrospectively observe the clinical efficacy of double filtration plasmapheresis(DFFP) in patients with lipoprotein glomerulopathy(LPG).

**Methods:** 17 Patients with biopsy-proven LPG in our center who received DFFP treatment from 2010 to 2016 were involved, clinical parameters before and after DFFP treatment were recorded and analyzed.

**Results:** 15 of the patients underwent 3-10 courses of DFFP, and 2 patients were unable to tolerate DFFP due to allergic reactions. All patients received fenofoate or statins and other relevant symptomatic treatments. After short-term DFFP treatments, serum creatinineScr, 1.76±0.87mg/dl vs 1.55±0.83mg/dl,P=0.01), plasma apolipoprotein E(7.94±1.87mg/dl vs 3.58±1.32mg/dl,P=0.01)and proteinuria (4.68±2.50g/24h vs 2.70±2.20g/24h,P<0.001),were relieved significantly. 1 patient (6.7%) achieved complete remission of proteinuria, and 5 patients (33.3%) achieved partial remission of proteinuria. Four patients underwent repeated renal biopsy after DFFP treatment, and 2 of them received 10 courses of DFFP were observed disappearance of intraglomerular lipid accumulation, and negative ApoE staining. While 2 patients who underwent only 3 and 4 courses of DFFP respectively showed no significant pathological improvement. After a median follow-up of 7 months(SCR 31.51), all patients had elevated ApoE level, 4 patients showed an elevation trend of Scr. 3 of the 4 patients who had got partially or completely remission of proteinuria after DFFP tend to be stable after 12 months follow-up.

**Conclusions:** Short-term efficacy of DFFP in patients with LPG was definite. However, Scr and ApoE levels rebounded in some patients during long-term follow-up.

**PO1165**

**Disease Course of Hyperkalemia in Patients on Hemodialysis**

Bruce S. Spinowitz,1 Steven Fishbane,2 Masafumi Fukagawa,3 Martin L. Ford,4 Nicolas J. Guzman,5 Anjay Rastogi,6 1New York Presbyterian Queens, Queens, NY; 2Zucker School of Medicine at Hofstra/Northwell, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY; 3Tokai University School of Medicine, Isehara, Japan; 4King’s College Hospital NHS Trust, London, United Kingdom; 5AstraZeneca BioPharmaceuticals Research and Development, Gaithersburg, MD; 6David Geffen School of Medicine, Los Angeles, CA.

**Background:** Hyperkalemia (HK) preceding hemodialysis (HD) is associated with increased risk of mortality and hospitalization. Longitudinal data on serum potassium (sK+) in this population is sparse. This post-hoc analysis of data from the placebo (PBO) arm of DIALIZE (NCT03303521) explored the course of HK in HD pts.

**Methods:** In DIALIZE, 196 pts were randomized 1:1 to PBO (n=99) or sodium zirconium cyclosilicate (SZC) (n=97) 5 starting dose once daily on non-dialysis days for 8 weeks (8w), comprising a 4-week SZC dose-titration phase (max 15 g) to achieve target pre-dialysis sK+: 4.0-5.0 mmol/L, and a 4-week stable-dose evaluation phase. All pts received HD TIW and dietary counselling. Post-hoc analysis of PBO pts by baseline (BL) pre-dialysis sK+ included mean pre- and post-dialysis sK+ by visit, and proportions of pts who had mean pre-dialysis sK+ of 4.0-5.0 and 4.0-5.5 mmol/L by visit (including pts receiving rescue therapy).

**Results:** Mean pre-dialysis sK+ after the long interdialytic interval was 5.9 mmol/L at BL (Day 1) and 5.7 mmol/L at end of treatment (EOT; Day 57) (Figure). Across all BL pt strata, mean pre-dialysis sK+ remained 5.0 mmol/L for all study visits (Figure). For pts with BL pre-dialysis sK+ <5.5, 5.5-6.0, 6.0-6.5, and 6.5 mmol/L, mean pre-dialysis sK+ at EOT was 5.4, 5.9, 5.6, and 5.9 mmol/L, respectively (Figure). Over 8w, only 7.0- 23.1% and 31.1-60.6% of PBO pts had a pre-dialysis sK+ of 4.0-5.0 and 4.0-5.5 mmol/L, respectively, at any study visit. Mean post-dialysis sK+ was 3.9 mmol/L at BL and at EOT.

**Conclusions:** In pts receiving PBO and counselling following a HK event, mean sK+ remains high over 8w. Most pts remain hyperkalemic over this period and are therefore at continued risk of adverse outcomes.

**Funding:** Commercial Support - AstraZeneca
Hemodialysis and Frequent Dialysis - 3

PO1167
Feasibility Study of Wrist-Based Wearable Activity Trackers in Hemodialysis Patients

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Background: Wearable activity trackers allow physicians to access patient's physical activity (PA) outside the dialysis clinic. Hemodialysis (HD) population have an increased cardiovascular mortality and they are less active than their healthy counterparts. We aim to assess the feasibility of use of a wearable trackers in a HD population.

Methods: HD patients from 4 NYC clinics were enrolled in the study starting from June 2018, followed up to 1 year. Patients ≥18 years on maintenance HD, able to walk, owning a smartphone, tablet or PC were included. Each patient received a wrist-based monitoring device (Fitbit Charge 2) to wear for a year. They were trained how to use and sync data. A stepwise intervention was created. After 3 in-person visits are completed, patients were deemed non-adherent and withdrawn. Events such as device failure or broken band were counted as an in-person visit. We used Kaplan-Meier analysis to study time to withdrawal for non-adherence and predictors of time to withdrawal were assessed by univariate Cox Regression. The end of the observation period was May 8, 2020.

Results: 118 patients were studied. Patients were 54±12 years old with a HD vintage of 5.2±5.1 years, 37% lived alone, 59% unemployed, 57% were African American, and 42% had an education level of some college or higher. Seventeen patients were withdrawn due to non-adherence. Mean and median time to withdrawal were 280 days (95%CI 260-301) and 359 days (95%CI 324-365). The probability of retention is shown in Fig.1. There was no association found between age, gender, race, living status, and education and time to withdraw due to non-adherence.

Conclusions: Only a small number of patients were withdrawn due to non-adherence, and the average time to withdraw was 9 months. We believe that the use of a wrist-based wearable device for remote patient monitoring, at least up to one year, is feasible in the HD population.

Funding: Private Foundation Support

PO1168
Evaluation of Biomarkers in Chronic Hemodialysis (HD) Patients Dialyzed with Optiflux High-Flux Dialyzers

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Background: Optiflux® (OPTI) dialyzers are single-use, high-flux dialyzers available in the following sizes: F160NR (1.5 m²), F180NR (1.7 m²), F200NR (1.9 m²), and F250NR (2.5 m²). They are designed to enhance small and middle molecule clearance without increasing albumin loss. Epidemiologic data has shown low serum albumin (sALB) to be a marker of increased mortality risk in dialysis patients (pts). Thus, loss of albumin should be avoided especially in pts with low sALB. This retrospective study aimed to assess changes in biomarkers in pts dialyzed with Optiflux dialyzers for 6 months, including a subset of pts with low sALB levels at baseline.

Methods: 976 in-center HD pts treated exclusively with Optiflux dialyzers for 6 months without liver disease, cancer, HIV, or history of drug abuse were analyzed in this study. Pre-HD labs at the first month of data collection (M1) and Month 6 (M6) were compared using paired t-test. A sub-analysis of pts with hypoalbuminemia (sALB ≤3.5mg/dL) at M1 was conducted. All analyses were performed separately for each dialyzer. Pts dialyzed with F200NR and F250NR were combined into 1 group.

Results: Mean biomarker levels during M1 and M6 are presented for the dialyzer groups (table). Most notably, significant increases in mean sALB and hemoglobin were observed in all groups. In the sub-analysis of pts with hypoalbuminemia at M1 (n=156), 87% of pts had increases in sALB by M6 (48/59=81.4% in F160NR, 82/92=89.1% in F180NR, and 5/5=100% in F200NR and F250NR) and 53.8% (84/156) achieved sALB ≥3.5 g/dL at M6.

Conclusions: During a 6-month follow-up, HD patients dialyzed with Optiflux dialyzers showed increases in serum albumin and hemoglobin while maintaining dialysis adequacy.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO1169
Postoperative Outcomes After Bariatric Surgery in Chronic Dialysis Patients: A Meta-Analysis and Systematic Review

Dharmenaan Pamlathu5inagam,1 Carmel Hawley,2 Elaine Pascoe,3 David W. Johnson,2 Magid Fahim,2 Logan Hospital, Loganholme, QLD, Australia; 3Princess Alexandra Hospital, Woolloongabba, QLD, Australia; 1The University of Queensland Faculty of Medicine, Herston, QLD, Australia.

Background: Renal transplantation improves longevity and quality of life for patients on chronic dialysis. However, obesity is a growing surgical contraindication in this group such that bariatric surgery is increasingly being considered as a bridge to transplantation. The risks and benefits of bariatric surgery in the dialysis population have not been synthesized.

Methods: Authors performed a systematic review of observational studies indexed in Embase, MEDLINE and CENTRAL till April 2020 that reported postoperative outcomes in chronic dialysis and non-dialysis patients undergoing bariatric surgery. Summary level data on patient demographics and comorbidity were extracted. The primary outcome was death (30-day or in-hospital mortality), secondary outcomes were myocardial infarction, surgical site infection, pneumonia, unplanned return to theatre, sepsis, and rates of kidney transplantation. Random effects meta-analysis was performed to derive summary risk estimates.

Results: Four cohort studies involving 4,096 chronic dialysis and 732,204 non-dialysis patients undergoing bariatric surgery were included. Sleeve gastrectomy (34%), and roux-en-Y gastric bypass (24%) were the most common procedures performed followed by gastric band or biliopancreatic diversion. There were increased odds of postoperative mortality (0.4%-0.5% vs 0.1%, OR 4.7, 95%CI 2.2-9.9, P=0.00), myocardial infarction (0.5%-0.5% vs 0.1%, OR 3.4, 95%CI 2.1-5.0, P=0.00), and pneumonia (0.3%-0.9% vs 0.2-0.4%, OR 2.3, 95%CI 1.1-4.5, P=0.00) in dialysis patients compared to non-dialysis patients. Patients on dialysis also had increased odds of return to theatre compared to non-dialysis patients (3.2-3.4% vs 1.4-2.0%, OR 2.2, 95%CI 1.7-3.0). There were no differences in the odds of surgical site infections, bleeding, or thromboembolic complications. Rates of renal transplant wait-listing among dialysis patients undergoing bariatric surgery were not reported in any of the studies.

Conclusions: Chronic dialysis patients have substantially increased odds of postoperative mortality and myocardial infarction. However, the absolute rates of complications are low and may not be prohibitive if they facilitate successful renal transplantation. Systematic reporting of both the benefits and risks of bariatric surgery in dialysis patients is needed.

Funding: Private Foundation Support

PO1170
Peridialytic Serum Cytokine Levels and Their Relationship with Postdialysis Fatigue and Recovery in Patients on Chronic Hemodialysis

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Background: The etiology of postdialysis fatigue (PDF), an intermittent but debilitating fatigue occurring in 40-80% of chronic hemodialysis (HD) patients after HD treatment, is still unclear. In other illnesses, such as inflammatory diseases, mounting

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evidence points toward the involvement of the immune system in the development of fatigue symptoms. Altered serum levels of inflammatory cytokines have also been shown in chronic HD patients and positive associations between interleukin-6 (IL-6) and fatigue symptoms in general in this patient population have been recently reported. Therefore, we investigated whether fatigue specifically occurring after HD (PDF) or the time needed to recover from HD treatment (TIRD) were related to pro- and anti-inflammatory cytokines (i.e., IL-1β, IL-6, TNF-α and IL-10) or their intradialytic changes (if any).

Methods: Serum levels of IL-1β, IL-6, TNF-α and IL-10 were measured immediately before and after HD in 45 chronic HD patients using commercially available kits on an ELLA™ automated immunoassay system. The presence and severity of PDF as well as TIRD duration were assessed by self-report measures.

Results: Thirty-three patients (74%) reported PDF, with a median PDF severity index of 3.30 [IQR: 3.00-4.30] on a scale from 1 to 5. Median TIRD was 120 min [IQR: 60-480]. PDF severity correlated strongly with TIRD, r = 0.85, p < 0.001. Only predialysis IL-10 serum levels significantly and positively correlated with PDF severity (r = 0.43, p = 0.003). Postdialysis cytokine levels and their intradialytic changes were not significantly related to PDF.

Conclusions: The present study does not support the hypothesis that the immune system may be involved in the development of PDF or TIRD. The positive, but countervailing relation between predialysis anti-inflammatory IL-10 levels and PDF severity warrants further research. However, the present findings do not necessarily undermine the previously found positive relationship between IL-6 levels and chronically fatigued experience in HD patients, as fatigue as response to treatment may have other determinants than a more chronically fatigued.

POI171
Tryptophan Removal in ESRD Patients Treated with High-Flux and Medium Cut-Off Dialyzers During Hemodialysis and Hemofiltration
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Background: Tryptophan (Trp) loss in kidney failure patients is likely to be associated with poor nutritional status and depletion due to dialysis. However, Trp removal with medium cutoff (MCO) membranes has not been investigated. Here, we compared Trp reduction ratios (RR) between an MCO dialyzer and a high-flux polysulfone (HFPS) dialyzer.

Methods: Clinically stable, anuric hemodialysis patients on thrice-weekly HD were enrolled. Over the course of 4 weeks, each subject traversed through the following combinations with 2 study treatments per week, 4 hours per HD session: post-dilutional hemofiltration (HiFlux) with FX120 (Fresenius Medical Care), HD with FX120, HDF with Theranava 400 (Baxter), HD with Theranava 400 (Fig.1). All subjects exercised using stationary bicycles during HD. Blood samples were collected before dialysis (B0) and at 230 min (B230) upstream of the dialyzer. Trp in plasma was analyzed by liquid chromatography–mass spectrometry. RR was calculated using signal intensities for Trp according to RB=-(B0-B230)/B0, with correction for hemoconcentration using hemoglobin levels (Schneidtiz, ASAIO 2012).

Results: Twelve subjects completed the study (30% female, 43.8±18.5 years old). With HD, RR was comparable between the MCO dialyzer and the larger HFPS dialyzer (median RR 0.29 for MCO, 0.33 for HFPS; surface areas 1.7 m² vs. 2.5 m², respectively). In HDF, our data suggest somewhat greater Trp loss with the MCO dialyzer despite its lower surface area (1.7 m² vs. 2.5 m²). There was no difference in EPO, phosphate, and urea RR between any of the four groups.

Conclusions: Adding a medium cut-off (MCO) dialyzer to HDF does not add benefit. The ESRD RR with HFHiex exceeds the one of a MCO dialyzer. HDF provides benefit over HD between the BZM RR regardless of the dialyzer used.

Funding: Commercial Support - Fresenius

POI173
pH-Dependent Protein Binding Properties of Uremic Toxins In Vitro
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Background: Patients with chronic kidney disease undergoing dialysis treatment have worse clinical outcomes. One cause is the interactions between various uremic toxins and organ/tissues. Protein-bound uremic toxins (PBUTs), such as indoxyl sulfate (IS) and p-cresyl sulfate (PCS), are difficult to remove by conventional dialysis treatment owing to their high protein binding property. A possible treatment strategy is to weaken the protein binding property of PBUTs. Acidic and alkaline pH change the conformation of proteins, which may be associated with the binding of uremic toxins. We examined the influence of pH on the protein binding properties of PBUTs in vitro.

Methods: Albumin concentration at pH 2 to 13 was analyzed using circular dichroism. Albumin reacted with IS at pH 4 to 11. The protein binding behavior was examined using isothermal titration calorimetry and free IS concentration was measured by mass spectrometry. Bovine serum with IS, PCS, indole acetic acid (IAA), or phenyl sulfate (PhS), as well as serum from hemodialysis patients, were adjusted to a pH of 4 to 11, and the concentration of the free IS was measured.

Results: Albumin partially unfolded at pH <4 or >12. Calorimetric analyses revealed weakened interaction between IS and albumin at pH <4 or >10. The concentration of free IS in the presence of albumin was significantly increased at pH 4 (99.4±1.38 μg/dL) and pH 11 (22.4±1.38 μg/dL) compared to pH 7 (17.2±0.87 μg/dL) (both p<0.01). Addition of bovine serum to IS, PCS, IAA, or PhS at the physiological concentration of uremic patients and adjustment of pH from 4 to 11 resulted in increased concentrations of the free form of the solutes at acidic and alkaline pH, compared with the concentrations at neutral pH. Adjustment of serum from 19 hemodialysis patients from pH 4 to 11 resulted in increased concentrations of the free forms of IS, PCS, PhS, and IAA at acidic and alkaline pH. (e.g., IS: pH 4, 152.5±77.6 μg/dL; pH 11, 153.8±135.5 μg/dL vs pH 8, 38.8±33.4 μg/dL; p<0.01, respectively).

Conclusions: Acidic and alkaline pH changed albumin conformation and weakened protein binding property of PBUTs in vitro. The findings could inform strategies to increase the removal of PBUTs with convection/diffusion in hemodialysis treatment.
PO1174

Associations Between Prelude eGFR Category and Trajectories of Uric Acid and eGFR Prior to Dialysis Transition Among US Veterans
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Background: Prior studies have demonstrated that elevated uric acid is associated with declining kidney function. However, how uric acid and estimated glomerular filtration rate (eGFR) levels change with progression toward end stage renal disease have not yet been fully characterized. We sought to examine trajectories of eGFR and uric acid 1 year prior to ESRD transition across strata of eGFR 5 quarters prior to transition.

Methods: From a cohort of US veterans who transitioned to dialysis between 10/2007-03/2015, we identified 15,725 patients with a pre-dialysis eGFR measurement 5 quarters prelude (15 months) before transitioning to ESRD and at least 1 uric acid measurement prior to ESRD. Trajectories were modeled across eGFR strata using mixed effects models with random slope and random intercept.

Results: The mean age of the cohort was 67±11 years old and included 2% females and 35% African American. In addition, the mean prelude quarter 5 uric acid level was 8±2 mg/dL and the median eGFR was 21±1.73m2. While the trajectories of uric acid were relatively stable for most strata, eGFR steadily declined across all strata. However, in the final 3 months prior to ESRD transition (PQ2 to PQ1), those in the highest PQ5 eGFR category (≥45 ml/min/1.73m2) had a sharp decrease in eGFR and corresponding sharp increase in uric acid, while there were notable trends for other strata. (Figure)

Conclusions: Patients with the most rapid renal function decline also had a sharp increase in uric acid 3 months prior to transition to ESRD. The mechanism behind this relationship is currently unknown, and should be investigated in future studies. Future studies should also examine the clinical implications of elevated uric acid in patients transitioning to dialysis earlier due to a rapid renal function decline.

PO1175

Insulin Resistance and Hemodialysis
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Background: Insulin resistance is an important risk factor in Chronic Kidney disease (CKD) patients. We analysed insulin resistance indices in hemodialysis (HD).

Methods: Subjects with CKD not on dialysis (CKD), and on HD (HD) were included. Age, gender, Body mass index (BMI), Waist-Hip ratio (WHR) were noted. Fasting blood glucose, fasting insulin (Ins), C-peptide (Cp), bicarbonate (HCO3), calcium (Ca), phosphorus (Pi), Vitamin D (Vit D), parathyroid hormone (PTH), Albumin (Alb), Ferritin, C-reactive protein (CRP) were measured. HOMA-insulin resistance using Ins (IR-Ins) and Cp (IR-Cp), Insulin sensitivity and Beta cell function using Ins (IS-Ins, BS-Ins) and Cp (IS-Cp, BS-Cp) and C-peptide resistance index (CRI) were calculated.

Results: 20 patients with CKD, 22 on HD were analysed. In HD, IR-Cp had significant positive correlation with eGFR, and CRI with HCO3, Vit D, Ca, Pi, IR-Cp and negatively with PTH, CRP,eGFR. In CKD, IR-Cp had significant positive correlation with PTH,eGFR and negatively with HCO3,Ca. CRI had significant positive correlation with HCO3, Vit D, Ca, Pi, negatively with PTH, IR-Cp. Between groups, IR-Ins, IR-Cp, IS-Ins, IS-Cp and BS-Ins had significant difference (Table 1).

Conclusions: IR-Ins, BS-Ins, IS-Cp, CRI were higher in HD, while IR-Cp,IS-Ins were higher in CKD. Cp based indices could be better markers of IR.

PO1176

Effect of Citrasate Dialysate on Intact Parathyroid Hormone (iPTH) in Prevalent Hemodialysis (HD) Patients: A Matched Retrospective Cohort Study
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Background: Citrate-acidified dialysate (CAD) has anti-coagulation properties compared to acetate-acidified dialysate (AAD), due to its binding of calcium. PTH regulates the calcium concentration through its actions on bone and kidney. The objective of this study is to assess any long-term changes in iPTH levels when patients (pts) are switched from AAD to CAD.

Methods: A retrospective cohort study of 3 clinics converting from AAD to CAD during 2009 to 2011 matched to 12 geographically proximate AAD clinics, on the same month as CAD conversion. Clinics were selected before year of 2013, so that the follow-up did not include time when the management of mineral bone disease changed at large dialysis organizations (LDOs). In-center HD pts included in the analysis received HD treatment for at least 6 months before (baseline, BL) and 6 months after (follow up, FU) CAD conversion. BL and 6-month FU average values of clinical measures were compared within and between CAD and AAD clinics. Measures included pre-dialysis iPTH and serum calcium (sCa), prescribed (Rx) dialysate calcium (dCa). Rx calcium-based phosphate binders (Ca-based PB), Cinacalcet and IV Vitamin D (iVitD).

Results: Changes in iPTH and sCa were not significantly different from BL to FU between CAD and AAD clinics (Table). Mean iPTH decreased by 17 pg/mL (4.1%, p<0.05) in CAD clinics and increased by 13 pg/mL (3.8%, p=0.13) in AAD clinics. However, Rx dCa increased in CAD clinics, but not in AAD clinics. Increases of Ca-based PB and Cinacalcet prescriptions were greater in AAD clinics. No significant differences were observed in changes of iVitD over time between CAD and AAD clinics.

Conclusions: Similar trends in iPTH and sCa were observed in clinics switched from AAD to CAD and geographically-matched clinics with continuous use of AAD.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

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Comparison between groups

* p<0.05 from paired t or McNemar’s test
+2 sample t test and repeated measures logistic regression for continuous and categorical variables
PO1177

High-Volume Hemodiafiltration Reduces Pre-Dialysis Beta-2 Microglobulin Concentration Compared with High-Flux Hemodialysis: A Post Hoc Analysis of the HDFit Trial

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Background: High-volume hemodiafiltration (HDF) is a diffusive-convective modality that provides higher clearance of middle-size uremic toxins, such as beta-2 microglobulin (β2M), compared to predominantly diffusive high-flux hemodialysis (HD). Previous studies have shown HDF may reduce circulating pre-dialysis concentrations of β2M compared to low-flux HD. We studied to what extent HDF reduces pre-dialysis β2M concentrations compared to high-flux HD.

Methods: HDFit randomized patients with a permanent vascular access time on HD between 3 and 24 months to either high flux HD or high volume HDF (convective volume (CV) target of 22L/session) treatment. Patients were followed for 6 months. Measurements of circulating pre-dialysis β2M levels were made at baseline, 3 and 6 months during mid-week session. Linear mixed effects models were used to test a change in β2M levels over time.

Results: A total of 195 patients (mean age 53±15 years, albumin 4±0.4 g/dL) were randomized (HDF n=97, HD n=98). Patient characteristics were balanced across intervention groups. Median treatment time was 235 min in both groups. Monthly mean CV ranged from 27.1 to 27.5L/treatment; the target CV was achieved in 96 out of 97 intervention groups. Median treatment time was 235 min in both groups. Monthly mean β2M levels between HDF and HD.

Conclusions: In this post-hoc analysis of the HDFit trial, we describe for the first time that high-volume HDF sustainably reduces pre-dialysis β2M concentration compared to high-flux HD. High convective volume was easily achieved with online HDF. Our findings suggest that HDF can be readily implemented and that this treatment modality yields a sustained higher control of middle-size uremic toxins.

Funding: Commercial Support - Fresenius Medical Care

PO1178

Hand Grip and Leg Muscle Strength in Hemodialysis Patients and Its Determinants


Background: Chronic kidney disease is associated with chronic inflammation and progressive loss of peripheral muscle strength and the ability to exercise, and these changes are more pronounced in people on hemodialysis (HD). We evaluated the hand grip and leg muscle strength in patients receiving HD and tried to find factors associated with muscle strength.

Methods: We screened hand grip (opposite to fistula side) and leg muscle strength (both sides) at single center (n=112) by using digital hand and leg dynamometer (T.K.K.5401 and 5710e/5715, Takei scientific instruments Co. Ltd., Niigata, Japan).

Results: Mean age was 62.6 years, and 73.2% of patients were men. Diabetes was the cause of kidney failure in 50% of patients and median HD vintage was 34 months. 77.7% of patients answered ‘yes’ to regular home exercise and 33% of patients regularly participated in the hospital based latex-band exercise. Hand grip strength (HGS) and leg muscle strength (LMS) showed good correlation (r = 0.715, p < 0.001). HGS (25.3 vs. 17.0 kg) and LMS (30.1 vs. 20.4 kg) were in men (p < 0.001 and p < 0.001, respectively). Older patients (≥ 60 years) showed decreased LMS than others in men and women (p = 0.01 and p = 0.04, respectively), but HGS was not different by age. Patients doing regular exercise or hospital based exercise showed higher HGS (24.2 vs. 18.6 kg, p = 0.01) but LMS did not show statistical significance (29.3 vs. 23.6 kg, p = 0.19). Serum albumin and creatinine showed positive correlation with HGS and LMS, and hs-CRP was negatively correlated only with HGS. Multiple linear regression analysis proved male sex, younger age, and any type of exercise were factors associated with better HGS and LMS.

Conclusions: Sex, age, and exercise were the most important determinants of muscle strength in HD patients. We need to encourage patients to do regular exercise and introduce new feasible form of exercise for HD patients.

Funding: Private Foundation Support

Table 3. Multiple linear regression analysis of the factors related with hand grip and leg muscle strength

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient (β)</th>
<th>p-value</th>
<th>Coefficient (β)</th>
<th>p-value</th>
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</thead>
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<td>HGS</td>
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<td>0.70</td>
<td>-0.005</td>
<td>0.70</td>
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<tr>
<td>HSP</td>
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<td>0.41</td>
<td>0.125</td>
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<tr>
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<td>0.104</td>
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</tr>
<tr>
<td>Serum creatinin</td>
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<td>0.015</td>
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</tbody>
</table>

BMI, body mass index; hs-CRP, highly sensitive C-reactive protein.

PO1179

Effect of Intradialytic Exercise on the Removal of Tissue Sodium During Hemodialysis

Hsin-Yu Fang, Luis M. Perez, Ryan J. Larsen, Alexis King, Brett Burrows, Kenneth R. Wilund. University of Illinois at Urbana-Champaign, Urbana, IL.

Background: Emerging evidence using 23Na-MRI shows that sodium can be stored in the skin and muscle. Hemodialysis (HD) patients appear to have higher tissue sodium concentration (Na*) compared to healthy controls, though tissue [Na+] appears to be partially reduced during HD. In this study, we thus aimed to determine whether intra-dialytic cycling (IDC) potentiates the removal of tissue [Na+] during HD.

Methods: Seven HD patients (sex: 57% male; age: 60±6.4 y; BMI: 36±4 kg/m2; spKt/V: 1.4±0.32; dialyse [Na*]: 136±1.90 mEq/L; UFR: 7.7±3.4 mL/kg/hr; thrice-weekly HD) underwent 23Na-MRI scans (3T system) before and after HD, on both a control (CON) and exercise (EX) day. Patients performed 30 minutes of IDC during the first hour of HD on the EX day and received standard care on the CON day. [Na*] of the medial (MG) and lateral (LG) gastrocnemius, soleus (SO), tibialis anterior (TA), and the whole lower leg (WL) were quantified from MRI images by trend analysis. Plasma [Na+] was also assessed by an colorimetric enzymatic assay (Piccolo). Repeated measures ANOVA was used to examine changes in muscle and plasma [Na*] between the EX and CON treatments from pre to post HD.

Results: There was a significant treatment by time interaction for [Na*] in WL (P=0.036) and SO (P=0.16), with the EX treatment attenuating the drop in [Na*] during HD compared to the CON condition in both WL and SO (Figure1A-B). [Na*] of MG (P=0.02), LG (P=0.001),TA (P=0.001), and plasma ([Na*]) were reduced during HD, but these changes did not differ by treatment (treatment x time interaction P = N.S. for all; Figure1C-F).

Conclusions: Contrary to our hypothesis, it appears that IDC may attenuate, instead of potentiate, the magnitude of tissue [Na+] removed during HD. However, this was not a consistent finding across all muscle beds analyzed. More studies are needed to examine if this result is a manifestation of the timing of MRI, the limited sample size, or other factors.

Funding: Private Foundation Support

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Underline represents presenting author.
Exercise Training to Improve Patient-Important Outcomes in Adults Undergoing Maintenance Dialysis: A Systematic Review and Meta-Analysis of Randomised Controlled Trials

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Background: Multiple trials have assessed the potential for exercise training to improve outcomes in adults undergoing dialysis. However, uncertainties exist in its relevance and sustainable benefits for patient-important outcomes.

Methods: We conducted a systematic search of the Cochrane Kidney and Transplant Specialised Register for randomised controlled trials of structured exercise programs of eight weeks or more in adults undergoing maintenance dialysis (hemodialysis or peritoneal dialysis) compared to no exercise or sham exercise. Two authors independently assessed the trials for eligibility, extracted the data and assessed the risk of bias. We conducted random-effects meta-analyses.

Results: We identified 93 studies involving 4634 participants and 71 studies involving 3973 participants contributed to the meta-analyses. The interventions lasted from 8 weeks to 2 years and most often took place thrice weekly during hemodialysis treatments. Overall, the quality of the included studies was low. In adults undergoing dialysis, compared with no or sham exercise, exercise training may improve fatigue, the physical component of health-related quality of life (HR-QoL;MD 0.45, 95% CI 2.2 to 6.8 points/100: low certainty evidence), depressive symptoms (SMD 0.73, 95% CI 0.39 to 1.07: moderate certainty evidence), pain (MD 6.1 95% CI 0.5 to 11.7 points on a 100-point scale: low certainty evidence), functional capacity measured in terms of the 6 Minutes-Walk Test (MD 49.9 meters, 95% CI 37.2 to 62.6; moderate certainty evidence) and the Sit-To-Stand test (MD 2.4 cycles, 95% CI 1.8 to 3.1; moderate certainty evidence). The impact on depression was greatest for those who had maintained exercise beyond 4 months (SMD 1.26, 95% CI 0.72 to 1.80). We could not determine the impact of exercise training for all-cause mortality, cardiovascular events, the mental component of HR-QoL, blood pressure and the safety of exercise training for adults undergoing maintenance dialysis due to the very low quality of the evidence.

Conclusions: In adults undergoing maintenance dialysis, exercise training is likely to improve depressive symptoms and functional capacity and may improve fatigue, the physical component of quality of life and pain.

Funding: Government Support - Non-U.S.

Comparative Risk of Fall-Related Fractures Among Hemodialysis Patients Newely Initiating Zolpidem vs. Trazodone Therapy

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Background: Zolpidem, a non-benzodiazepine hypnotic, and trazodone, a sedating antidepressant, are the most common medications used to treat insomnia in the United States. Both drugs have side effects (e.g. drowsiness, dizziness, cognitive and motor impairment) that increase the risk of falls and fall-related fracture events. Despite widespread zolpidem and trazodone use, little is known about the comparative safety of these medications in hemodialysis patients, a vulnerable population with an exceedingly high fracture rate.

Methods: We conducted a retrospective cohort study using an active comparator new-user design to investigate the association between zolpidem vs. trazodone initiation and the 30-day risk of hospitalized fall-related fractures among Medicare-enrolled hemodialysis patients in the United States Renal Data System Registry (2013 - 2016). We used an intention-to-treat analytic approach and propensity score weighted survival models, adjusted for numerous demographic and clinical covariates, to estimate hazard ratios (HRs) and their 95% confidence intervals (CIs). Death was treated as a competing event.

Results: A total of 31,055 hemodialysis patients were included in the study, 18,941 zolpidem initiators (61%) and 12,114 trazodone initiators (39%). Newly initiating zolpidem vs. trazodone therapy was associated with a higher risk of hospitalized fall-related fractures, HR [95% CI] = 1.71 [1.11, 2.63]. The association was more pronounced among individuals previously exposed to higher zolpidem doses (1.92 [1.14, 3.21]) and in subgroups with fall-related risk factors, such as older and frailter patients (1.89 [1.14, 3.09]) and 2.49 [1.31, 4.73], respectively) and individuals using other medications with central nervous system activity (2.04 [1.14, 3.37]). Sensitivity analyses using longer follow-up durations, evaluating a broader definition of hospitalized fracture), and employing an on-treatment analytic approach yielded similar results (data not shown).

Conclusions: Hemodialysis patients newly initiating zolpidem had a higher risk of hospitalized fall-related fracture compared to patients initiating trazodone, suggesting that trazodone may be a safer pharmacologic treatment option for the management of insomnia in this vulnerable population.

Funding: NIDDK Support, Other NIH Support - NHLBI

Relationship of Peripheral Nerve Function with Mobility in ESKD

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Background: Mobility limitation is widely prevalent in patients undergoing dialysis and is associated with frailty, disability, hospitalizations and mortality. Motor and sensory nerve impairments are reported in ESKD but their relationship with mobility is poorly studied. We tested the hypothesis that objective measures of nerve function in the lower extremity are associated with mobility limitation.

Methods: Twenty-five subjects with ESKD underwent nerve testing after their routine dialysis session. Nerve testing was done using the Natus Viking Quest NSC system and vibration detection threshold (VDT) was measures with a Medoc VSA-3000 analyzer. Predictors were nerve action potentials (amplitude) and nerve conduction velocity (NCV) in motor (peroneal) and sensory (sural) nerves as well as VDT quantitatively measured at the pulp of the big toe. Gait speed (mobility outcome) was measured over 4 meters and the better of 2 attempts used. Leg extensor strength, a covariate was measured by a dynamometer. Patient symptoms were assessed using the Neuropathic Pain Questionnaire.

Results: Subjects were 23-74 yr, 14 male, 23 black, 14 diabetic, median dialysis vintage 4.5 yrs. Median gait speed was 0.70 m/s (IQR 0.61-0.86). Neuropathic pain was noted in ~57% patients, but did not correlate with objective measures of nerve function or gait speed. Median vibration detection threshold was 51u (IQR 26-104) and showed significant negative correlation with gait speed (p < 0.01). Higher sensory (sural) nerve onset and peak latency and lower sensory conduction velocity were correlated with lower gait speed (all p < 0.01). Higher peroneal motor nerve amplitude was positively correlated with gait speed (p < 0.05). Higher VDT remained significantly associated with gait speed in multivariable regression model adjusted for demographics, diabetes, dialysis vintage and muscle strength (model R²=0.74).

Conclusions: In patients with ESKD, objective measures of nerve function are associated with mobility dysfunction regardless of diabetes, muscle strength and dialysis vintage. In contrast, subjective assessment of neuropathy is not associated with mobility dysfunction. These results demonstrate that the neuropathy of ESKD is a contributing factor to the widespread impairment in mobility observed in patients undergoing dialysis and that additional testing is required for diagnosis.

Funding: Private Foundation Support

Native Hawaiian/Pacific Islander Data in the USRDS

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Background: The United States Renal Data System (USRDS) has reported very high ESRD incidence and prevalence rates among patients designated as Native Hawaiian or Other Pacific Islander (NHP/I) race. Xiang et al. (2019 NKF Spring Clinical Meeting) reported a “denominator problem,” caused by a large percentage of NHP/I individuals reporting multiple races in the US census. By counting only single-race individuals, resulting dominators are too small, leading to rates that appear to be too large. We sought to assess whether reporting of race is accurate for these individuals by examining reported country of origin on the CMS 2728 Medical Evidence (ME) form.

Methods: Using data from the ME form for patients initiating dialysis in 2016, we examined the accuracy of the country/area of origin field, which is required to be filled out only when NHPI race is chosen. We assumed all those reporting the US as the country of origin were correct.

Results: The figure displays country/area of origin or ancestry for the 1578 patients who reported NHPI race, for the top 25 countries, which accounts for 90.8% of all NHPI patients. Only 38.7% of them came from countries that are actually part of the census definition of NHPI. The largest misclassified countries were Philippines (19.2%) and Mexico (2.5%).

Conclusions: The apparently high rates of ESRD among NHPI individuals have gained increasing attention. Our finding of inaccurate understanding of the US census definition of NHPI leading to numerators of rates that are too large, combined with the already important problem of the US census single vs. multiple race denominator, makes it difficult and perhaps even impossible to calculate accurate incidence and prevalence rates for this race group. Improvements in capturing accurate race information at the time of ESRD initiation are needed.

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PO1184

Workforce Capacity for ESKD Care: An Analysis from the Global Kidney Health Atlas Study

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Background: Despite the rising burden of chronic kidney disease, recent surveys reveal a global shortage of nephrologists and other kidney healthcare professionals. The objective of the second iteration of the International Society of Nephrology’s (ISN) Global Kidney Health Atlas was to assess inter- and intra-national variability in the capacity for end-stage kidney disease (ESKD) care.

Methods: Data were collected in two steps: desk research and a cross-sectional survey. Desk research used data from online sources, such as the Central Intelligence Agency World Factbook and the World Health Organization Global Observatory. The survey was administered online to key stakeholders worldwide, and all country-level data were analyzed by ISN region and World Bank income classification.

Results: The results of desk research showed that the general healthcare workforce density varied by income level: high-income countries had more healthcare workers per 10,000 population (30.30 physicians; 79.21 nursing personnel; 7.20 pharmacists; 3.47 surgeons) than low-income countries (0.85 physicians; 5.02 nursing personnel; 0.10 pharmacists; 0.03 surgeons). A total of 182 countries responded to the survey, with 160 (88%) countries responding to questions pertaining to the ESKD workforce. Nephrologists were primarily responsible for providing care to ESKD patients in 92% of countries. Global nephrologist density was 9.95 per million population (ppm) and nephrology trainee density was 1.42 ppm. High-income countries reported the highest densities of nephrologists and nephrology trainees (23.15 ppm and 3.83 ppm, respectively), whereas low-income countries reported the lowest densities (0.24 ppm and 0.11 ppm, respectively). Compared to higher income countries, more low-income countries reported shortages of all types of ESKD healthcare providers, including nephrologists, transplant surgeons, peritoneal dialysis providers, and peritoneal dialysis access surgeons, and peritoneal dialysis access interventional radiologists.

Conclusions: In this global survey, a significant trend was demonstrated in workforce capacity and distribution for ESKD care across countries. There was limited capacity in low income compared to high income countries. National and international policies are required to build a workforce that can effectively address the growing burden of ESKD.

PO1185

Patient Activation in Prevalent Hemodialysis Patients in the United States

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Background: Patient activation (PA) is the product of knowledge, skills and confidence that enable a person to manage their health and care. PA is associated with healthy behaviors, disease management and hospitalization rates. This study aimed to investigate the status and correlates of PA among prevalent HD patients in the US.

Methods: We surveyed patients from 10 HD centers using the Patient Activation Measure (PAM-13), which reports a score out of 100 and is categorized into four levels (higher scores or levels denoting higher activation). We described the distribution of PA status, and investigated associations with demographics, vintage, education level and HD center.

Results: 925 respondents completed the survey out of 1374 patients (response rate 67%). Mean age 62 ± 14 years, 40% female, and median vintage 41 months (IQR 19-77). Mean PAM score was 56 ± 13, and 14%, 50%, 25%, and 10% were in levels 1 to 4 respectively. Mean PAM scores were higher in younger patients (<55yrs: 59 ± 14, 55 to <65yrs: 55 ± 14, 65 to <75yrs: 55 ± 14, ≥75 yrs: 54 ± 12; p<0.001). Higher PAM scores were observed with higher education (College: 60 ± 14, High School: 57 ± 14, <High School: 51 ± 10; p<0.001) and in blacks (58 ± 15) compared to non-blacks (55 ± 13; p=0.008). Mean PAM scores varied significantly across centers ranging between 52 and 61 (p=0.004). In regression analysis, there were lower odds of having high activation (levels 3 or 4 vs levels 1 or 2) in association with age (for every 10 years: aOR 0.79 [95% CI: 0.71 – 0.87]) and male sex (0.72 [0.53 – 0.96]). Compared to having less than high school diploma, high school diploma and college were associated with high activation (2.36 [1.60 – 3.47], and 3.52 [2.25 – 5.54] respectively). HD center differences remained significant after adjustment. However, vintage, race, and ethnicity did not have a significant association with activation in the adjusted model.

Conclusions: Patient activation is low in a high proportion of HD patients. Older age, less education and male gender were associated with lower activation. This study is the first to report activation status among individuals on HD in the US, identifying an opportunity to direct resources to high-risk groups and develop programs to improve activation.

PO1186

Analysis of Psychological Detachment of Primary Caregivers of Maintenance Hemodialysis Patients

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Background: Long term care for maintenance hemodialysis patients will bring physical, mental and economic burden to the caregivers. If the caregivers cannot detach during non working hours, it will affect their physical and mental health. The goal was to Analysis the psychological detachment level of primary caregivers of maintenance hemodialysis patients and its influencing factors.

Methods: By convenient sampling method, 240 caregivers of maintenance hemodialysis patients in our hospital from June to September 2019 were selected and investigated by using Psychological Detachment Scale, Zarat Burden Inventory Scale, and Warwick-Edinburgh Mental Well-being Scale.

Results: The total score of psychological detachment of caregivers in maintenance hemodialysis patients was 9.8 ± 3.4, which was negatively correlated with the burden of caregivers (P < 0.01), and positively correlated with the total score of Warwick Edinburgh positive mental health(P<0.01) and psychological detachment level was high at 53.2% and low at 46.8%. The main influencing factors of caregiver’s psychological detachment were time of care, type of character, burden of care, positive mental health, duration of dialysis and types of complications(P<0.01).

Conclusions: Medical staff should pay attention to the psychological status of caregivers and take positive measures to improve the level of psychological detachment and promote their physical and mental health.

PO1187

Factors Contributing to Primary Care Provider (PCP) Use in ESKD Patients After Starting Hemodialysis (HD)

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Background: While the importance of primary care is well-recognized, PCP use among HD patients has not been well-characterized and factors contributing to PCP use are unknown.

Methods: We characterized change in PCP use (aPC visit) 1 year before and 1 year after dialysis start among adults a67 years old with Medicare coverage initiating in-center HD between 2008-2014 (data from the United States Renal Data System). We used multivariable logistic models adjusting for demographics, clinical characteristics, and pre-ESKD nephrology care to identify factors associated with continuity of PCP care (defined as PCP use pre- and post-HD start) and new initiation of PCP care post-HD start.

Results: Among 111,424 older HD patients, 34% did not use PCP care post-HD start. Among patients with PCP use pre-ESKD, 85% did not continue to use PCP care post-HD start. Among patients without PCP use pre-ESKD, 70% did not initiate PCP care post-HD start. Black race, Medicare insurance, impaired functional status, and residence in less urban or higher poverty neighborhoods were associated with lower odds of continuity of PCP care or initiating PCP care after HD start. (Table)

Conclusions: Among older incident HD patients, continuity of PCP care and initiation of PCP care were lower among patients who were black, of lower socioeconomic status, key ages, with lower income, and living in higher poverty neighborhoods.
Factors Associated with Continuity of PCP Care and Initiation of PCP Care after Starting HD

PO1189

Fully Immersive Virtual Reality-Based Mindfulness Intervention in Hemodialysis Patients: A Pilot Study Assessing Safety and Utility

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Background: Virtual reality (VR) is an evolving technology that is becoming a more common treatment for pain management and psychological phobias. While non-immersive VR (i.e., Nintendo Wii) has been used in trials involving hemodialysis (HD) patients, no studies to date have used fully immersive VR as a tool for intervention delivery. Because HD treatment and fully immersive VR have similar potential adverse side effects (e.g., fatigue, nausea), the current pilot trial tests the initial safety and utility of fully immersive VR during maintenance HD treatment sessions.

Methods: HD patients (n=20) were enrolled in a single-arm pre-post pilot study. Participants were exposed to our fully immersive VR program, Joviality™, which delivered mindfulness training and guided meditation using the Oculus Rift head-mounted display. Participants experienced our 25-minute program on two separate occasions during HD treatment sessions. Participants recorded their level of HD treatment and/or motion-related symptoms prior to VR exposure and then again immediately following each VR exposure using the Simulator Sickness Questionnaire (SSQ). Validated utility measures included participant’s ability to be fully immersed in the virtual environment, interact with virtual objects, and find our VR program user-friendly.

Results: Mean age was 55.3 (±13.1) years; 80% male; 60% African American; and mean dialysis vintage was 3.56 (±3.75) years. The SSQ displayed significant decreases in total composite symptom score following VR Exposure 1 (22.6 vs. 11.2; p=0.03). Decreases were evident after Exposure 2, though these were non-significant (11.97 vs. 7.29; p=0.18). Participants reported high levels of spatial presence in the VR world with mean scores of 5.03/7.0 and high ratings of our VR program as easy to operate, with average System Usability Scores of 82/100.

Conclusions: HD patients routinely suffer from fatigue, nausea, and dizziness during HD, and we hypothesized that fully immersive VR may exacerbate these symptoms. By contrast, we saw a significant reduction in severity of symptoms on at least one of the two exposure days. Fully immersive VR may be a safe mode of intervention delivery during HD.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

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Mariachi Madness: A Unique Presentation of Acyclovir Toxicity
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Introduction: Acyclovir and valacyclovir (pro-drug) are often prescribed for treatment of infections caused by herpes viruses. Neurological toxicity consisting of hallucinations, seizures, and coma are rare reported side effects occurring predominantly in renal failure as a result of the renal clearance of the drug.

Case Description: A 71-year-old woman with end stage renal disease from amyloidosis on maintenance hemodialysis presented with recent onset of confusion, slurred speech, weakness, and intractable auditory hallucinations described as “Mariachi music.” She had been recently treated for herpes keratitis four days prior to presentation. On exam she was noted to be inattentive with disorganized thought-processes, diffuse hyporeflexia, generalized myoclonus, and up-beating nystagmus with superior gaze. A medication reconciliation revealed that she had been prescribed valacyclovir at a dose of 1,000 mg three times daily. She had additionally continued previously-prescribed prophylactic acyclovir at a dose of 200 mg twice daily. Urgent hemodialysis was performed for presumed acyclovir toxicity. An acyclovir level drawn 2 hours after initiation was elevated at 2.6 mcg/mL (typical therapeutic level 0.14 – 1.2 mcg/mL).

After a four-hour session of hemodialysis her mental status improved, and her movement symptoms resolved. The following morning a repeat acyclovir level was 1.1 mcg/mL. An additional session of hemodialysis was performed due to persistent altered mentation with subsequent resolution to baseline. She was transitioned to topical ganciclovir for her keratitis and discharged home.

Discussion: This case describes the rare yet potentially underrecognized syndrome of acyclovir neurotoxicity, manifesting as delirium with prominent auditory hallucinations and myoclonus. Such toxicity is more likely to present in patients with acute or chronic renal failure given the drug’s pharmacokinetics. Both acyclovir and valacyclovir are dialyzable (30-60% drug removal in a four-hour session). Given these medications are commonly prescribed, as well as the severity of neurotoxicity and the rapid improvement with hemodialysis, it is critical to maintain a high index of suspicion and begin treatment promptly. The views expressed in this abstract are those of the authors and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense (DoD), or the U.S. Government.

Rescue Hemodialysis for Paroxysmal Hyperammonemic Encephalopathy Sans Cirrhosis
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Introduction: Ammonia is a product of protein catabolism that is converted to less toxic urea before excretion by the kidneys in urine. Hyperammonemia can be associated with coma, cerebral edema, and herniation. Ammonia levels do not correlate linearly with encephalopathy, especially in patients with chronic hyperammonemia.

Case Description: A 63-year-old female with a history of Roux-en-Y gastric bypass surgery > 20 years ago and malnutrition presented with three weeks of encephalopathy. Initial workup, including head CT and EEG, was negative. She was noted to have normal liver function and an elevated ammonia level of 110 μmol/L which was not responsive to conventional therapies. Continuous veno-venous hemodialysis (CVVHD) was successfully employed to prevent neurologic catastrophe. After discontinuation of CVVHD, she experienced recurrence of hyperammonemic encephalopathy prompting the use of hemodialysis (HD) intermittently throughout the hospital stay. We believe this patient’s paroxysmal hyperammonemic encephalopathy is a consequence of progressive metabolic disarray following gastric bypass surgery coupled with an exceptionally poor diet.

Discussion: There is historical precedent for extracorporeal blood purification in hyperammonemic states, typically related to pediatric inborn errors of nitrogen metabolism or fulminating liver failure with hyperammonemic encephalopathy. Recurrent hyperammonemic encephalopathy in the absence of liver failure has been described after bariatric surgery. Ammonia, a small, water-soluble molecule without significant protein binding, is cleared well with dialysis. Due to a large volume of distribution, ammonia levels frequently rebound after discontinuation of HD. Intermittent HD allows for the highest rate of reduction of ammonia, though CVVHD may be superior in severe encephalopathy. This patient’s ongoing need for HD, either chronically or episodically during decompensations, remains to be determined.
reduce platelet counts. A few isolated case reports have observed thrombocytopenia in patients on dialysis therapy. Although emergent dialysis is urgent, thrombocytopenia at 

Case Description: We report a case of an 82 year old man with a history of hyperten-
sion, an abdominal aortic aneurysm Stage 5 chronic kidney disease and AV

malformations admitted to with recurrent GI bleeding and acute kidney injury. Admission labs were significant for Hgb 4.9, Plt 209, Hct 16.0, BUN 166, Cr 5.3, 5.7, Bicarbonate 7 and Phosphorous 7.5. The bleeding site was found to be the transverse colon, which was ligated with resolution of the bleeding. Interim hemodialysis was initiated thrice weekly using an F810NR polysulfone hemodialysis membrane. On admission, his platelet count was 233,000. However, each morning after a hemodialysis treatment, his platelet count was ~40% lower than that of the previous day, but then increased until the next dialysis session. Over the course of the admission, his platelet count therefore progressively fell, reaching a nadir of 37,000 on hospital day 38. The patient was anticoagulated with citrate and did not receive heparin. His heparin- 

accompanied by itching, in the absence of any other symptoms. Recognition of a yellow dialyzer in a timely manner can assist in discerning if the etiology is medication related or hyperbilirubinemia related where the yellow color is thought to be due to entrapment of unfiltered bilirubin-albumin complexes by the dialysis membrane. Hopefully this recognition can improve outcome.

Discussion: Dialyzer membrane was changed to Cellentia-H cellulose triacetate single-use, hollow-fiber, high-flux hemodialyzer. Over the following week he underwent 3 additional dialysis treatments, over which time his platelet count rose to 120,000 and the post-dialysis drop in platelet count was no longer observed.

PO1195

Drug Condusion: A Case of Valacyclovir-Induced Neurotoxicity


Introduction: Medication dose adjustment in ESRD is paramount to avoid serious adverse effects. Valacyclovir(VA) is ~90% renally excreted after conversion to acyclovir, & cause life-threatening valacyclovir induced neurotoxicity(VAN). Prompt recognition and treatment(dialysis) to reduce mortality is crucial. We present a case of VAN in ESRD.

Case Description: 69-year-old male with ESRD on hemodialysis(HD),DM, HTN,CAD, prostate cancer presented with 1 day of confusion, weakness, flighth of ideas, auditory/visual hallucinations & persecutory delusions. 3 days prior he was given VA 500mg bid after telemedicine encounter for a rash. On exam, BP 238/106, heart rate 71,797.8f, he was oriented to person, time & place, had atomic aphasia, impaired short term memory & confusion. There was no skin rash. Labs noted Hb 11g/dL,WBC 10.2,PLT 170, Na136,K5.6,BUN 70, creatinine 9.2 & calcium 10. Head CT showed no abnormalities. He underwent emergent HD for acute encephalopathy due to VA use & during HD, his confusion & confabulation improved. The morning after HD he returned to baseline mental status & was counseled on the importance of discussing new medications with his nephrologist so dosage adjustments can be made appropriately.

Discussion: VA is a prodrug of Acyclovir & is ~90% renally excreted. Appropriate dose adjustment based on CrCl must be considered in CKD/ESRD to prevent serious adverse events. Our case caused life threatening valacyclovir induced neurotoxicity (VAN). Prompt recognition and treatment(dialysis) to reduce mortality is crucial. We present a case of VAN in ESRD.

PO1196

A Case of a Yellow Dialyzer in a Hemodialysis Patient

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Introduction: Yellowish discoloration of a dialyzer during hemodialysis (HD) can have various diagnostic and therapeutic implications, however its recognition must be made in a timely manner. Here we present a case of a patient whose dialyzer color was noted to be yellow after his HD session.

Case Description: A 65-year-old African American male with ESKD secondary to hypertension and diabetes mellitus, on intermittent hemodialysis for 9 years was noted to have a yellow dialyzer post hemodialysis. His only complaint during dialysis was severe itching for two days. On exam, he had no sceleral or palatal icterus. Stat outpatient laboratory testing revealed a total bilirubin of 13.1 mg/dL, with a direct bilirubin of 7.2, 10.0 mg/dl which led to his hospital admission. Further laboratory testing revealed an AST of 188 U/L, ALT of 188 U/L, alkaline phosphatase of 857 U/L, a normal amylase and lipase, and negative viral testing for hepatitis A, B, C, CMV, and EBV. Autoimmune work up was significant: anti-mitochondrial, and anti-smooth muscle antibody. An abdominal ultrasound showed mildly thickened gallbladder, without stones, sludge or ductal dilatation. Doppler showed no portal or hepatic vein thrombosis. A CT scan of his abdomen showed no discernable liver or gallbladder injuries. He denied herbal medications and had no history of jaundice or history of hepatitis. There was suspicion for drug induced liver injury caused by hyalurazine and high dose statin. Patient had a planned liver biopsy however he decapitated rescheduled, and had a cardiac arrest which led to his demise.

Discussion: Although yellow dialyzers have been described they are still quite a rare entity. In this case, the presence of a yellow dialyzer was one of the only two presenting symptoms for this patient, the other being itching. Itching, which occurs in dialysis patients could have easily been disregarded if it were not for the dialyzer discoloration. Not all yellow dialyzers display the yellow color in the absence of any symptoms. Recognition of a yellow dialyzer in a timely manner can assist in discerning if the etiology is medication related or hyperbilirubinemia related where the yellow color is thought to be due to entrapment of unfiltered bilirubin-albumin complexes by the dialysis membrane. Hopefully this recognition can improve outcome.

PO1197

Life Finds a Way: Two Successful Pregnancies in a Woman Without Kidneys

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Introduction: Bilateral nephrectomy is a controversial and rarely used approach to control refractory hypertension in patients with anatomic end-stage renal disease (ESRD) who require dialysis. This extreme measure results in complete dependence on dialysis to maintain metabolic homeostasis. This procedure has become rare due to advances in pharmacotherapy. There are relatively few pharmacologic options available for ESRD patients. We present the first known case of successful pregnancy in a woman on intermittent hemodialysis (iHd) without kidneys due to bilateral nephrectomy.

Case Description: The patient is a 31-year-old female who had ESRD secondary to hypertension and atypical hemolytic uremic syndrome (aHUS). She was diagnosed with aHUS condition during her first pregnancy and was initiated on biweekly infusions of eculizumab after delivery. Seven months after delivery, she underwent bilateral nephrectomy to control her hypertension. Two years following nephrectomy, she presented to the Emergency Department (ED) with dyspepsia. Her urine β-HCG was positive and ultrasonography confirmed an intrauterine pregnancy. Throughout this pregnancy, she required iHD six days weekly. She delivered at 27 weeks gestation and was transferred to the maternal-fetal intensive care unit (NICU) where she was discharged home in healthy condition. Two years later, the patient presented to the ED and was again found to be pregnant. She was managed with HD six days weekly. This child was born at 23 weeks gestation and was discharged home after several weeks in the NICU.

Discussion: The patient is a 31 year-old female who had ESRD secondary to hypertension and atypical hemolytic uremic syndrome (aHUS). She was diagnosed with aHUS condition during her first pregnancy and was initiated on biweekly infusions of eculizumab after delivery. Seven months after delivery, she underwent bilateral nephrectomy to control her hypertension. Two years following nephrectomy, she presented to the Emergency Department (ED) with dyspepsia. Her urine β-HCG was positive and ultrasonography confirmed an intrauterine pregnancy. Throughout this pregnancy, she required iHD six days weekly. She delivered at 27 weeks gestation and was discharged home after several weeks in the NICU.

PO1198

First Report of Simultaneous HBsAg and Anti-HBs Reactivity in a Hemodialysis Patient

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Introduction: Of great concern to dialysis units is the presence of bloodstream pathogens. The incidence of HBV infection is quite low in the United States, however outbreaks of hepatitis B in hemodialysis units have occurred. CDC guidelines recommend hemodialysis patients be screened for HBV surface antigen (HBsAg) surface antibody (anti-HBs) and core antibody (anti-HBc) on admission to the dialysis unit. We present an unusual case of a patient with both HBsAg and anti-HBs positive who required hemodialysis (HD).

Case Description: A 78-year-old Chinese female with past medical history of CKD stage V, Type 2 DM, hypertension, chronic HBV with no prior treatment, presented to the ED with signs of fluid overload. In the ED she was hypertensive to 170/107. Lab tests resulted at 28 IU/ml. HBsAg positive, as well as anti-HBs positivity. Confirmatory HBV quantitative PCR testing resulted at 28 IU/ml.

Discussion: Classically, anti-HBs antibodies neutralize and clear HBsAg from peripheral blood. Therefore, the presence of anti-HBs is considered an indicator of ongoing HBV infection. The typical serological feature of chronic HBV infection is circulating HBsAg and lack of anti-HBs. However, the coexistence of HBsAg and anti-HBs has been reported to be as high as 8% of chronic HBV patients. The coexistence of HBsAg and anti-HBs is generally explained by the phenomenon of “escape mutation”. Point mutations or deletions in the pre-S' gene of HBsAg may give rise to
PO1199

Dialysis Disequilibrium Syndrome and Cerebellar Herniation with Successful Reversal Using Mannitol

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Introduction: Dialysis disequilibrium syndrome (DDS) is a complication of hemodialysis. Symptoms can include headaches, seizures, and even death. An extensive literature review yielded 13 documented reports of patients suffering from cerebral herniation secondary to DDS with poor outcomes.

Case Description: 47-year-old male with hypertension presented to the emergency department (ED) with complaints of abdominal pain. Initial laboratory studies were concerning for thrombocytopenia and acute renal failure. The patient was urgently admitted to the Intensive Care Unit (ICU) and hemodialysis was initiated. Approximately 20 minutes into the hemodialysis session, the patient became unresponsive. A right eye gaze deviation and right-sided fasciculations of the upper and lower extremities were observed. Hemodialysis was discontinued and a head CT was obtained. Imaging revealed pontine edema with mass effect and cerebellar tonsillar herniation (Figure 1). Intravenous mannitol was initiated. Within 30 minutes of initiation of the mannitol infusion, the patient regained consciousness. Follow-up neurological exam showed resolution of the right-sided fasciculations and gaze palsy. The follow-up head magnetic resonance imaging (MRI) showed resolution of the midline shift and tonsillar herniation.

Discussion: Historically, even with swift intervention, cerebral herniation due to DDS carries a grim prognosis. Current guidelines stress the importance of preventative measures and the use of IV mannitol if cerebral herniation is suspected. The case reported herein is the first documented account of reversal of the clinical and imaging findings of tonsillar herniation secondary to DDS using intravenous mannitol.

PO1200

Gross and Microscopic Evidence of Platelet Clumping in the Extracorporeal Circuit Causing Thrombocytopenia in a Patient on Continuous Renal Replacement Therapy

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Introduction: Thrombocytopenia has been reported coincident with continuous renal replacement therapy (CRRT). We present a patient who developed thrombocytopenia on CRRT with gross and microscopic evidence of platelet clumping in the extracorporeal circuit.

Case Description: An 83 year old female with atrial fibrillation developed acute kidney injury requiring CRRT in the setting of ischemic bowel. Heparin was started due to suspicion of embolic phenomena. CRRT with citrate anticoagulation was begun using the NxStage System One (Purema H) without immediate issues. However, coincident with a progressive thrombocytopenia to a nadir of 75 x 10^3/uL, the care team noticed a white substance at the venous header of the dialyzer (Figure 1). Heparin was stopped due to concern for heparin-induced thrombocytopenia. CRRT was stopped and the dialyzer was sent to Pathology for evaluation. The white substance was found to be composed of many platelets with entrapped white blood cells and red cells, consistent with platelet clot. CRRT was withheld for 2 days with improvement of platelet count from 75 to 140 x 10^3/uL before the patient was restarted on CRRT due to clinical need; platelets subsequently decreased to 79 x 10^3/uL with reappearance of the white substance in the dialyzer. HIT testing was negative. The patient expired several days later when her family requested comfort care.

Discussion: Thrombocytopenia is frequently seen in critically ill patients, and it is often difficult to pinpoint a specific cause. In our case, gross and microscopic evidence of platelet clumping were seen in the CRRT filter coincident with thrombocytopenia, which remitted when off and then recurred when restarted on CRRT. Care teams should examine the dialyzer carefully when there is unexplained thrombocytopenia, as platelet activation and trapping within the circuit may be responsible.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Association Between Serum Alkaline Phosphatase Levels and Stroke Risk in Patients Receiving Maintenance Hemodialysis: The Q-Cohort Study

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Introduction: Elevated serum alkaline phosphatase (ALP) levels have been associated with increased risks of all-cause and cardiovascular mortality in patients receiving hemodialysis (HD). However, little is known about the impacts of serum ALP levels on the occurrence of stroke, including brain hemorrhage and brain infarction. This study aimed to explore the association between serum ALP levels and brain hemorrhage or brain infarction separately in HD patients.

Methods: A total of 3,497 maintenance HD patients registered in the Q-Cohort Study, a multicenter observational cohort study in Japan, were examined. The primary outcomes were the first-ever incidence of either brain hemorrhage or brain infarction during the follow-up period. The covariate of interest was serum ALP levels. Patients were divided into tertiles based on the serum ALP levels at baseline (ALP (U/L): T1, <69.3; T2, 69.3–98.4; T3, >98.4). The risks for brain hemorrhage or brain infarction were estimated using a Cox proportional hazards model and a Fine-Gray proportional substitution hazards model with all-cause death as a competing risk. The restricted cubic spline model was used to plot the multivariable-adjusted association between serum ALP levels and hazard ratios (HRs) and 95% confidence intervals (CIs) for brain hemorrhage or brain infarction.

Results: During the follow-up period of four years, 89 patients developed brain hemorrhage and 195 patients developed brain infarction. The risk of brain hemorrhage in the highest tertile (T3) was significantly higher than that in the lowest tertile (T1): multivariable-adjusted HR [95% CI], 1.93 [1.15–3.35], subdistribution HR, 1.91 [1.10–3.30]. Furthermore, restricted cubic spline curves showed that higher serum ALP levels were significantly and incrementally associated with an increased risk for brain hemorrhage. In contrast, no significant association was identified between serum ALP levels and the risk of brain infarction.

Conclusions: Higher serum ALP levels were associated with an increased risk of brain hemorrhage in patients receiving maintenance HD. Our results suggest that ALP might play some roles in the pathogenesis of brain hemorrhage in HD patients.

Funding: Private Foundation Support

PO1202

Tailoring the Dialysis Prescription in Patients at Risk for Dialysis Disequilibrium Syndrome


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Introduction: The dialysis disequilibrium syndrome (DDS) is a potentially fatal, preventable syndrome in uremic patients treated with dialysis. Urea kinetics can be used to tailor the dialysis prescription to a goal urea reduction ratio (URR) of less than 40%.

Case Description: A 22-year-old female patient presented to the emergency department with severe renal failure and a failing transplant secondary to noncompliance with medications for 1 year. Serum creatinine was 32 mg/dl, blood urea nitrogen (BUN) 226 mg/dl, potassium 9.2 meq/l and serum total carbon dioxide content 6 meq/l. Intermittent hemodialysis was started using a dialyzer with a mass transfer coefficient (koA) of 1200 ml/min, a blood flow rate of 250 ml/min, a dialysate flow rate of 500 ml/min and zero ultrafiltration. She was given 12.5 g of mannitol to reduce the risk of post-dialysis encephalopathy. After 1.5 hours of dialysis, the patient developed generalized seizures secondary to brain edema. BUN 6 hours after dialysis was 137 mg/dl. She was declared brain dead 4 days later.

Discussion: The dialysis disequilibrium syndrome results from osmotic shifts between the blood and the brain compartments. Rapid changes in BUN are known to contribute, but other osmotic substances may contribute to the development of DDS as well. Patients at risk for DDS include those with very elevated BUN, concomitant hypernatremia, metabolic acidosis, and those with low total body water volumes. There is no absolute cut off value for URR that is guaranteed to prevent DDS. However, a URR of 40–45% over 2 hours and a total decrease in serum osmolality no more than 24 mosm/kg per 24 hours are recommended. A simplified relation between Kt/V and URR is provided by the equation: k/V= -ln (1-URR). A URR of 40% is roughly equivalent to a k/V of 0.5. Thus, targeting a k/V of 0.5 is a reasonable goal for the initial treatment. k can be plotted on the nomogram in figure 1 (used with permission) for a given dialyzer kA and blood flow rate. Using a 400 kA dialyzer at a blood flow rate of 200 ml/min for 120 minutes in a patient with a V of 30 l, the estimated k/V is 0.45 and the estimated URR is <40%.

When low-efficiency dialyzers are not available, other measures to lower clearance such as reversing dialysis lines or CRRT need to be considered. Sodium modeling and mannitol may also mitigate rapid changes in osmolality.

PO1204

Effects of Improvements in Nutritional and Physical Conditions on Life Prognosis in Elderly Hemodialysis Patients in Japan

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Background: The increase in the number of elderly dialysis patients is an urgent worldwide issue. Among these patients, malnutrition and physical-function decline are often observed. Therefore, we conducted a nationwide cohort study using the elderly hemodialysis patient database (n=38227) of the Japanese Society for Dialysis Therapy to investigate the relationship of their nutritional and physical conditions with their risk of one-year death.

Methods: Malnutrition and poor performance status (PS) were defined as being indicated by low serum albumin levels, and high score of the modified Eastern Cooperative Oncology Group PS, respectively. After a one-year follow-up of changes in these factors, the relationships between the changes in these factors and the risk of one-year death were evaluated using Cox proportional hazards models adjusted for baseline characteristics.

Results: Among the patients examined, 57.9% were males; age, 73±6.0 years; diabetes mellitus, 33.7%; serum albumin level, 3.7±0.3 g/dl. The prevalence of patients in the low-albumin/poor-PS group tended to increase with age: 65 to 69 years, 14.0%; 75 years or older, 22.7% (Figure A). The low-albumin/poor-PS group showed a higher risk of all-cause death than the high-albumin/good-PS group: adjusted hazard ratio (aHR), 2.77 (95% CI, 2.24, 3.44) (Figure B). The 0.1 g/dl improvements in serum albumin levels and 1 point improvement in PS scores were independently associated with better life prognosis; aHR 0.93 (0.92, 0.95); aHR 0.76 (0.71, 0.81). These results were confirmed in subgroups categorized on the basis of age, and the presence of DM.

Conclusions: Malnutrition and PS decline are risk factors for death in elderly hemodialysis patients, and should be evaluated and treated simultaneously. It is expected that the treatments of patients with these factors will improve their life prognosis independent of their baseline characteristics.
PO1205
Ultralfiltration Accuracy of the Tablo® Hemodialysis System During 24-Hour Therapy
Michael A. Aragon, Amy Kerdock, Josh Schumacher. Outset Medical, Inc., San Jose, CA.

Background: Ultrafiltration (UF) accuracy is vital to ICU management of patients with kidney failure. Replacement options include intermittent hemodialysis, continuous renal replacement therapy and slow low efficiency dialysis. Regardless of therapy, clinicians need confidence that the dialysis device chosen will accurately remove volume to achieve the prescribed goal. The Tablo Hemodialysis System is an all-in-one system with on-demand water purification and dialyse production indicated for use in clinic, hospital, and home settings. Prior reports have demonstrated UF accuracy over a wide range of conditions up to 12 hours. The objective was to report on the accuracy of Tablo’s unique flow balancing technology over 24 hours of continuous therapy utilizing HD, isolated ultrafiltration, or a sequential therapy mode.

Methods: Bench testing was conducted to evaluate UF accuracy across clinically relevant parameters during a simulated 24-hour treatment with a single cartridge. Ten distinct treatment conditions were created. Effluent was weighed and compared to the prescribed goal at treatment completion. Treatment conditions included: most Qb HD, UF Only, and Sequential therapy (HD—UF only, UF only—HD), blood flow rates (Qb) from 150-400 ml/min, dialysate flow rates (Qd) from 50-300 ml/min, UF goals from 0 to 1.9 l/hr, and low and high venous and arterial pressure.

Results: Thirty simulated treatments were performed. Twenty-four treatments were performed with Qb from 150-250 ml/min and 6 were performed with Qb 300 or greater. Twenty-seven treatments had fluid removal goals between 250ml/hr to 2000ml/hr and 3 treatments were performed with a UF goal of 0ml/hr. Ninety-three percent of treatments were within 20ml/hr of accuracy (< 480ml of total error). Sixty-seven percent of treatments were within 10ml/hr of the prescribed UF goal (< 240ml of total error). Blood flow and UF rate showed correlation to UF accuracy with minimum error between Qb 200-300ml/min and UF rate between 0-1000ml/hr. There was no impact to UF accuracy from treatment mode or dialysate flow rate.

Conclusions: Tablo’s proprietary flow balancing technology maintains a high level of UF accuracy across a wide range of 24-hour treatment prescriptions. Optimal accuracy was noted at parameters typically prescribed in continuous renal replacement therapy.

Funding: Commercial Support - Outset Medical, Inc.

PO1206
Unfavorable Vintage: Dialysis-Related Amyloidosis Discovered at Transplant
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Introduction: Despite its life-sustaining potential, prolonged dialysis and inadequate clearance of middle molecules can have untoward consequences. Largely undiagnosed, dialysis-related amyloidosis (DRA) is an effect of prolonged dialysis vintage. We present a case of DRA in a patient with nearly 25 years of dialysis-dependence, diagnosed histologically at time of transplant.

Case Description: A 60-year-old man with hypertension, on dialysis since 1996, presented for renal transplant evaluation. Hematology labs showed normal serum protein electrophoresis but elevated free kappa (κ) level to lambda (λ) light chain ratio of 10.9. Bone marrow biopsy was normal but patient was found to have elevated serum β2 microglobulin (β2m) at 23.6 μg/ml. He was listed and immediately received a deceased donor transplant. Intraoperatively, biopsy of a large iliac lymph node was submitted which showed Congo Red positive staining by light microscopy for amyloid but was negative for serum amyloid. Intraoperatively, biopsy of a large iliac lymph node was submitted which showed Congo Red positive staining by light microscopy for amyloid but was negative for serum amyloid.

PO1207
Baclofen Pump Causing Electroencephalography Seizures
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Introduction: Baclofen is a centrally acting muscle relaxant that inhibits monosynaptic and polysynaptic reflexes at the spinal cord level resulting in relief of muscle spasticity. Baclofen is commonly used orally and intrathecally. We present the case of a patient on intrathecal baclofen through a pump presenting with respiratory failure and seizures.

Case Description: A 59 year old male with Atrial fibrillation, right MCA stroke and resultant left hemiparesis was under treatment with intrathecal baclofen through a pump. He underwent fluoroscopy guided pump refill and was found unresponsive later that night. EMS was called and he was intubated en route to the ED. He was hypotensive with recorded blood pressures 48/26-84/45 mm Hg. He had two seizures in ED and received IV lorzepam. Initial labs showed lactate 11.9 mmol/L, PCO2 80 mm hg, pH 6.9 and creatinine 2.0 mg/dl. Urine was positive for opiates and benzodiazepines. CT head did not show acute changes and was consistent with previously seen right cerebral encephalomalacia. He received intravenous fluids and creatinine improved to 0.9 mg/dl with resolving oliguria. Electroencephalography (EEG) was concerning for status epilepticus and he was transferred to our center for further management. Baclofen level was 0.13 mcg/ml. The acute encephalopathy, status epilepticus and respiratory failure were attributed to baclofen toxicity and nephrology was consulted for emergent dialysis. He underwent a 4 hour hemodialysis session using a Nipro 17H filter and maximum blood flow with dialysate flow at 600 ml/min. A post hemodialysis baclofen level was undetectable. Continuous EEG on the day after the hemodialysis session had improved.

Discussion: Role of hemodialysis in life threatening baclofen toxicity in a patient with AKI and improved renal function is not well described. Baclofen is small molecule with a molecular weight of 213g/mol that is primarily excreted unchanged by the kidneys with an apparent volume of distribution of 59 liters and is 30 percent protein bound. A single hemodialysis session may be adequate to clear baclofen in patients without advanced CKD. It is pertinent to recognize baclofen as possible cause of encephalopathy and seizures and consider hemodialysis in severe cases.

PO1208
Hep B or Not Hep B: The Mystery of Hepatitis B Serology in a Dialysis Patient
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Introduction: Dialysis patients are susceptible to viral infections due to impaired cellular immunity. HepB remains a major problem in these patients. Hemodialysis, transfusions, frequent admissions and surgery, all increase risk of infections. While the introduction of vaccines and infection control measures have limited the spread of hepatitis infection within dialysis facilities, outbreaks occur and prevalence remains high. Serology testing is used to screen and identify infected patients. Interpretation of these serologies, as in our case, can be challenging.

Case Description: 83 y/o female with HTN, DM and ESRD on HD. Admitted from a NH with viral prodrome and tested +ve for COVID-19. Nephrology consult was requested for maintenance HD. She had HBsAg assay which came back positive. Full Hep B panel showed HBsAb +ve, HBcAb +ve (IgM), HepB DNA PCR -ve, HBeAg & Ab-ve. Surprisingly, old records showed HBsAg positivity 6 months prior to admission and the rest of the serology was identical to this admission. Within the last 6 months, she have had multiple HBsAg tests that all came back -ve. Up to this point, she wasnt receiving HD in dedicated HepB machines. Decision was to apply segregation and to contact the health department to track down all patients that were dialyzed with the same machines.

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Discussion: The prevalence of HepB in dialysis patients is 1%. Cirrhosis, which can result from HepB, is associated with a 35% increased mortality in dialysis and patients. To prevent transmission, measures include barrier procedures, routine screening, disinfection and vaccination. Failure to use dedicated machines may increase incidence of HepB. Serology can identify infected patients. Screening consists of HBsAg, anti-HBs, and anti-HBc. If anti-HBs is negative, HepB can be definitely excluded. Anti-HBc positivity, we believe that she was infected in the past. Interestingly, the HBc-IgM was always \(+ve\) and DNA was always \(-ve\). The occasionally positive HBsAg is bizarre. This can be seen in patients receiving vaccination but it doesn’t apply to our patient. We don’t have an explanation for this. Anti-HBs in the absence of DNA and HBsAg recommendations to guide clinicians in such cases. In our patient, we decided to consider her a chronic HepB patient for the purpose of dialysis segregation, however, she does not meet criteria for chronic HepB and will unlikely require treatment.

PO1209 Temporal Change in Formula-Derived Creatinine Index as a Surrogate for Lean Muscle Mass Correlates Well with Change in Post-Hemodialysis Weight
Xiao Ling, Andrew I. Chin. University of California Davis, Sacramento, CA.

Background: In hemodialysis (HD) patients, creatinine kinetic modeling to derive a Creatinine Index (CI) is a measure of lean muscle mass. Loss of lean muscle mass is associated with poor outcomes. This modeling process is complex and not routinely performed. A simplified formula for CI was developed in a previous study. We sought to determine if temporal change in the calculated CI using the simplified formula correlated with more commonly available data used in routine clinical care of HD patients.

Methods: We retrospectively queried long-term HD patients without residual function who had available serum creatinine, urea kinetic, and clinical care data at least 18 months over a 24 month span. We used the simplified formula previously published for creatinine index: CI (mg/kg/day) = 16.21 + 1.12 (1 [if male], 0 if female) - 0.06 x age (years) ± 0.08 x sPcr x Urea x 0.009 x Creat (pre-dialysis). Regression lines were created for each parameter over the 24 months. Slopes of the change in CI, post-HD wt, urea generation rate (G) and kinetic modeled distribution of urea (V) were compared by paired t-tests.

Results: We included 455 long-term HD patients without residual renal function (we measure this routinely) with at least 18 out of 24 months of complete data. Mean HD vintage was 46 months. We found the slope of CI to be poorly correlated to V or G, but did not compare favorably to change over time slopes for V and post-HD weight.

Conclusions: In this retrospective analysis in HD patients, the temporal change of calculated Creatinine Index as an indicator of lean muscle mass compared best with change in post-HD weight. While the volume of urea distribution is related to body composition, the change V over time surprisingly did not mirror that of calculated CI. We also compared the slope of V to that of post-HD weight and found a strong association. The simplified equation for CI, applied to our population in Northern California, may correlate poorly with lean muscle mass.

Funding: Clinical Revenue Support

Comparisons of slope of regression lines for stated factors

PO1210 Crit-Line Blood Volume Monitoring in a Community Hemodialysis Unit
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Background: A quality improvement (QI) project on fluid management using Crit-Line Blood Volume Monitors (CLM) was conducted by a nephrologist in one community hemodialysis unit in Texas. A goal of the QI project was to decrease the blood pressure medication burden to facilitate better ultrafiltration during treatment. This analysis examines the changes in blood pressure (BP) medication (Med) and associated changes in post-dialysis weight and systolic BP.

Methods: Chronic HD patients of the nephrologist leading the QI project, receiving care at the CLM project site, were included. A total of 24 months of QI project data were included in this analysis. Time was divided into 1-month Baseline, 3-month training period, and 7-month follow-up. The physician reviewed each Crit-Line session and directed the staff to challenge the patient’s weight based on a positive refill curve. In order to facilitate further fluid removal, the vasodilating anti-hypertensive medication was discontinued. Thereafter, the other anti-hypertensive medications such as beta-blockers and RAAS inhibitors were added or discontinued.

Results: Patients (n=43) were on average 63 years old, with a HD vintage of 5 years and 79% \(+ve\) to post-HD weight, 77% \(+ve\) to post-HD systolic BP. Patients with \(+ve\) post-HD systolic BP had an \(+ve\) post-HD weight. During follow-up, 16.7% of patients discontinued BP med, 28.6% reduced BP med pills/day, 4.8% increased BP med pills/day, and the remaining had unchanged BP med. Changes in post and pre HD systolic BP and post-HD weight are presented in the table.

Conclusions: In a single-center QI project addressing fluid management through relative blood volume monitoring, 46% of patient were able to reduce (28.6%) or discontinue (16.7%) blood pressure medication. In patients able to discontinue the medications, had the largest decrease in post-HD weight.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

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PO1213

Use of Triferic and Outcomes of Hemodialysis-Dependent Patients: Initial Analysis Using 2016-2017 USRDS

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Background: Use of iron oxide nanoparticles (IONP) to replace iron losses in CKD-HD patients has been associated with increased risk of infections. We have examined patient outcomes with ferric pyrophosphate citrate (FPC; Triferic®), a novel iron compound delivered via the hemodialysate, relative to the general U.S. hemodialysis patient population receiving IONPs in US Renal Data System (USRDS). A single outpatient free-standing hemodialysis center with ~57 adult CKD-HD patients between 2016 and 2017, converted to FPC in January 2017. Unadjusted all-cause and infection related hospitalizations and mortality were examined pre-FPC and post-FPC and compared with the general USRDS data during the same period.

Methods: USRDS methods were utilized for calculation of the crude hospitalization and mortality rates. For each calendar study year, the period at risk begins at the later date of either January 1 or day 91 of ESRD, and censoring occurs at death, or December 31.

Results: Consistent with findings from USRDS, unadjusted all-cause hospital and mortality rates for the general ESRD population in 2016 were 2.12 hospital admissions, 16.0 hospital days, 0.35 infection-related admissions, 3.05 infectious hospitalization days per patient-year, and 164 deaths per 1,000 patient years. Notably, patients in 2017 exhibited similar rates compared to 2016. In contrast, patients treated in the facility using Triferic experienced a reduction in both mortality and infection-related hospitalizations. Specifically, mortality rates reduced 58% from 101 per 1,000 patient-years in 2016 to 42 in 2017. Infectious hospital admission reduced 73% from 0.49 admissions per patient-year in 2016 to 0.13 admissions in 2017. Furthermore, infection-related hospital days reduced 82% from 3.86 days per patient-year in 2016 to 0.71 in 2017.

Conclusions: This observational study suggests that use of ferric pyrophosphate citrate as iron replacement therapy is associated with reduction in all cause and infection-related hospitalizations and mortality. Further analysis is needed to confirm the findings from this initial analysis after controlling a variable of patient case-mix factors and dialysis center characteristics with a larger sample size.

Funding: Commercial Support - Rockwell

PO1214

Association of Geriatric Nutritional Risk Index with Decline in Residual Kidney Function in Incident Hemodialysis Patients

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Background: Malnutrition is highly prevalent and is a significant contributor to adverse outcomes among hemodialysis patients. Residual kidney function (RKF) provides effective and continuous clearance of both small and middle molecules, plays an important role in nutritional status. However, the impact of malnutrition on the decline of RKF has not been well studied. The objective of this study was to investigate the association of baseline Geriatric Nutritional Risk Index (GNRI) with a decline in RKF over 1 year after dialysis initiation among hemodialysis patients.

Methods: We included 6,649 hemodialysis patients who initiated dialysis treatment in a large United States dialysis organization between January 1, 2007, and December 31, 2011. Rapid decline in RKF was defined as the percent change in residual urea creatinine (KRU) greater than 50% per year. The associations of GNRI with decline in RKF were retrospectively examined across three strata of GNRI [low (GNRI <92), middle (GNRI 92-98), high (GNRI >98) GNRI group] using logistic regression models adjusted for clinical characteristics and laboratory values. Then, we used the linear mixed-effects model allowing for a random intercept and slope using unstructured covariance matrices to estimate the magnitude and decline of RKF over 1 year according to the GNRI groups.

Results: The median GNRI and baseline KRU were 107.7 and 3.4 mL/min/1.73m², respectively. Lower GNRI was associated with a smaller proportion of diabetes, lower baseline KRU, BMI, nPCR, and serum albumin. Adjusting for patient’s differences, there was an inverse relationship between lower GNRI and a higher odds of rapid decline in RKF [adjusted odds ratio: 1.97 (1.61-2.41) and 1.48 (1.25-1.76) for low and middle GNRI groups, (reference: high GNRI group)]. KRU trajectories showed greater KRU decline over time in lower GNRI.

Conclusions: Lower GNRI was associated with a rapid decline in RKF, especially in the first 3 months after transitioning to hemodialysis.

PO1215

Prognostic Nutritional Index and Mortality Among Maintenance Hemodialysis Patients

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Background: Malnutrition and inflammation are associated with the mortality of dialysis patients. Prognostic Nutritional Index (PNI), which is composed of serum albumin levels and total lymphocyte count, has been suggested as a simple and useful prognostic marker in postoperative cancer patients. We evaluated the usefulness of PNI for predicting mortality in hemodialysis patients.

Methods: This retrospective cohort study included the patients who started hemodialysis in a large U.S. dialysis organization from 2007 to 2011. We examined the association between the quartiles of PNI and mortality using Cox regression model.

Results: The mean age (and standard deviation) of total 101,616 patients was 63±15 years, and 26,622 died during the median follow-up period of 1.4 years. Higher quartiles of PNI were associated with lower mortality; case-mixed adjusted hazard ratios (95%CI) were 0.66 (0.64-0.68), 0.49 (0.48-0.51), 0.35 (0.34-0.37) among patients with PNI 39.5–43.1, 43.1–46.6, and 46.6< (reference: PNI <39.5). PNI showed higher mortality predictability than serum albumin levels and total lymphocyte count; AUROC (95%CI); 0.74 (0.74-0.75), 0.743 (0.73-0.748), 0.711 (0.706-0.716), NRI (95%CI); 0.436 (0.418-0.454), 0.410 (0.392-0.429), 0.174 (0.156-0.192), IDI (95%CI);0.032 (0.032-0.033), 0.032 (0.030-0.033), 0.003 (0.003-0.004), respectively. The difference in the AUROC was statistically significant between PNI and its components. In subgroup analysis PNI well predicted mortality in younger than 75 year-old patients.

Conclusions: Higher PNI was associated with lower mortality in hemodialysis patients. Compared with serum albumin levels and total lymphocyte count, PNI seems to be a useful predicting marker of mortality.

Figure: Mortality risk associated with PNI

PO1216

Hemodialysis-Assisted Management of Severe Hypoglycemia

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Introduction: Many medications are cleared by hemodialysis (HD) but the effectiveness of clearance depends on drug characteristics including molecular weight, protein binding, volume of distribution and water solubility. The effectiveness of HD in clearing endogenous insulin has not been well studied. We present a case of refractory hypoglycemia in a patient with ESRD, which was likely due to ciprofloxacin (cipro)-induced insulin release that was successfully managed with HD.

Case Description: A 77 year old man with ESRD receiving chronic HD and no previous history of diabetes, was admitted for management after he pulled out his tunnelled HD catheter. The patient had HCV-induced cirrhosis and had been receiving outpatient cipro for spontaneous bacterial peritonitis prophylaxis. Initial electrolytes did not warrant urgent HD so was admitted to medical floor pending new HD catheter placement. During first several days after admission, the patient had persistently low blood glucose (BG) despite not receiving any hypoglycemic medicines and receiving continuous infusion of dextrose solution and repeated boluses of 50% dextrose. Prior to receiving HD, serum insulin was elevated at 42 ng/ml and 148 ng/ml despite hypoglycemia and c-peptide was ~40ng/ml consistent with excessive endogenous insulin secretion. The patient was suspected to have cipro-induced hyperinsulinemia. Emergently HD was performed to
increase clearance of cipro and insulin. After 1 HD session, insulin level decreased to 14.6 with improved BG levels. The patient was maintained on octreotide with stable BG levels without further IV dextrose administration.

Discussion: Fluoroquinolones have been associated with hypoglycemia in diabetic and non-diabetic persons. Animal studies have suggested fluoroquinolones can block the ATP-sensitive K+ channels in B-cells and increase the insulin secretion. Although our patient received his chronic dose of cipro (250mg daily), it is possible that lack dialysis for several days may have led to accumulation of cipro. The effect of HD on immune reactive insulin (IRI) was evaluated by Masanori et-al, in diabetic and non-diabetic patients. Although pro- and post-dialyzer samples revealed evidence of significant HD clearance of endogenous insulin. It is therefore likely that HD reduced insulin in our patient by reducing cipro-induced endogenous insulin secretion and via clearance of insulin.

PO1217 Low-Sodium Home-Delivered Meals Reduce Thirst and Xerostomia in Patients on Hemodialysis

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Background: Hemodialysis (HD) patients are often advised to restrict dietary sodium and fluid. Thirst and xerostomia contribute to non-adherence with fluid restricted diets resulting in fluid retention and chronic volume overload. Dietary sodium restriction may reduce thirst and xerostomia, which may, in turn, reduce fluid intake and retention. The purpose of the study was to determine if 4-weeks of low-sodium home-delivered meals reduces HD patient’s subjective thirst and xerostomia.

Methods: Twelve HD patients had 3 low sodium meals/day (Mom Meals, Inc) delivered over their home for 4 weeks. On average they were on 17 medicines among which 7 (Mean) had prior evidence to induce xerostomia. Subjective thirst and xerostomia were measured at 3 time points: baseline (BL), after 4 weeks of low sodium meals (INT), and 4 weeks post-meals (POST[SA1]). Thirst was measured using the dialysis thirst inventory scale (DTI) that had 7 domains describing thirst, and numerical rating scale for 12 items. Xerostomia was measured with a numerical rating scale for dry mouth (NRX-X) and the xerostomia inventory scale (XI) that had 11 domains describing dry mouth symptoms.

Results: Participant’s mean thirst during the day, thirst after HD, thirst’s influence on social life, dry mouth feeling, total XI, NRX-T, NRX-X were significantly lower during INT compared to BL (MeansSD scores from BL to INT: 3.1±2.1; 2.5±2.2 to 2.2±1.3; 2.9 to 1.9±0.9 on the scale of 1-5; 28.5±12 to 19.3±9 on the scale of 1-55; 6±3 to 2.8±2 and 5.5±3 to 3.1±2 on the scale of 0-10, respectively; p<0.05). The score of thirst’s influence on social life and NRX-T were significantly higher in POST compared to INT (MeansSD scores from INT to POST: 1.3±0.9 to 1.7±1; 2.8±2 to 4.5±2.6; p<0.05). NRX-T is significantly lower in POST compared to BL (MeansSD scores from BL to POST: 6.3±4 to 4.5±2.6; p<0.05).

Conclusions: Multiple domains of subjective thirst and xerostomia decreased after 4 weeks of home-delivered low sodium meal consumption but generally returned close to baseline 4 weeks after cessation of the meal delivery. The feasibility and efficacy of long-term meal provision for reducing thirst, xerostomia, and chronic volume overload need to be further evaluated in future studies.

PO1219 End-of-Life Care Experiences and Beliefs Among African American Hemodialysis Patients

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Background: Prior work has shown that African Americans with end-stage renal disease (ESRD) are less likely than their White counterparts to have discussed end-of-life (EOL) care preferences with their providers, and more likely to prefer life-extending treatment. We sought to determine if patient demographic and institutional factors are associated with African American ESRD patients’ experiences and beliefs on EOL care.

Methods: Self-identifying African American adults receiving hemodialysis at three university-affiliated dialysis units completed surveys about their prior EOL care planning and preferences in various EOL situations. We used bivariable and multivariable logistic regression to analyze the association between EOL care views and several covariates including age, gender, education level, income, insurance, and previous experiences with EOL care discussions.

Results: From June to September 2019, 101 patients completed the study. The mean age was 58.7 years, 52% identified as female, and 42% have been on dialysis for >5 years. Almost 69% of patients reported they had never discussed EOL care with any healthcare provider; 95% (64/69) reported their providers never initiated EOL care conversations with them, the remaining 5% thought their providers initiated these conversations. Almost 66% of patients believed end stage renal disease and any significant deterioration of health are EOL care conversations and any clinical or demographic covariates. The proportion agreeing that at the EOL if was to “withdraw treatments,” 2) “withdraw treatments,” and 3) “to withhold nutrition and fluids” were 78%, 71%, and 63%, respectively. Previous experience with EOL care discussions with either family or healthcare providers was significantly associated with a decreased likelihood to prefer life-extending treatments at EOL (p<0.05).

Conclusions: A majority of African American patients with ESRD reported never having any EOL care discussions. Most of these patients are open to speaking about EOL care and they believe that their healthcare providers but are unwilling to initiate discussions. Furthermore, past experience with EOL care discussions with either family or medical team is associated with a decreased preference for aggressive life-extending care. Despite provider and patient discomfort with EOL care discussions, healthcare providers should familiarize their African American patients with ESRD to identify how medical care at EOL can be more congruent with their values and needs.

Funding: Private Foundation Support

PO1220 Impact of a Palliative Hemodialysis on Quality Standards and Hospice Utilization

Minna Park, Jeffrey I. Silberzweig. Rogosin Institute, New York, NY.

Background: Minimal data exists regarding effect of palliative dialysis on clinical outcomes and quality measure. Frail, elderly patients may find thrice weekly, 3-hour hemodialysis treatments burdensome. Numerous barriers exist to providing palliative dialysis, including quality standards set by the ESRD Quality Incentive Program (QIP). This study shows the impact of reduction in dialysis frequency and time on quality standards and hospice utilization in the seriously ill elderly.

Methods: A retrospective chart review was performed on four deceased patients who received palliative dialysis in one ambulatory dialysis center. Quality standards reviewed included: dialysis adequacy (Kt/V), metabolic control, nutrition, heoglobin and ultrafiltration rate. Clinical outcomes were also reviewed.

Results: All four patients were elderly with reduced functionality, heavy symptom burden and difficulty tolerating regular hemodialysis sessions. Patients were deceased at three hour hemodialysis sessions twice weekly. Despite decreased treatment time and frequency, most quality measures did not differ from baseline. Duration of palliative dialysis ranged from 2-11 weeks. Most patients tolerated palliative dialysis, remained free of hospitalization, successfully transitioned to hospice and did not experience serious clinical events. Lack of need for dialysis. On quality measurements were attributed to patients poor oral intake, loss of body mass and minimal weight gains between dialysis sessions. Patients were observed to have a better quality of life and better utilization of time with family.

Conclusions: Palliative care, incorporating the patient and family, appears to be a good option for patients and families who are not ready to withdraw from dialysis. Palliative dialysis allows patients a slower transition to end-of-life care with more support and proper preparation in line with patients’ wishes. In addition, with our recent experiences with covid 19 infections, this practice might be a possible option for someone with serious illness, hoping to avoid unwanted hospitalization and aggressive medical treatment. Goals of care conversation, timely plan of care for transition of care and close monitoring of patients are essential for palliative dialysis.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
POI1221

Surprise Question: A Mortality Predictor in Hemodialysis Patients?
Patricia Valerio, Ana Farinha, Centro Hospitalar de Setubal EPE, Setubal, Portugal; Fresenius Medical Care Portugal, Setubal, Portugal.

Background: Surprise question (SQ), used in Palliative Care (PC) and Oncology, has already been tested to assess prognosis in several chronic diseases. In Portugal, as worldwide, an elderly and fragile hemodialysis (HD) population has been emerging. Tools to screen patients who might benefit from end of life care would be useful. The present study aims to test SQ mortality prediction value in a Portuguese cohort of HD patients, answered by nephrologists and nurses. The study ran between November 2018 and November 2019.

Methods: We design an observational prospective study. All patients on regular HD for more than 3 months were included. Experienced nephrologists and dialysis nurses, but without PC training, answered SQ at the beginning of the follow-up. We collected demographic, clinical and analytical data. At the end of follow-up, we analyzed evolution during follow-up and survival status.

Results: We included 194 patients, median age of 69.9 y-o. Median age-adjusted Charlson Comorbidity Index (aCCI) was 6 (5-8). Table 1. After one year of follow-up 22 (11.3%) patients have died. Nephrologist and nurse SQ were both good predictors for mortality within one year, with an OR 7.44 (IC95% 2.92-20.74) and 8.47 (IC95% 3.08-30.34) respectively (both with a p-value <0.001). Institutionalization, aCCI, albuminemia and hospital admissions during follow-up also seems to be important predictors. Table 2. With multivariate analysis, SQ for nephrologists and nurses are no longer statistically significant: OR 1.25 (IC95% 0.31-5.11) and 3.09 (IC95% 0.81-11.86), respectively.

Conclusions: Our results showed that SQ answered by nephrologist and nurse are not good mortality predictors, reflecting this method subjectivity and the lack of PC training. Probably, SQ should be reserved to professionals with PC training, a profound gap in nephrologists training in Portugal.

POI1222

Code Status Variability in a Regional Hemodialysis Program
Danielle Moorman, Samuel A. Silver, Hasitha Welihinda, Eduard A. Iliescu. Queen’s University, Kingston, ON, Canada.

Background: Patients with end stage kidney disease (ESKD) treated with hemodialysis (HD) have poor life expectancy and may not benefit from aggressive measures at the end of life. Previous studies suggest variability in Do Not Resuscitate (DNR) orders in patients treated with HD but they are limited by missing code statuses and inability to adjust for demographics. In our regional HD program, with complete code status ascertainment that is updated annually, our objective was to examine DNR variability while accounting for demographic factors.

Methods: We conducted a cross-sectional study of DNR prevalence in October 2019 in patients treated with in-centre HD in a regional program, which consists of a main centre and six smaller centres. Patients are transferred to smaller centres based on location. Each centre has an attending nephrologist who reviews code status yearly with every patient. Unadjusted DNR prevalence are compared using the Chi-square test and multiple logistic regression is used to control for covariates (age, sex, race, dialysis vintage, HD unit).

Results: We included 374 patients, 193 (52%) from the main centre and 181 (48%) from its satellite units. Mean age of patients is 67.2±14.3 years, 52% male, 87% Caucasian, and dialysis vintage 5.2±5.3 years. Code status was full code in 78% and DNR in 22% with significant variation across sites (range of 9% to 46%, p =0.02) (Figure 1). Variation remained significant (p = 0.03) after controlling for covariates.

Conclusions: Variability in code status at different HD centres in our regional program persisted despite accounting for differences in patient age, sex, race, and HD vintage. This finding suggests factors related to the HD centre may affect code status decisions, such as local culture, question phrasing, and views of the treating nephrologist. Future studies are planned to determine if a standardized approach to discussing code status would normalize rates.

POI1223

Polypharmacy and Frailty Among Hemodialysis Patients
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Background: Most patients undergoing maintenance dialysis have multiple comorbidities, most of which require long term medication management and can inevitably lead to polypharmacy. Frailty is also highly prevalent among dialysis patients and has been associated with poor outcomes. With higher frailty and comorbidity rates among dialysis patients, it remains unclear if polypharmacy is still associated with the incidence of frailty among dialysis patients. The aim of this study was to examine the independent association between polypharmacy and frailty among hemodialysis patients.

Methods: We examined 337 patients enrolled in the ACTIVE/ADIPose dialysis cohort study. The number of prescribed medications and frailty were assessed at baseline, 12, and 24 months. We used logistic regression with generalized estimating equations to model the association of the number of medications and frailty over time; competing-risks regression to assess incidence of frailty.

Results: The mean number of medications was 10 ± 5, and 94 patients (28%) were frail at baseline. Patients taking greater than 11 medications showed higher odds for frailty as compared with patients taking less than 8 medications (OR 1.54, 95% CI 1.05-2.26). During two years of follow-up, 87 patients developed frailty among the non-frail patients at baseline. Compared with patients taking less than 8 medications, the incidence of frailty was approximately 2-fold in those taking greater than 11 medications (sub-distribution hazard ratio [SHR] 2.15, 95% CI 1.32-3.48).

Conclusions: Using a higher number of medications was associated with frailty and the incidence of frailty among hemodialysis patients. Minimizing polypharmacy may reduce the incidence and prevalence of frailty among dialysis patients.

Figure 1: Unadjusted DNR prevalence in hemodialysis units across a regional dialysis program.
Veterans Administration Medical Center, Durham, NC; 2 Duke Clinical Research Institute, Durham, NC; 3 Durham Veterans Administration Medical Center, Durham, NC.

Background: Sudden cardiac arrest is the leading cause of death for hemodialysis patients, and often occurs during treatment in hemodialysis units. Resuscitation guidelines emphasize the need for rapid delivery of effective chest compressions to improve survival. How different methods of patient positioning (in the dialysis chair or on the floor) affects chest compression quality is unknown.

Methods: This was a prospective randomized cross-over study to assess the quality of chest compressions performed on a simulation manikin (Laerdal SimMan3G). Dialysis staff were recruited from a single center and asked to perform 2 minutes of compressions on the manikin positioned: 1) on a gurney with a code-cart backboard (baseline); 2) on the floor; 3) in a reclined dialysis chair; and 4) in a reclined dialysis chair with a backboard placed underneath. The sequence of manikin positions was randomized to reduce carryover effects and assessments were conducted 48 hours apart to reduce participant fatigue. Mean compression depth, %compressions at appropriate depth, %compressions fully released and %compressions at adequate rate were assessed for each position and for each participant. Paired sample T-tests were performed to assess the mean differences in compression measures between positions and baseline.

Results: 13 dialysis staff members including 7 RNs, 3 MTS and 3 providers participated in the study. Compared to baseline, mean compression depth (6.5 mm) and % compressions fully released (26%) were significantly worse for compressions performed in the dialysis chair, and quality reductions persisted even when a backboard was utilized in the dialysis chair (see Figure 1). No significant differences in compression quality measures were observed with manikin positioning on the floor compared to baseline.

Conclusions: Performing CPR in a reclining dialysis chair results in significant reductions in CPR quality. This should be considered in developing dialysis-specific CPR protocols, and further studies should investigate the relative merits of different patient positioning options for optimal CPR delivery.

Funding: NIDDK Support

PO1226

Association Among Iron, Coronary Artery Calcification, and Mortality in Hemodialysis Patients

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Background: Coronary artery calcification (CAC) is recognized as one of the main causes of cardiovascular disease and death in hemodialysis (HD) patients. It has been reported in HD patients that iron may be a contributing factor of calcification. Previous studies have shown that higher CAC scores contribute to the high incidence of cognitive deficits in ESRD-HD subjects.

Methods: This study included 173 HD patients. Clinical data and Agastson’s coronary artery calcification score (CACS) were obtained at baseline. Two groups comprised patients with CACS ≥400 (n=109) and patients with CACS <400 (n=64). Logistic regression analyses for CACS ≥400 and Kaplan-Meier survival and Cox proportional hazard analyses were conducted.

Results: The median (interquartile range) age and dialysis vintage among all subjects were 67 (60–75) years and 73 (37–138) months, respectively. Serum iron (Fe) and transferrin saturation (TSAT) levels were significantly lower, but age, dialysis vintage, C-reactive protein (CRP), and albumin-adjusted serum calcium (Ca) levels were significantly higher in patients with CACS ≥400 than in patients with CACS <400 (P<0.05). No significant differences in the dosage of phosphate binders, active vitamin D, cinacalcet, and iron were observed. In the univariate logistic regression analysis, CACS ≥400 had a significant association with TSAT ≥200, Fe ≥80 μg/dL, age, and dialysis vintage (P<0.05). In the subsequent multivariate analysis, including all variables that showed significance in the univariate analysis, excluding Fe ≥80 μg/dL, and well-known risk factors for coronary artery calcification in HD patients (diabetes mellitus, Ca, phosphate, and CRP), TSAT ≥200% remained independently and significantly associated with CACS ≥400 (odds ratio 0.44, P<0.01). HD patients with Fe ≥80 μg/dL showed significantly higher 5-year survival. However, patients with serum ferritin ≥36.6 μg/mL (median ferritin value in this study) showed significantly lower 5-year survival than patients with ferritin <36.6 μg/mL, and ferritin ≥36.6 μg/mL was a significant predictor of a 1-year all-cause mortality in HD patients (hazard ratio: 2.71, P<0.05).

Conclusions: In HD patients, there is an association among iron, CAC, and mortality, and TSAT ≥200% was found to be an independent and significant factor in the prevention of CACS ≥400.

Funding: Private Foundation Support

PO1227

Valvular Heart Disease in Prevalent Hemodialysis Patients

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Background: Valvular heart disease is observed in patients with Chronic Kidney Disease. Previous large studies found a prevalence rate of 14%-16% of valvular heart disease (VHD) in hemodialysis patients (2018 USRDS; Hickson et al., 2016). KDIGO consensus group identified several evidence gaps where research is necessary in order to improve our understanding of diagnosis and management of VHD. The aim of our study is to assess the burden of VHD in a haemodialysis cohort in one center in the UK.

Methods: A single-center, retrospective, cross-sectional study of echocardiographic findings in prevalent hemodialysis patients. Patients were considered to have VHD if they had significant aortic or mitral valve disease (AVD, MVD) based on standard echocardiographic criteria. Medical records were reviewed for clinical information.

Results: This study included 425 haemodialysis recipients. Mean age was 61 years, (SD: 14.96). The cohort was predominantly male (59.3%). The mean BMI was 27.69 (SD: 5.99). 37.1% had a history of smoking. The median renal replacement therapy vintage was 3.19 years (IQR: 1.96, 5.61). With median hemodialysis vintage of 2.93 years (IQR: 1.76, 5). 85% of patients had hypertension, 41% had diabetes, 29% had coronary artery disease (CAD) and 13% had a history of congestive cardiac failure (CCF). Atrial Fibrillation (AF) was present in 11.5%. 34% (n=143) had evidence of VHD. 18% had evidence of AVD (n=78); Aortic Regurgitation in 11%, and Aortic Stenosis in 7% of patients. 20% of patients (n=85) had MVD with Mitral Regurgitation in 18% of patients and Mitral Stenosis in 0.7% (n=3). 5% of patients had cardiothoracic intervention (n=21) for VHD. Compared to patients who had no evidence of VHD, those with VHD were significantly older (p < 0.001), had lower creatinine BMI (P=0.001), and had decreasing AF, CAD and CCF (p<0.05). These patients had a significantly longer dialysis vintage (p=0.001). Patients, who had VHD, had a tendency to higher serum calcium, although this did not reach statistical significance (p=0.057). Similarly, diabetes was also higher in the MVD cohort (44.3% vs 34.3%, p=0.059).

Conclusions: 34% of patients had significant VHD, higher than the previously published figures. The lower prevalence of diabetes in the VHD cohort makes the metabolic milieu an additional important risk factor in VHD. Timely echocardiographic studies are essential to identify patients with significant VHD.

Funding: Commercial Support - Alkahest Inc.
POI1228

The Effect of Intradialytic Potassium and Magnesium Fluctuations on Cardiovascular Functioning in ESRD Patients Undergoing In-Center Hemodialysis

Andy Chiu,1 Gonzalez Matsumura Umemo,1 Michael I. Rauchman,2,3 Frank J. O’Brien.1 Washington University in Saint Louis, Saint Louis, MO; 2Saint Louis VA Medical Center John Cochran Division, Saint Louis, MO.

Background: Patients with ESRD receiving in-center hemodialysis (HD) have an age-adjusted rate of mortality 4 times the general population. Increased mortality has been attributed to fatal arrhythmias. Mechanisms and risk factors for this are unknown. It has been postulated that changes in serum levels of Potassium(K)/Magnesium(Mg) with HD contribute to arrhythmia generation. Limited data is available to guide personalization of K prescription of HD to reduce this risk. No data exists describing the serum changes in Mg pre-, intra-, and post-HD. We examine the correlation between electrolyte fluctuations, arrhythmia generation, and heart rate variability (HRV) in ESRD patients undergoing in-center HD.

Methods: Single center, prospective, cross-sectional pilot study. 25 patients enrolled to achieve an 80% power. Demographic data, dialysis vintage, and HD prescription were recorded. Arrhythmia data was collected by placement of Holter monitor prior to 1st weekly HD session and recorded continuously for 5 days ending at completion of 3rd weekly HD session. Serum samples were obtained at time intervals 30, 60, 90, and 120 minutes during 1st weekly HD session for electrolytes. Pre and Post HD serum electrolyte analysis occurred during all 3 treatments. Associations were examined by count regression utilizing Poisson or negative binomial methods.

Results: 25 patients were included in data analysis. Mean age 63 and primarily African American (73%). 73% of individuals were dialyzed utilizing 2mmol/L Ectopy data and serum potassium / magnesium data are summarized in Table 1.

Conclusions: There is a trend towards increased ectopy (particularly on HD day 1) and decreased HRV on HD days. There is a trend towards hypo-K post-HD after HD sessions 2 and 3. Serum Mg levels remained stable pre and post HD throughout all HD sessions. Data derived in this study will be utilized to guide a larger future study with the goal towards personalized HD treatments.

Results:

<table>
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<th># of Patients</th>
<th>Mean Pre K</th>
<th>Mean Post K</th>
<th>Mean Pre Mg</th>
<th>Mean Post Mg</th>
<th>Mean Post K (mmol/L)</th>
<th>Mean Post Mg (mmol/L)</th>
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<td>7</td>
<td>4.7 (4.0-6.0)</td>
<td>3.8 (3.0-5.3)</td>
<td>2.2 (1.9-3.0)</td>
<td>1.9 (1.6-2.2)</td>
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<td>3.3 (3.0-4.0)</td>
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<td>1.9 (1.6-2.2)</td>
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<tr>
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<td>4.7 (4.0-5.4)</td>
<td>3.4 (3.0-4.0)</td>
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<td>1.9 (1.6-2.2)</td>
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<tr>
<td>Mean Pre K (mmol/L)</td>
<td>4.7 (4.0-5.4)</td>
<td>3.3 (3.0-4.0)</td>
<td>2.3 (2.0-3.0)</td>
<td>1.9 (1.6-2.2)</td>
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<tr>
<td>Mean Post K (mmol/L)</td>
<td>3.8 (3.0-5.3)</td>
<td>2.2 (1.9-3.0)</td>
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POI1229

Human Factors Testing of the Quanta SC+ Haemodialysis System: Demonstrating Ease of Use with Minimal Upfront Training in Health Care Practitioners and Patients

Paul Komenda, John Millad, Kathryn Compton. Quanta Dialysis Technologies, Alcester, United Kingdom.

Background: Quanta Dialysis Technologies has developed a compact, powerful personal haemodialysis system intended for home and self-care use designed in collaboration with patients and healthcare practitioners. Human factors testing is necessary to demonstrate ease of use with minimal up-front training.

Methods: In compliance with FDA guidance and EU standards, the user interface of the system was evaluated through human factors testing to assess the safe and effective use of SC+. This included a series of user-based tasks whereby representative users independently setup SC+ into a simulated treatment, managed alarms to resolution and external SC+ cleaning/disinfection. All participants received an introduction to SC+ and completed a competency sign off at the end of training. 15 healthcare professionals (6 renal nurses, 8 dialysis technicians, 1 patient care technician) received up to 4 hours of structured training followed by a 1-day learning decay period. In addition, 10 lay users (8 dialysis patients, 2 caregivers) received between 5.5 and 7.5 hours training followed by a 2-day learning decay period.

Results: Between the two user groups, there were a total of 8,110 opportunities for use errors to occur. Despite minimal training and representative learning decay, only 4 significant use events were observed requiring some user manual enhancements. Other use errors captured were minor or could not be mitigated further due to clinical practices and shared inherent risks across all haemodialysis systems.

Conclusions: The results of the human factors testing demonstrated that healthcare practitioners, patients and caregivers successfully operated SC+ independently with a high level of use safety, despite minimal training and learning decay. The SC+ user interface is optimised for safe and effective use under FDA guidance and EU standards.

Funding: Commercial Support - Quanta Dialysis Technologies

POI1230

Inpatient Dialysis Provider Type and Duration of Hospital Admissions of Dialysis Patients

Joshua W. Morrison, Daniel Liu, David L. Mahoney, Jeffrey A. Giulian. DaVita Inc, Denver, CO.

Background: Inpatient dialysis treatments may be performed by hospital staff or by a contracted dialysis provider. In this study, we compared duration of hospitalizations of dialysis patients who were admitted to hospitals performing in-house dialysis to that of patients who were admitted to hospitals contracting with a dialysis provider.

Methods: Data for this analysis were derived from the electronic medical records of a large dialysis organization. We identified patients who were hospitalized between Jan 2017 and Sept 2019. Length of stay was compared for patients who were admitted to hospitals performing dialysis in-house versus patients who were admitted to hospitals that contracted with the dialysis organization.

Results: During the study period, we identified 155,458 hospitalizations among 64,662 patients at 572 hospitals in which dialysis was performed by in-house staff. There were 226,059 hospitalizations among 87,213 patients at 797 hospitals in which dialysis was performed by the dialysis organization. There were no meaningful differences in patient characteristics or reasons for admission among patients admitted to hospitals performing dialysis in-house compared to those of patients admitted to hospitals contracting with the dialysis organization. The mean length of stay for patients admitted to hospitals providing dialysis in-house was 6.0 days versus 5.7 days for patients admitted to hospitals contracting with the dialysis organization, a difference of 5.0%. We made similar observations for hospitals with ≤400 beds, hospitals that were not affiliated with an academic medical center, and hospitals designated trauma levels II to V. These differences were attenuated at hospitals with >400 beds, academic medical centers, and level I trauma hospitals.

Conclusions: These results suggest that use of a contracted dialysis organization may shorten the length of stay for patients who require dialysis during hospital admissions and this trend was more pronounced in smaller, non-university-affiliated hospitals.

Funding: None
The Impact of CRRT Modality on Filter Life

Lewis Magn, Iro Honkanen, Rebecca L. Hegeman, Chou-Long Huang, Prerna Kumar, Swe Zin Mar Winhtuoto, Christie P. Thomas, Melissa L. Swee, Benjamin R. Griffin. University of Iowa, Iowa City; IA.

Background: Increasing CRRT filter lifespan would save money, decrease iatrogenic blood loss, increase the time CRRT is actively running, and waste less nursing time. Filter clotting is a common reason for filter loss that can potentially be reduced. CRRT can be performed using convective clearance as in CVVH or diffusive clearance as in CVVHD. Whether convection or diffusion prolongs filter life over the other is unknown, but there are plausible arguments for both. CVVHD has no significant hemocoagulation within the circuit, whereas CVVH is subject to hemocoagulation as fluid is removed across the filter. However, pre-filter CVVH results in hemodilution prior to entering the filter that may mitigate the effects of the filter hemocoagulation. We hypothesize that filter life is longer in patients treated with CVVHD vs CVVH.

Methods: In this unblinded prospective randomized trial, patients are assigned to either pre-filter CVVH or CVVHD. The standard treatment protocol at the University of Iowa is to use citrate anticoagulation with a blood flow rate of 200 mL/min and a dose of 25 mL/kg/hr. Using a power of 0.8 and an alpha of 5%, and historical filter loss attributable to clotting of 60%, a total of 1,010 filters are needed to show a hazard ratio of at least 1.3 for filter loss. The primary outcome is average filter life, and secondary outcomes are mortality, intensive care unit LOS, hospital LOS, and renal recovery.

Results: Beginning March 25, 2020, we have enrolled 30 patients using a total of 90 filters (Table 1). The average filter life in CVVH filters is 36.8 ± 26.8, compared to 37.0 ± 31.9 hours in CVVHD filters (p=NS).

Conclusions: Data from 2 months of a planned 12-month prospective study comparing filter life in CVVH vs CVVHD shows no significant difference in filter life.

Table 1: Patient characteristics

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<tr>
<td>CVVHD</td>
<td>37.0 ± 31.9</td>
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Hemodialysis and Frequent Dialysis - 4

PO1232

Acute Dialysis in a High-Dependency Unit: A New Service with a Long-Term Legacy

Nasreen Samad,1,2 Fanel Ace,1 Nick Lever,2 Ian R. Carrasco Barber.3 Barts Health NHS Trust, London, United Kingdom; ‘Queens Hospital, London, United Kingdom.

Background: Continuous Renal Replacement Therapy (CRRT) in the intensive care unit (ICU) was stretched to the limit during the COVID-19 pandemic. COVID-19 was complicated by ARDS with dialysis requiring Acute Kidney Injury (AKI) patients admitted to ICU, in addition to chronic dialysis patients with COVID-19 requiring ICU admission. During the peak of COVID-19 there was a critical national shortage of consumables and dialysis fluids. In the United Kingdom (UK) required for CRRT in ICU. The ICU Service at Queens hospital, Romford, UK was no exception, the need to develop a viable urgent alternative therapy. A modified prolonged intermittent haemodialysis treatment 4-8 hours every day in selected patients was set up in the high dependency unit. This method required the installation of additional equipment and staff training.

Methods: During the peak of the COVID-19 pandemic, 5 beds in HDU were created with mobile reverse osmosis (RO) units to provide acute dialysis. Within 10 days of service approval, the dedicated area in HDU was equipped with all necessary laboratory, water, and consumables. In the interstial nursing training was provided by the senior dialysis nurse from the satellite dialysis unit based in the hospital who also supervised all sessions of dialysis 6 days a week. Patients selected were relatively stable with or without the need for assisted ventilation and inotrope requirement with Needlescreen up to 0.6mcg/kg/min. Dialysis treatment was provided 6 days for 4-8 hours per session.

Results: 12 COVID-19 patients received haemodialysis in the newly established HDU dialysis unit between 30th April to 30th May 2020. 5 had AKI associated with COVID-19 and 7 admitted with dialysis requiring Acute Kidney Injury (AKI) patients admitted to ICU, in addition to chronic dialysis patients with COVID-19 requiring ICU admission. Of the 12 patients 4 died, of whom 2 with AKI and 2 were on chronic dialysis. Of remaining 8, 5 patients were on chronic haemodialysis while 2 AKI patients continue to require haemodialysis and one became dialysis independent.

Conclusions: Prolonged intermittent renal replacement therapy in HDU was a viable alternative during the COVID-19 pandemic. The process was safe and manageable. The resources acquired during COVID-19 pandemic can be utilised in managing AKI and acutely ill chronic dialysis patients in a hospital where this service was not available before the pandemic.
Methods: In patients with central-venous catheter we measured central-venous oxygen saturation and hemoglobin levels during HD using the Crito-Line Monitor (Fresenius Medical Care North America, Waltham, USA). We measured CO using the Task Force Monitor (CNSystems, Graz, Austria). We tested the time series for stationarity using the Dickey-Fuller test, employed differencing to make the time series stationary, analyzed the association between the time series using cross-correlations and Granger Causality test.

Results: We studied 13 patients (59±14 years, 5 (38%) male, 93±22 kg pre-dialysis weight 170±7 cm tall) during 34 hemodialyses. Averaged across all treatments, CO and eUBBF were 4.7±1.0 and 1.3±0.4 L/min, respectively. CO showed a weak downward trend during hemodialysis. Cross-correlations showed no meaningful relationship between CO and eUBBF; Granger causality index was less than 20% in 8 treatments, albeit without clearly discernable patterns.

Conclusions: CO and eUBBF remained considerably stable during HD. Cross-correlations showed no significant relationships and Granger causality test suggests some form of a relationship which requires some further investigation. The clinical usefulness of eUBBF and future investigations will need to take additional parameters and dynamic relationships into account. Figure 1: Dynamic of CO and eUBBF flow during 34 HD; correlation coefficient from cross-correlations and Granger Causality index at a lag of -2 minutes.

PO1237

Accelerated Renal Replacement Therapy: Single-Institution Experience in Calculating Delivered Clearance During the COVID-19 Pandemic

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Introduction: Continuous renal replacement therapy (CRRT) is commonly used in the intensive care unit (ICU) setting. A minimum delivered dose 20 ml/kg/hr is associated with improved survival. Previous studies have revealed significant discrepancy between prescribed and delivered CRRT dosing. Before the COVID 19 pandemic, CRRT was the main modality used at our medical center. But to accommodate the increase need for RRT and our limited resources, accelerated renal replacement therapy (ARRT), providing the same total CRRT clearance but in half the time, was used. To ensure that the delivered dose was appropriate given the reduction in time, we calculated delivered clearance.

Case Description: ARRT prescribed dose was based on patient’s weight and time on therapy to achieve the equivalent 20cc/kg/hr over 24 hours. Delivered clearance (k) was calculated using the following formula K= Qd / Qt ∗ Quf / weight ∗ 24 hours where Qd = spent dialysate Qr = replacement fluid rate and Quf = net fluid removal rate. FUN = efluent urea nitrogen BUN= blood urea nitrogen. Hourly flowsheet with total time, Quf, Qd, and Qr were recorded during treatment by bedside nurse and reviewed to calculate the delivered clearance. 8 patients underwent 14 uninterrupted ARRT treatments. Total treatment time ranged from 8-10.5 hours. FUN/BUN ratio ranged from 0.5 to 1.05. The ratio between delivered clearance to prescribed clearance ranged from 0.83-1.08. Only 6 treatments (43%) achieved goal clearance.

Discussion: ARRT delivered clearance was only achieved 43% of time. While ARRT is a feasible modality when resources are limited, close monitoring of achieved clearance is needed to ensure that adequate dialysis is being delivered. Careful patient selection is important as delivered dose may be more difficult to achieve in obese patients. Although ARRT may be a practical alternative, continuous therapy would be ideal in the critical setting.

PO1238

Can COVID-19 Personal Hygiene and Social Distancing Reduce Bacteremia and Peritonitis Rates in Dialysis Patients

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Background: During COVID-19 pandemic affecting United Kingdom(UK) from March till May 2020 with social distancing guidelines in place (hand washing 5 times a day, 2 meter separation) and shielding in high risk individuals (including renal replacement therapy patients) and strict personal protective equipment (PPE) use in dialysis units we proposed the hypothesis that it may have positive impact on bacteremia in hemodialysis(HD) and peritonitis in peritoneal dialysis(PD) patients.

Methods: We compared Staphylococcus Aureus (SA) bacteremia in HD patients and PD peritonitis rates over three months March, April and May 2020 and compared the results with similar duration during 2019. We also viewed SA colonization rate in a satellite unit during this period.

Results: Quarterly Staph. Aureus bacteremia results showed yearly rate on 31 May 2019, 31 August 2019, 30 November 2019, 28 February 2020 and 31 May 2020 as 0.014, 0.021, 0.039, 0.038 and 0.024 respectively. However yearly PD peritonitis rates were significantly down from 0.386 to 0.238 from January 2019 to April 2020. MRSA colonization data from one satellite unit showed 2 out of 105 patients colonised in January 2019, of whom one decolonized by April 2020 while 16 patients in the same unit had MSSA colonization in January 2019 which was 15 out of 103 patients in February 2020 suggesting no significant difference in SA colonization rate.

Conclusions: Improvement in peritonitis rates is indicative of personal behavioural change with regards to common sense hygienic principles being very important in PD. However, in HD patients it had no impact on bacteremia at similar time one year ago indicating that possibly colonisation with MSSA/MRSA are important and strategies to de-colonisation of HD patients may help reduce episodes of bacteremia. There was some reduction in bacteremia rate from preceding quarter ending February 2020 to quarter ending May 2020 although not to May 2019 level. It will be difficult to say at this stage if this trend will be sustained in coming months.
PO1239
Effect of Lockdown to Stop Spread of COVID-19 on Physical Activity Levels of Hemodialysis Patients
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Background: On March 20, 2020, to stop the spread of the COVID-19, the New York State Governor issued a strict stay at home order for all tasks that were deemed as “non-essential” starting March 22 at 8PM. We would like to determine what change, if any, in physical activity levels (PAL) took place because of the lockdown order in HD patients.

Methods: HD patients were enrolled from 4 clinics in New York City starting in May 2018 and followed for a period of up to 1 year. Patients ≥18 years, on HD ≥3 months, able to walk, and owning a smartphone were enrolled. PAL was defined by steps taken per day measured by with a wrist-based monitoring device (Fitbit Charge 2). Patients still in the study as of March 22, 2020 were included in the study cohort. Average steps per day was calculated for Jan 1-Feb 13, 2020 and the five weeks prior to and after the lockdown went into place. A linear mixed-effect model was used to estimate the average steps per day and 95% confidence intervals. Socioeconomic parameters such as age, race, employment status, and education level were taken at the beginning of the study.

Results: 42 patients were included in this analysis. At enrollment patients were 55.1±11 years old, with a dialysis vintage of 4.5±4.4 years, and a BMI of 28.9±8.6 kg/m². 33% lived alone, 48% were single, 50% unemployed, 69% were African American, and 50% had an education level of some college or higher. Results on average steps per day are presented in Figure 1. Steps per day decreased significantly after the lockdown order with the most significant drop when the COVID-19 pandemic was declared a national emergency

Conclusions: There was a decrease in PAL due to the mandated lockdown. As sedentary behavior is a risk factor for negative outcomes in the HD population, we must implement interventions to promote PAL, such as intradialytic exercise.

Funding: Commercial Support - Fresenius Medical Care

PO1240
Affecting Factors on Circuit Lifespan in Continuous Renal Replacement Therapy
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Background: CRRT is a useful dialysis modality in hemodynamically unstable patients. But despite use of anticoagulants, clotting of circuit frequently occurs, which reduces efficiency of dialysis and causes the consumption of RBC, platelets, and coagulation factors. Especially, the more severe patient is, the lower blood flow into circuit due to hypotension can lead to decrease circuit lifespan. This study aims to investigate the factors that affects CRRT circuit lifespan.

Methods: This is a retrospective observational study. From January 2018 to December 2019, 38 patients who underwent CRRT in the ICU were enrolled. Outcomes were defined as the time of first clotting in circuit from CRRT initiation and the number of clotting during total application period. We statistically analyzed association of circuit lifespan with patient’s clinical characteristics.

Results: The results showed that first circuit clotting was significantly related to serum bicarbonate (r=0.453, p=0.005) and creatinine levels (r=0.359, p=0.026). The total number of circuit clotting were related to RBC and platelet transfusion respectively (r=0.779, p<0.001 / r=0.652, p=0.001). Blood pressure, infection, blood flow of circuit showed no relationships with circuit lifespan. The use of heparin and nafamostat increased circuit lifespan with patient’s clinical characteristics.

Conclusions: Circuit lifespan in CRRT is shorter in more serious metabolic acidosis and renal failure. Transfusion of RBC and platelet also reduces the circuit lifespan.
PO1242

Home Dialysis and Kidney Transplant Assessments in the ESRD Treatment Choices Payment Model

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Background: The End Stage Renal Disease (ESRD) Treatment Choices (ETC) Model is a proposed mandatory payment model that assigns financial bonuses and penalties to dialysis facilities as a function of home dialysis prevalence and kidney transplant incidence among patients with Medicare fee-for-service coverage. We used claims data to estimate distributions of facility-level home dialysis prevalence and kidney transplant incidence.

Methods: Using Medicare Limited Data Sets, we identified all Part B claims for outpatient dialysis for the treatment of ESRD in 2017. In each dialysis facility with a 132 adult patient-months, we estimated the percentage of patient-months with any home dialysis treatment. Using Part A claims in 2017, we also estimated the number of kidney transplants among dialysis patients in the facility.

Results: We identified 6263 dialysis facilities and 3,645,655 dialysis patient-months. Overall home dialysis prevalence was 10.8%. The distribution of facility-level home dialysis prevalence exhibited three features, as displayed: (1) over 54% of facilities with exactly 0% home dialysis prevalence; (2) among facilities with any home dialysis utilization, a unimodal distribution with peak prevalence near 12%; and (3) a small subset of facilities (4%) with home dialysis prevalence >90%. Regarding kidney transplant incidence, over half of facilities had 1+ transplant. The 75th and 90th percentiles of transplant count were 2 and 4, respectively.

Conclusions: In patients with Medicare fee-for-service coverage, facility-level home dialysis prevalence exhibits a nonnormal distribution, while kidney transplant incidence typically manifests few (or no) events per year. Both patterns will complicate statistical analysis of performance in the ETC model. Alternative methodology should consider assessments in regional clusters of facilities.

Funding: Commercial Support - Fresenius Medical Care

PO1243

Identifying Barriers to Implementing an Assisted Home Hemodialysis Program in Canada

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Background: Policy changes such as the Advancing American Kidney Health Initiative and the impact of the COVID-19 pandemic will accelerate the trend for more home dialysis. Expanding the pool of patients eligible for HHD will require health care practitioner assisted models to be developed and deployed. We hypothesize that many barriers to delivering assisted HHD (aHHD) exist and implementation of a successful program would require meaningful input from frontline home dialysis nurses. Our primary objective of this study is to survey these key stakeholders to identify these barriers.

Methods: We conducted a semi-structured focus group of leaders within our large Canadian home dialysis program to anticipate key aspects of implementing aHHD, including gauging local demand, identifying eligible patients, and recognizing essential operational components. From this, we constructed questionnaires for frontline nursing staff within HHD, peritoneal dialysis (PD) and assisted PD (aPD) programs. We performed a qualitative analysis to identify common themes and implementation barriers.

Results: Twenty-six responses from three sites were received. 20/21 PD nurses reported existing aPD programs expanded the eligible pool of PD patients. 5/5 HHD nurses felt an aHHD program would keep more patients on the modality and prevent technique failure. Only 2/5 felt aHHD should be offered as a transition to HHD. While 18/21 PD nurses reported they could easily identify patients for aPD, only 2/5 HHD nurses agreed. Patients with sensory deficits, functional impairments, and limited support networks were felt to benefit most from aHHD. Lack of confidence and phobias were not agreed upon. Behavioral and safety issues, clinical instability, and inability to manage device malfunction may be barriers to aHHD. Machine set-up, take-down, and establishing access were thought to be essential services. PD nurses felt clinical assessments should be routine. Few nurses felt complete assistance was necessary.

Conclusions: Our findings suggest there is a strong local demand for aHHD provided there is a clear criterion for enrollment and operational plans are well established. Frontline nurses have identified several important barriers to implementation which we will acknowledge and address when deploying our assisted home program over the upcoming year.

Funding: Commercial Support - Fresenius Medical Care

PO1244

Timed Repetitive Controlled Rotations of the CAR-170-C NXSTAGE Chronic Cartridge Hemodialysis Filter: An Original Newfangled Maneuver to Enable Heparin-Free Frequent Daily Home Hemodialysis

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Introduction: Heparin-free hemodialysis is usually obligatory in immediate post-operative states, bleeding diathesis and in critically ill patients. Conventionally, this is achieved through normal saline flushes, and regional citrate anticoagulation.

Case Description: An 87-yr white male with ESRD and atrial fibrillation on Wartarin, on maintenance daily Home Hemodialysis (HHD) with a NxStage machine, developed intra-abdominal abscess and sepsis following an urgent laparoscopic appendectomy. He required emergent pericardioacndescesis for cardiogenic shock from hemorrhagic pericardial effusion. Upon discharge, he was to continue heparin-free HHD. Despite the use of increasing volumes of normal saline flushes, his system clotted every day during HHD, therefore compromising his ability to carry out HHD. Our HD Senior Technician, had astutely observed that by a controlled timed manual and repeated to and fro rotation of the horizontally aligned CAR-170-C NXSTAGE Chronic cartridge, 60 degrees back and forth clockwise and counterclockwise, along the long axis of the filter, every 15 minutes, the filter stopped clotting. He has since then not needed saline flushes for smooth heparin-free HHD for several months.

Discussion: This is the first such report in the English literature. More studies are justified. We have hypothesized a mechanism and have named this the ‘Adam Locke Onuigbo Maneuver’. If confirmed by subsequent research, we propose that a miniaturized motor set-up that would be programmed to mimic these timed controlled partial rotations of the horizontally aligned CAR-170-C NXSTAGE Chronic cartridge could translate to a commercial success with major clinical benefits to patients needing heparin-free hemodialysis in all settings.

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PO1245

The Use of Etelcalcetide in a Special Cohort of Home Hemodialysis Patients with Severe Secondary Hyperparathyroidism
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Background: Secondary hyperparathyroidism (SHPT), is a common complication of chronic kidney disease. Its clinical consequences include extraskeletal vascular and valvular calcifications, changes in bone metabolism resulting in renal osteodystrophy, and an increased risk of cardiovascular morbidity and mortality. Etelcalcetide is an intravenous calcimimetic that increases sensitivity of the calcium-sensing receptor to calcium and decreases PTH, so it’s indicated for the treatment of secondary hyperparathyroidism (SHPT) in dialysis patients. In this observational study we are reporting our experience in treating SHPT by Etelcalcetide, in a very special cohort of sick, highly comorbid, bed, and home bound hemodialysis patients, at home with the assistance of a hemodialysis nurse, we called the program as Nurse Assisted Home Hemodialysis (NAHHD).

Methods: This is a retrospective observational sixth months study. Thirty home HD patients, managed by NAHHD program, were included in this study, average age 59.6 (26-87)year, 60% female, Etiology of ESRD was DM in 63%, 53% of them have hypertension. Vascular access AVF & AVG 60%, CVC 37%. Average comorbidities 9.4 (6-16). Patients were either naïve (30%) or switched from cinacalcet to Etelcalcetide due to non-compliance 50%, PTH resistance 31%, and bad tolerance of Cinacalcet 19%.

Results: The medication was well tolerated, two patients had GI side effects (6.5%), only with high dose of Etelcalcetide. The results of treating secondary hyperparathyroidism by Etelcalcetide in a special cohort of the patients for 6 consecutive months are illustrated in the graph.

Conclusions: This study showed that Etelcalcetide is efficient and well tolerated in this special group of sick, highly comorbid, bed and home bound home hemodialysis patients. The drug was well tolerated with minimal GI side effects.

Funding: Government Support - Non-U.S.

PO1246

Clinical Characteristics, Practice Pattern, and Outcome of Home Hemodialysis in India

Background: Maintenance hemodialysis is growing steadily and is the dominant renal replacement modality and Home HD has been in recent times. But, the profile, treatment characteristics could be different from the western context but it remains unknown.

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stress. Recent data demonstrated the role of TonEBP in EMT of cancer cells, however the exact mechanisms how TonEBP regulated cell phenotype were not known. The aim of this study is to investigate the role of TonEBP in hyperosmolarity-induced EMT of MCs and its mechanism.

Methods: The expressions of TonEBP and other osmotic stress-related genes including, sodium-myoinositol cotransporter (SMIT), betaine/g-aminobutyric acid transporter (BGT1) and aldose reductase (AR) were evaluated. EMT was evaluated by morphological changes of MCs and the expressions of E-cadherin and a-smooth muscle actin (a-SMA) after stimulation of high glucose (HG, 30-120 mM) and mannitol (30-120 mM). E-cadherin promoter activity was confirmed by luciferase assay. Binding of TonEBP- or β-catenin to E-cadherin promoter was identified by chromatin immunoprecipitation (ChIP) assay. The interaction between TonEBP and β-catenin was analyzed by immunoprecipitation.

Results: Both HG or mannitol enhanced the expression of TonEBP as well as SMT, BGT1 and AR from the concentration of 30 mM. HG induced EMT of MCs with a decrease in E-cadherin promoter activity, however mannitol did not induce EMT. HG (>30 mM) induced nuclear translocation of TonEBP which was associated with an enhanced binding to p-catenin. Mannitol also promoted nuclear translocation of TonEBP only at the highest concentration we tested (120 mM), however it was not associated with nuclear binding of TonEBP to p-catenin. In addition, mannitol induced a transient increase in nuclear β-catenin only with the highest concentration (120 mM) whereas HG showed a persistent increase in nuclear β-catenin.

Conclusions: This study demonstrated the role of TonEBP in peritoneal EMT for the first time. Not the increased expression of TonEBP per se but binding of TonEBP and β-catenin to the E-cadherin promoter is a key mechanism by which TonEBP induced EMT of MCs.

PO1249

CD4+ ICOS-Expressing T Cells Contribute to Peritoneal Fibrosis in Patients Receiving Peritoneal Dialysis

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Background: Long-term peritoneal dialysis (LPD) can affect the morphology and function of the peritoneum, which causes peritoneal fibrosis one of the major causes of peritoneal dialysis (PD) failure. Reliable treatment strategies that successfully prevent progressive peritoneal fibrosis are still lacking. We performed single-cell RNA sequencing (scRNA-seq) on PD fluid from patients at different stages.

Methods: Firstly, PD fluid from patients with short-term peritoneal dialysis (SPD) (< 6 months) and LPD (>3 years) were collected for scRNA-seq analysis, and genomic interaction differences of each sample were observed and analyzed. Secondly, peritoneum of PD patients and healthy inpatients were collected, and the expression of ICOS on CD4+ T cells and ICOSL, COL1A1, COL1A2, FN, CDH, IL6 on peritoneal mesothelial cells (MSC) was detected by qPCR, ELISA, flow cytometry and immunofluorescence. Thirdly, CD4+ T cells and ICOS+ T cells in PD fluid were co-cultured with MSC cell lines, then stimulated with anti-ICOS monoclonal antibody. Lastly, we used gene pathway analysis and KEGG analysis to find out the possible mechanism pathway.

Results: A total of 13,167 T cells and 6,090 MSC from 8 PD fluid biopsies were included. Through scRNA-seq analysis, we found that under the stimulation of high glucose and other components in PD fluid, compared with SPD patients, the proportion of ICOS+CD4+ T cells within T cells and ICOSL/MSC within MSC from LPD patients was respectively increased by multiple of 0.58 and 0.29. Furthermore, the expression of COL1A1, COL1A2, FN, IL6 also increased in PD fluid and peritoneum from LPD patients. CD4+ ICOS+expressing T cells interact with MSC by increasing the expression of profibrogenic proteins through ICOS/ICOSL pathway, then accelerate the progress of peritoneal fibrosis. Hence, an anti-ICOS antibody can alleviate peritoneal fibrogenesis by interfering with the interaction between MSC and ICOS+CD4+ T cells, providing a new therapeutic target for progressive peritoneal fibrosis.

Conclusions: CD4+ ICOS+expressing T cells contribute to peritoneal fibrosis, the anti-ICOS antibody can alleviate peritoneal fibrogenesis by interfering with the interaction between MSC and ICOS+CD4+ T cells, providing a new therapeutic target for progressive peritoneal fibrosis.

ICOS expression in T cells from SPD and LPD patients

PO1250

Geographic Variation of Home Dialysis Utilization in the United States

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Background: Increasing home dialysis utilization is an aim of the Advancing American Kidney Health Initiative. We estimated geographic variation in home dialysis utilization in a contemporary population of end stage kidney disease (ESKD) patients. We also assess the extent to which race and payers—possible systemic barriers to home dialysis—account for this variation.

Methods: Using USRDS Standard Analysis Files, we identified all prevalent ESKD patients on December 31, 2017 and ascertained the dialysis modality—in-facility hemodialysis, home hemodialysis (HHHD), or peritoneal dialysis (PD)—of each patient on that date. We categorized patients into 306 Hospital Referral Regions (HRRs), according to ZIP code of the dialysis facility. We estimated the standardized home dialysis ratio (SHDR) for each HRR, with expected home dialysis utilization as a logistic regression of age, sex, primary cause of ESKD, and ESKD duration. Subsequently, we added race and payer to the regression.

Results: The cohort comprised 513,669 patients. Home dialysis utilization was 12.0% (8.1% HHHD, 10.2% PD). Among HRRs, 5th and 95th percentiles of observed utilization were 5.3% and 23.2%, respectively, whereas 5th and 95th percentiles of SHDR were 0.43 and 1.82, as displayed. There were 87 HRRs (28%) with SHDR significantly <1.0 (P < 0.05) and 116 (38%) with SHDR significantly >1.0. Of the 10 HRRs with largest percent decreases, seven—Los Angeles, Houston, Manhattan, Dallas, East Long Island, Philadelphia, and San Antonio—had SHDR significantly <1.0. The addition of race and payer improved the discrimination of logistic regression, with black race and concurrent Medicaid enrollment as negative predictors of home dialysis utilization. However, the distribution of SHDR did not greatly compress. There were 29 HRRs (9%) with SHDR that decreased from significant to non-significant and 22 (7%) with SHDR that was revised from non-significant to significant.

Conclusions: Large geographic variation in home dialysis utilization exists. Race and payer are associated with utilization, but adjustment for these factors does not alter variation in SHDR.

Funding: NIDDK Support

Standardized Home Dialysis Ratio

PO1252

Higher Utilization of Peritoneal Dialysis Following the Executive Order on Advancing American Kidney Health

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Background: On July 10, 2019, the president of the United States issued an Executive Order on Advancing American Kidney Health (AAKH). As part of the order, the Centers for Medicare and Medicaid Services (CMS) issued a proposed rule regarding the End Stage Renal Disease Treatment Choice (ESTC) Model, which would employ payment mechanisms in Medicare Part B to incentivize home dialysis and kidney transplantation.

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In the revised SHDR, expected home dialysis utilization also reflects race and payer.
We assessed whether the period following the Executive Order was characterized by an increase in peritoneal dialysis (PD) utilization in incident end-stage kidney disease (ESKD) patients undergoing dialysis.

**Methods:** We analyzed submissions of form CMS-2728 (“ESRD Medical Evidence Report”) among patients with dialysis initiation in 2017-2019, according to an April 2020 extract from the Renal Management Information System. For each calendar month in 2017-2019, we estimated the percentage of patients whose primary type of dialysis was PD. We used logistic regression to assess whether PD utilization during each quarter of 2019 exceeded corresponding norms in 2017-2018, with adjustment for age, race, and sex.

**Results:** The cohort comprised 375,815 incident ESKD patients undergoing dialysis. PD utilization increased each year, to an apex of 12.0% in 2019. In September and October 2019, PD utilization exceeded 13.0%, as displayed. Relative to corresponding quarters in 2017-2018, adjusted odds ratios of PD utilization in 2019 were 1.06 (95% confidence interval, 1.02-1.11) during January-March, 1.08 (1.04-1.13) during April-June, 1.16 (1.11-1.21) during July-September, and 1.16 (1.16-1.21) during October-December.

**Conclusions:** The Executive Order on AAKH and the proposed ETC Model together marked the advent of a period of significantly higher PD utilization among incident ESKD patients.

**Funding:** NIDDK Support

**PO1254**

Disparities in Home Dialysis Care and Links to Kidney Transplantation: Inequities Among African American ESRD Patients in Detroit, Michigan

**Background:** African Americans with ESRD continue to fare worse than their White counterparts for graft and patient survival after kidney transplantation. These disparities may partly reflect differential use of peritoneal dialysis (PD) and hemodialysis (HD) among African Americans who undertake maintenance renal replacement therapy – although PD and preemptive transplants are linked to longer survival and better kidney transplantation outcomes, emerging studies suggest that African Americans less often receive PD than Whites. The current analysis sought to explore whether disparate use of PD would persist in the context of an inner-city hospital that serves a majority African American patient population, within a predominantly African American city.

**Methods:** We compiled electronic medical record data from 2012-2018 for African American (n = 1078) and White (n = 155) ESRD patients who initiated maintenance dialysis through either HD or PD. We also compiled data on successful kidney transplantation in these patients, as well as sociodemographic and health status data, including BMI, age, PRA peak, race, sex, diabetes, and hypertension.

**Results:** Fisher’s exact tests showed that African American patients were 2.28 times more likely to receive HD than PD as compared to White patients (p = .004), and that patients receiving PD were 2.09 times more likely to be transplanted (p = .01). Although attenuated, a robust relationship between PD and kidney transplantation persisted in a logistic regression that controlled for sociodemographic and health status variables (OR = 1.60, p = .10).

**Conclusions:** Disparities in use of PD can be observed even in the context of an inner-city hospital serving a predominantly African American population. Aligned with the Advancing American Kidney Health initiative to achieve 80% home dialysis by 2025, future research must identify and intervene on patient and clinician factors that contribute to lower PD use among African Americans.

**PO1255**

Home-Based Dialysis Care Among Veterans Within the Veterans Affairs Health Care System, 1995-2014

**Background:** Contemporary US policy is focused on proportionally increasing home-based dialysis care, however overall rates are lower in the US compared to other similarly developed countries. Use of peritoneal dialysis (PD), the most common home-based dialysis modality, is even lower among US Veterans. How the characteristics and rates of PD utilization among US Veterans vary by health system affiliation, is unknown.

**Methods:** Using United States Renal Data Systems (USRDS) combined with Medicare data for the years 1995-2014, we matched US Veterans initiating dialysis (n = 14,904) to Veterans and Medicare non-Veterans receiving care in the community. Matching was performed in a 1:1 ratio according to year of dialysis initiation (+/- 2 years), age (+/- 2 years), gender, race, and reported cause of kidney disease. A total of 668 veterans initiated PD within the VA, compared to 890 Veterans and 1,436 non-Veterans in the community.

**Results:** After adjustment for patient age, gender, race, ethnicity, and region of residence, odds (AOR) of PD initiation within the VA was highest among those with diabetes mellitus (AOR: 1.36; CI: 1.18-1.57), tobacco use (AOR: 1.59; CI: 1.25-2.02), and a history of cancer (AOR: 1.49; CI: 1.10-2.02) and lowest for those of Hispanic ethnicity (AOR: 0.73; CI: 0.56-0.95), history of heart failure (AOR: 0.74; CI: 0.62-0.88). In 1995-1996, patients receiving Medicare coverage within the community were most likely to utilize PD compared to Veterans within the community and within the VA (18.9% vs. 9.6% and 8.2%, respectively), an observation that remained consistent over time. PD utilization among African-American Veterans was lower overall, although more closely approached estimates in white Veterans in more recent years. Veteran survival vs. Medicare controls is shown in Figure 1.

**Conclusions:** While PD utilization among Veterans is lower within the VA, the observed mortality benefit for care receipt within the VA was reassuring.

**Funding:** NIDDK Support

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**PO1253**

Challenging Assumptions of Outcomes and Costs Comparing Peritoneal and Hemodialysis

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**Background:** Policy makers have suggested that increasing peritoneal dialysis (PD) use would improve end-stage kidney disease (ESKD) outcomes and reduce Medicare spending.

**Methods:** Using Medicare claims, we exploited an idiosyncratic Medicare coverage rule to conduct an instrumental variable analysis comparing mortality, hospitalizations, and Medicare spending between PD and hemodialysis (HD) in uninsured adults with incident ESKD. Uninsured patients usually receive Medicare at dialysis month four; however, those starting with PD receive Medicare at dialysis start and retroactive pre-dialysis coverage for the entire calendar month of dialysis start. Because pre-dialysis coverage is essential for PD catheter placements, the rule encourages more PD use among patients starting at the end of the month by increasing pre-dialysis coverage. We used dialysis start day as an instrumental variable to mitigate selection bias when comparing outcomes and costs of the two modalities.

**Results:** Starting dialysis later in the calendar month was associated with an increased probability of using PD at day 1 (absolute increase of 1.0% for every 10 days later in the month, 95% CI: 0.8%, 1.3%) and at month 12 (absolute increase of 0.7% for every 10 days later in the month, 95% CI: 0.4%, 1.0%). We observed no significant absolute difference between PD and HD for all outcomes: 12-month mortality, −0.4% (−3.4%, 1.8%), hospitalizations during months 7-12, 0.01% (−0.16, 0.17) per patient, and Medicare spending during months 7-12, $2,803 (95% CI: −$6,355, $508) per patient. We assessed the potential role of selection bias in prior studies by repeating the same analyses using traditional regression methods. In contrast to the instrumental variable model, when using traditional regression methods, PD was associated with statistically significant decreases in mortality but significant increases in costs.

**Conclusions:** Using an instrumental variable analysis, PD did not result in improved outcomes or lower costs when compared to HD. We observed evidence of selection bias when using traditional study methods. Policy makers eager to promote home dialysis should temper expectations of improved outcomes and reduced spending.

**Funding:** NIDDK Support

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PO1256
Trends in Automated Peritoneal Dialysis (APD) Prescriptions in Adult Chronic Dialysis Patients at a Large Dialysis Organization from 2015 to 2019
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Background: Benefits of patients dialyzing at home have been well-reported. Peritoneal dialysis (PD) has grown in recent years and is expected to grow further due to the recent executive order encouraging home dialysis. Trends in APD prescriptions have not been well-described in the literature. This current retrospective analysis aims to describe trends in APD prescriptions from 2015-2019.

Methods: All demographic, lab, and prescription data were retrospectively extracted and de-identified from a LDO’s (Fresenius Kidney Care) electronic data warehouse. Patients included in the analysis were adults with chronic kidney disease on dialysis, incident to APD from Jan 1, 2015 to Dec 31, 2019, completed APD training, had at least one APD treatment record, and no data quality issues with their records. Patients were stratified by the year they started PD (2015, 2016, 2017, 2018, 2019) and patients’ first APD prescription information was summarized.

Results: 16,047 patients were eligible for inclusion. The number of APD new starts eligible increased from 2,005 patients in 2015 to 4,751 patients in 2019, as did mean patient age (56.0 years in 2015 to 58.3 years in 2019, p<0.05). Fewer patients were prescribed daytime exchanges (7.6% in 2015 to 4.8% in 2019, p<0.05) and of those with daytime exchanges, the majority (~93% in all years) had 1 exchange. Table describes other prescription parameters by year.

Conclusions: Comparing 2019 to 2015 initial PD prescription patterns, there have been reductions in cycler volume, total number of exchanges, and prescriptions for prescribed daytime exchanges (7.6% in 2015 to 4.8% in 2019, p<0.05) and of those with daytime exchanges, the majority (~93% in all years) had 1 exchange. Table describes other prescription parameters by year.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

PO1257
Development of a Robust Peritoneal Dialysis Program
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Background: Despite ample evidence supporting the superior performance of Peritoneal Dialysis (PD) in a value-based healthcare system, this modality remains conspicuously underutilized in the USA. We implemented a multifaceted strategy to develop a high-performing PD facility in 28 months.

Methods: VIPKIH, a private PD Center, was created through an affiliation with a five-doctor nephrology group in Florida and Medicare Certified 8/2017. Our physicians adopted an “upstream” approach to patient selection by promoting timely access to care for CKD 3b-4/5. KD education was mandatory. Social Media storytelling fostered a vibrant virtual CKD community. Patient vetting incorporated multidisciplinary evaluation of support systems and socio-economic and cultural determinants of health within their specific ecosystem. Expedited referral to an expert surgeon for laparoscopic cather insertion was crucial. Home training and on-demand home visits were conducted routinely. 24/7 tele-access to clinicians and an open-door policy for non-routine care was instituted. Two satellite locations were available. FTE staff included an Administrator/Population RN, two PDRN, Assistant Administrator and PTE RD and MSW.

Results: From 9/2017 through 12/2019 (28 months), 66 patients were admitted to VIPKIH (Program Vintage 58 PD patient-years). Demographics: female 50%, 64.7 years (25-86), Caucasian 55%, African-American 23%, Hispanic 15%. Comorbidities: DM 47%, CHF 36%, DM/CHF 21%, Morbid Obesity 14%. As of 12/31/2019, 37 patients were on CCPD with good adequacy, 29 discharged: 1 Recovery, 7 Transplant, 3 Relocation, 4 Deceased, 1 Hospice, 13 Dropouts (5 peritonitis, 1 tunnel infection, 2 leaks, 1 inadequate dialysis, 3 disability, 1 burnout). Performance rates per 100 ESRD patient years (VIPKIH vs Benchmarks): Peritonitis (10 vs 25), tunnel infection (2 vs 8), admissions (72.6 vs 170), hospitalization days (631 vs 1120), 30 day readmission (16.7% vs 37%), ED/Short-Stay (12.1 vs 350), transplant (12.9 vs 3.5), mortality (6.9 vs 22.5).

Conclusions: Our outcomes reflect the delivery of exceptional PD care. Our pragmatic approach to developing a successful PD program encompasses humble leadership which lays the foundation for building powerful relationships between all stakeholders through effective communication, education, and collaboration, promotes shared decision-making and facilitates timely access to integrated, longitudinal, patient-centered care.

Funding: Clinical Revenue Support

PO1258
Acute Peritoneal Dialysis in Obese Patients During the COVID-19 Pandemic
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Background: Due to increased risk for infection, fluid leak, metabolic complications and poor uremic solute clearance, concerns have been raised in using peritoneal dialysis in obese patients. However, due to unprecedented need for renal replacement therapy (RRT) in New York City during the COVID-19 pandemic, acute peritoneal dialysis (APD) was initiated in patients regardless of body mass index (BMI).

Methods: 36 patients who received PD between April 8, 2020 and May 8, 2020 were categorized into 3 groups based on BMI calculated using admission height and weight. Group 1 with BMI < 30, Group 2 with BMI 30-40 and Group 3 with BMI > 40 kg/m². Treatment goals included correction of hyperkalemia, hyperphosphatemia, acid-base abnormalities, reduction in blood urea nitrogen (BUN), creatinine and maintaining euvolemia. All patients were initially started on manual exchanges every 1-2 hours (Total volume 18-20 L/24 hours) and eventually most were changed to automated PD (Total volume 18-20 L/24 hours). We compared the frequency of treatment-related complications among the groups.

Results: Of the 36 patients, 13 had BMI < 30, 18 patients had BMI 30-40, and 5 had BMI > 40, one of whom had BMI > 50 kg/m². Patients showed improvement in serum creatinine, BUN, phosphorous, potassium, and bicarbonate. All had adequate ultrafiltration and improved volume status after optimization of PD prescription. No differences were observed between groups in achievement of treatment goals. No patients in any group required discontinuation of PD because of treatment-related complications or insufficient dialysis.

Conclusions: APD was successfully performed in obese, and morbidly obese patients during the COVID-19 pandemic. Treatment goals were achieved based on relevant parameters and there were no increases of treatment related complications compared to non-obese patients. Acute PD should not be restricted based on elevated BMI.

PO1259
Comparing Mortality of Peritoneal and Hemodialysis Patients in an Era of Medicare Reform
Virginia Wang,1 Cynthia Coffman,2 Linda L. Sanders,2 Abby Hoffman,2 Caroline E. Sloan,2 Shou-Yih D. Lee,2 Richard A. Hirth,2 Matthew L. Maciejewski,1 Durham VAHCS, Durham, NC; 2Duke Univ, Durham, NC; 3Univ Mich, Ann Arbor, MI; 4UNC-CH, Chapel Hill, NC.

Background: Medicare’s 2011 prospective payment system (PPS) encouraged the expansion of peritoneal dialysis (PD), which is preferred by many patients and less costly than in-center hemodialysis (HD). Prior studies have shown PD to be associated with lower or equivalent mortality to HD. Expansion of PD services after the PPS may change

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
the relative mortality of PD and HD if PD is increasingly used by sicker patients. This may mitigate the comparative risk of mortality between PD and HD modalities in cohorts of patients spanning Medicare PPS.

Methods: From the US Renal Data System, we compared 2-year all-cause mortality in a cohort of incident dialysis patients in 2006-2013. Patients were censored at renal transplantation or the end of the year prior to follow-up. Baseline characteristics of HD and PD patients were assessed via standardized differences and Kaplan-Meier curves. To compare HD and PD 2-year survival, a Cox proportional hazards model was fit using inverse probability of treatment weights (IPTW, generated from patient demographic and clinical characteristics) by incident year, adjusting for patient and dialysis market characteristics.

Results: PD use in the first 90 days increased from 9.5% of incident patients in 2006 to 13.6% in 2013. Crude 2-year mortality was 16.7% for PD and 27.6% for HD. There were no differences in patient characteristics between pre- and post-policy cohorts. In IPTW-adjusted survival analysis across all incident years, no differences in 2-year mortality were found for those who attempted PD in the first 90-days of dialysis compared to patients receiving HD (example: HR, 0.93; 95% CI, 0.84 to1.04 for 2006 incident cohort). Mortality differences between PD and HD did not change over time (p=0.23).

Conclusions: In PD initiation over time occurred without changing the patient mix towards sicker patients. After adjustment, we found no evidence of mortality differences between PD and HD before and after payment reform. These findings suggest that Medicare PPS improved the value of dialysis care such that PD service use increased without adversely affecting patient mortality. Still, PD uptake in the US still lags that of many countries. Future policy initiatives may be needed to continue to increase clinically appropriate PD uptake.

Funding: NIDDK Support

PO1260 Duration of Serum Phosphorus Control Associated with Overall Mortality in Patients Undergoing Peritoneal Dialysis Jun Ai, Zhiwen Xiao, Nanfang Hospital, Southern Medical University, Guangzhou, China.

Background: Serum phosphorus (SP) level was closely associated with overall mortality and cardiovascular events, while the role of SP controlled duration was not fully recognized. Our study is to identify the relationships of SP controlled duration with clinical outcomes in patients undergoing peritoneal dialysis (PD).

Methods: This was a retrospective cohort study, including PD patients with regular follow-up in our center from Jan 1st, 2009 to Jun 30th, 2019. Clinical data were collected at baseline and at 3, 6, 9, 12, 18, 24, 30, 36, 48, 72, 96, and 120 months after dialysis. SP levels changed degree of SP over baseline, and SP controlled duration were analyzed with overall mortality, PD withdrawal, and combined endpoint. Degree of SP change over baseline (%)= (SP level at follow-up point - baseline SP level) x 100 / baseline SP level.

Duration of SP control (months) = PD vintage when patients reached hyperphosphatemia - PD vintage when patients decreased to less than 1.78 mmol/L after PD.

Results: 530 patients entered the analysis [the mean age was 45.4 ± 1.5 years old, 57.2% were male, the median PD vintage were 32 (15-54) months]. 86.0% patients had lower degree was associated with higher overall mortality [HR, 1.012 (1.004-1.020); p<0.001]. The median SP controlled duration was 13 (5-28) months, the longer SP controlled duration, the lower overall mortality [HR, 0.9680 (0.956-0.981); p<0.001], the lower SCR level at baseline (HR, 0.9941 [0.987-1.000]; p<0.001), and combination endpoint [HR, 0.9820 (0.976-0.989); p<0.001]. A categorized, patients whose SP never controlled had the maximum overall mortality (24.6%), the duration more than 12 months greatly improved the overall mortality [HR 0.197 (0.082-0.458); p<0.001]. After categorized, patients whose SP were tightly associated with overall mortality, PD withdrawal and combined endpoint. HR, 0.964(0.954-0.973); p<0.001. Patients whose SP never controlled had the highest overall mortality (24.6%), the duration more than 12 months greatly improved the overall mortality [HR 0.197 (0.082-0.458); p<0.001].

Conclusions: A total 612 incident PD patients between January 2006 and August 2019 were included in this study. The primary outcome was all-cause mortality and the main exposure of interest was a cumulative dose of statin. For defining the cumulative dose for statin, the definition of daily dose by World Health Organization was used. Patients who used statin for at least 28 cumulative defined daily doses (cDDD) after initiation of PD were defined as statin user. PD users receiving HD (example: HR, 0.93; 95% CI, 0.84 to1.04 for 2006 incident cohort).

Results: A total of 717 USPD patients were matched to HD-CVC patients. During follow-up (mean 1.2 ± 0.6 years in both groups), USPD patients were hospitalized at a rate of 1.21 admissions/patient-year (pt-yr), vs. 1.51 admissions/pt-yr for HD-CVC patients. This corresponded to a 24% lower rate of hospitalization among USPD patients (adjusted incidence rate ratio 0.76, 95% confidence interval [CI] 0.65 – 0.88). Mortality rates were likewise lower among USPD patients compared to HD-CVC patients (0.08 vs 0.11 deaths/pt-yr) although this trend did not achieve statistical significance (adjusted hazard ratio 0.84, 95% CI 0.68-1.04). No difference was found with respect to KDOQI score.

Conclusions: Among patients with little to no predialysis planning, use of USPD is associated with a lower subsequent hospitalization rate and a trend towards lower mortality rate, compared to HD-CVC. In areas where facilities and clinical expertise exist, more widespread adoption of USPD may lead to better outcomes among patients with limited predialysis planning.

PO1262 Efficacy of Statin Use in Patients Undergoing Peritoneal Dialysis Hyung Won Kim, Geouk Woo Ryu, Shinchun Kang, Yoo-Ju Nam, Beom Jin Kim, Yeoung University College of Medicine, Seoulmeun-gu, Seoul, Republic of Korea.

Background: The efficacy of statin use in patients with PD have not been proven in large studies. Because most of studies included only HD patients or a small number of PD patients, there is lack of evidence whether statin have positive effect on PD patients or not. The aim of this study was to reveal the efficacy of statin uses in PD patients.

Methods: A total 612 patients between January 2006 and August 2019 were included in this study. The primary outcome was all-cause mortality and the main exposure of interest was a cumulative dose of statin. For defining the cumulative dose for statin, the definition of defined daily dose by World Health Organization was used. Patients who used statin for at least 28 cumulative defined daily doses (cDDD) after initiation of PD were defined as statin user. PD patients receiving HD were defined as PD-CVC patients.

Results: During a median follow-up duration of 33.0 months (IQR, 15.0-63.0), the primary outcome occurred in 124 (20.2%) patients. The mean age at initiation of PD was 53.6±14.5 years and 329 (53.8%) patients were men. The number of statin users was 390 (63.5%) and the number of patients who use statin before starting PD was 311 (50.8%).

Statin use (as2c cDDD) was associated with a lower risk of all-cause mortality (HR, 0.32; 95% CI, 0.20-0.52) after adjustment and this association was also consistent regardless of the use of statin before PD initiation. Adjusted hazard ratios for the all-cause mortality were 0.87 (95% CI, 0.53-1.43), 0.39 (95% CI, 0.20-0.75), 0.41 (95% CI, 0.18-0.81), and 0.13 (95% CI, 0.06-0.26) for the 28-365, 366-730, and 731-1095, respectively, compared with cDDD<28. The risk reduction of statin may be dose dependent.

Conclusions: Statin use was associated with a reduced risk of all-cause mortality in incident PD patients with or without statin use before dialysis.


Background: With the exception of some national registries, data referred to mortality or hospitalization within a single large international peritoneal dialysis (PD) institution are seldom reported. Objectives: To study all-cause mortality, transplantation rate, hospitalizations and peritonitis rates in our large PD program during 2018.

Methods: Observational, prospective registry in 8 countries. The following variables were tracked: crude mortality rate and causes, hospitalization variables (number of hospitalization days per patient; number of hospitalization episodes per patient; number of days per hospitalization episode; causes of hospitalization; peritonitis rate/ episodes/ year and patient months at risk to a peritonitis episode) and transplantation rate.

Results: By the end of December 2018, 1207 pt. were treated (11 countries) but only 8 countries submitted data. Evaluated population as “patients treated at risk during the year”; AR (319.5), BO (173.5), DE (137), HU (103), PL (97), UR (69.5), CL (27), KZ (7). Crude mortality rate was 13.1%, same if first 90 days on therapy were excluded. Lowest mortality was seen in HU (9.9%) and highest in DE (19.3%). Causes of death: cardiac 32%, all type infections 22% [Sepsis 78%, PD related 11% (as 0.7% of total mortality), pulmonary 3.7%, others 7.4%], vascular 10%, gastrointestinal 3.3%, unknown 10.7% (1.6%, 0.7%, 0.7%, other 0.7%); 2.5% of patients had 2 or more follow-up death per patient-year and 7.6 days of hospitalization per patient-year. N. of days per hospitalization episode was 13.7. Causes of hospitalization: PD related 38%, cardiovascular 17%, non-PD infection sepsis 10.2% (higher in LA, 16.6%), vascular access 2.1%, unknown 4.5%, others 23.3%. Global peritonitis rate was 0.18 episodes/patient-year at risk (1 episode every 66 m). However, large differences were seen among countries. Transplantation rate was 6.5% (much higher in UR). PD was withdrawn in 35% of pt. Country specific data have been evaluated but are not shown here.

Conclusions: The use of a common registry in our institution increases quality and allows homogeneous comparisons across countries that if promptly addressed may increase patients’ outcomes. Our series may bring light into the PD community as one of the ever largest tracked in a single institution.
Approach to identify individual risk factors leading to the index hospitalization and targeted interventions are not directly designed into clinic workflow. Often, information regarding these specific risk factors are not exact. We identified a need to standardize practice in our PD clinic by conceiving an action checklist for nephrologists and nurses to minimize index admissions.

Methods: Our quality improvement project sought to identify risk factors by analyzing the cause of admission from our cohort of 103 PD patients over 8 months. We divided reasons for admission into related and unrelated to PD. Based on these categories, we created a list of potential contributory risk-factors for admission. We also surveyed providers to determine key technical components for a clinic checklist to encourage early recognition of the risk-factors.

Results: Of the 105 individual admission events identified from June 2018 to March 2019, 45% were identified as PD-related. Such admissions included peritonitis (34%), gastrointestinal dysfunction (9%), electrolyte derangement (13%), hypotension (12%), and respiratory dysfunction (10.6%) and catheter dysfunction (10.6%). 37 admissions (35%) were readmissions in the last 30 days, of which 60% were PD-related. From these results we designed a snapshot of trends of the prior 3 months’ vital signs, electrolytes, weights, PET results, PD adequacy results, urine volume, peritonitis history and current medications for clinicians to review pre-visit.

Conclusions: We are currently implementing this checklist in our monthly PD clinic visits. Though the idea was conceived prior to the pandemic, we have increasingly seen the benefit of a clinical trends snapshot readily available as we transition to Telehealth visits to prevent patients’ exposure to COVID-19. This method assists the clinician in triaging remotely. Ultimately, through utilization of this tool, we hope to unify our practice pattern in the clinic to reduce admission rates by promoting proactive, not reactive, interventions.

PO1267

Lung Comets and Hydration Status in Peritoneal Dialysis Patients

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Background: Multiple diagnostic options to determine hydration status in peritoneal dialysis (PD) patients are available. Multifrequency bioimpedance spectroscopy (MBHS) is a non-invasive method of estimating body composition, including total body water (TBW), extracellular water (ECW), intracellular water (ICW) and the ratio between both spaces (ECW/ICW). Lung ultrasoundography (LUS) and lung B-lines (lung comets) can be used for the evaluation of extravascular lung water. Ultrasound evaluation of inferior vena cava (UVIC) provides a non-invasive assessment of a patient’s hemodynamic and volume status. N-terminal pro-brain natriuretic peptide (NT-proBNP) is related to fluid status and fluid distribution. The aim of our study was to assess fluid status in PD patients comparing four different methods: MBHS, LUS, UVIC and NT-proBNP.

Methods: We performed a single-centre cohort study in 19 PD patients. The body composition was measured using the portable whole-body MBHS device, BCM® (Fresenius Medical Care, Germany), LUS with portable US device (Vscan, GE Corporate), UVIC index with SonoSite US device. NT-proBNP was measured in a one-step sandwich chemiluminescent immunoassay (Siemens Healthcare Diagnostics, Newark, USA).

Results: The mean age of patients was 54±10 years, mean dialysis vintage 53 (10-194) months were men. Thirteen (68.4%) patients had fluid overload (FO)>1.1 L. Data of patients are presented in table 1. We found a statistically significant correlation between the number of lung comets and ECW/ICW ratio (r=0.496, P=0.031) and NT-proBNP (r=0.759, P<0.0001). In contrast, there was no significant correlation between the number of lung comets and UVIC (r=0.221, P=0.364).

Conclusions: According to our results, LUS with lung comets, MBHS with ECW/ICW ratio and NT-proBNP are useful and complementary methods for evaluation of fluid status in PD patients.

PO1268

Outcomes of Urgent-Start Peritoneal Dialysis in a Retrospective Cohort


Background: Peritoneal dialysis (PD) has shown to have early survival benefit and increased patient satisfaction when compared to in-center hemodialysis. Despite this, 87% of patients with End Stage Renal Disease (ESRD) start hemodialysis, while only 10% of patients start RRT via peritoneal dialysis. The Advancing American Kidney Health Initiative was launched in July 2019, with the goal of having 80% of incident ESRD patients on a home modality or transplant by 2025. In this context, major changes will need to occur so patients starting RRT can have increased access to home dialysis. Conventional start peritoneal dialysis requires the PD catheter to rest for several weeks.
after insertion prior to use. This limits the use of PD for patients that need to start RRT urgently. An alternative is urgent start PD where the dialysis can be started as soon as 1 day after catheter insertion. There is growing evidence that urgent start PD is a safe and effective alternative to urgent start hemodialysis.

Methods: A retrospective analysis of patients that underwent urgent start peritoneal dialysis from 2013 to 2019 at the Washington University Home Modalities Dialysis Clinic was conducted. Complications (including catheter leak, catheter malfunction, infections and bleeding episodes), hospital admissions in the first 30 days after catheter placement and time patients remained on PD after urgent start were examined. Among 41 patients were started on urgent PD during the study period. 12 patients (29%) were started as an inpatient and 29 patients (71%) as an outpatient. Median time from catheter placement to initiation of dialysis was 5 days. Major complications including per-catheter leaks occurred in 3 patients (7.3%), catheter malfunction in 7 patients (17.1%), peritonitis within the first 4 weeks occurred in 3 patients (7.3%) and 2 patients (4.8%) developed an exit site infection. There was 1 patient that had a major bleeding event after catheter placement. 11 patients (27%) were admitted to the hospital within the first 30 days after urgent start PD. During the follow-up period, the median time patients were on PD after urgent start was 15.9 months, 16 patients (39.02%) transitioned to another form of RRT. PD was continued.

Conclusions: As has been demonstrated in previous studies urgent start PD remains a viable option for initiation of RRT and ensures increased access to home dialysis.

Megaloblastic Anemia in a Patient on Peritoneal Dialysis Returning from Kenya

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Introduction: We describe a case of atovaquone-proguanil (A-P)-related toxicity in a patient treated with peritoneal dialysis (PD).

Case Description: A 40-year old man treated with PD presented 48 hours after return from Kenya with a diffuse erythematous rash, dysphagia, fever and weight loss. Clinical evaluation showed a maintained general status, diffuse non-palpable purpura and tonsillitis. Laboratory testing revealed an elevated c-reactive protein and laboratory values. A-P was stopped. PD was continued.

Discussion: DNA synthesis requires the presence of thymidylate, a nucleotide present in cells in rate-limiting amounts. Both folate and vitamin B12 are crucial cofactors in the rate of formation of thymidylate. Vitamin B12/folate deficiency or drugs affecting the vitamin metabolism. Vitamin B12 deficiency or drugs affecting the vitamin metabolism.

Megaloblastic anemia appears as a potential nutritional-evaluation tool, with some authors defining protein-energy wasting as PA <4.5. Higher HSCBMCr would indicate either a muscle mass anemia or those with atrial fibrillation. Its adequate cut-off point in PD remains unclear. Reports in CKD/HF-patients suggest a cut-off point at 2.0, which added to a PA value <6, would work as markers of poor cardiovascular prognosis. But, how could these markers work in our population.

Methods: A prospective study included patients’ first simultaneous acquisitions of biochemical and peritoneal equilibration test (PET).

Phase Angle and Extracellular Mass to Body Cell Mass Ratio in Peritoneal Dialysis Patients


Background: Extracellular mass to body cell mass ratio (ECM/BMCr) is an important marker of malnutrition and a described independent predictor of long-term mortality. This study aimed to evaluate ECM/BMCr as a potential indicator of outcome in patients on PD.

Results: As has been demonstrated in previous studies urgent start PD remains a viable option for initiation of RRT and ensures increased access to home dialysis. The use of A-P is contra-indicated in CKD, due to the risk of proguanil accumulation and consecutive hematologic toxicity. Treatment is based on discontinuing PD was continued. Patients Undergoing Chronic Peritoneal Dialysis

PO1270 Serum Uric Acid, Mortality, and Decline of Residual Kidney Function in Patients Undergoing Chronic Peritoneal Dialysis

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Background: Hyperuricemia is known to be associated with cardiovascular (CV) events and mortality in patients with chronic kidney disease (CKD). However, in the particular case of patients on chronic dialysis, the relationship between serum uric acid (UA) values and all-cause mortality is less consistent. The aim of this study was to identify the correlation between UA, on one side, and all-cause mortality (primary endpoint) and the rate of decline of residual kidney function (RKF) (secondary endpoint), on the other, among patients undergoing chronic peritoneal dialysis (PD).

Methods: We conducted a single centre, retrospective, observational cohort study of 682 patients who started PD between 1990 and 2019. We recorded essential demographic, clinical and laboratory data at baseline, 6, 12 and 24 months. We categorized the study population according to the median of mean UA levels during the first 3 months on PD.

Conclusions: As has been demonstrated in previous studies urgent start PD remains a viable option for initiation of RRT and ensures increased access to home dialysis.

Phase Angle and Extracellular Mass to Body Cell Mass Ratio in Peritoneal Dialysis Patients


Background: Extracellular mass to body cell mass ratio (ECM/BMCr) is an important marker of malnutrition and a described independent predictor of long-term mortality. This study aimed to evaluate ECM/BMCr as a potential indicator of outcome in patients on PD.

Results: As has been demonstrated in previous studies urgent start PD remains a viable option for initiation of RRT and ensures increased access to home dialysis.
Conclusions: 24-hour ambulatory pulse pressure is the most significant predictor of peritonitis. Post hoc: for clinical outcomes in PD patients, and systolic blood pressure is an independent predictor for cardiovascular outcomes. Meanwhile, it suggests that the associations can be explained by vascular calcification and volume status in PD patients.

Funding: Other NIH Support - National Natural Science Foundation of China (NSFC: 81670892)

PO1273

Differences in Protein Energy Wasting Indicators by Peritoneal Dialysis Patients

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Background: In chronic kidney disease (CKD) population protein energy wasting syndrome (PEW) is a prevalent problem with a multifactorial etiology (uremia, low energy and protein intake, basal energy expenditure increased, inflammation, metabolic acidosis, nutrient loss during renal replacement therapy (RRT). In peritoneal dialysis (PD) patients with high peritoneal transport tend to have enhanced clearance of small solutes and shows low ultrafiltration capacity and higher inflammatory state, that impacts negatively in nutritional status. We evaluate the differences in nutritional status indicators and the association of high type transport peritoneal with protein energy wasting (PEW) syndrome.

Methods: Cross-sectional study of a cohort of 36 patients with CKD on automated peritoneal dialysis (APD) [18 men, 18 women; age, 55.1 ± 13.3 years; dialysis duration, 7 ± 6 years]. Peritoneal transport characteristics were classified after a peritoneal equilibration test (PET). The PET study reasons were: baseline study, low ultrafiltration, underdialysis and after an event of peritonitis. Patients were classified according to peritoneal characteristics as a low transporter (LT) [low/low average] and as high transporter (HT) [high/high average transporters]. Weight and height were measured using standard procedures and body composition was assessed by multifrequency bioelectrical impedance analysis.

Results: HT individuals have lower albumin concentrations than LT (3.3 ± 0.42 vs 3.7 ± 0.39, p=0.026). Higher glucose absorption from dialysis solution (p=0.036) and a trend toward in higher c reactive protein plasma concentrations (p=0.089) was observed in the HT group. Higher prevalence of PEW condition (50 vs 23%) was observed in HT group without statistical significance (p=0.144). Higher malnutrition status using malnutrition inflammation score and PEW criteria was observed in HT-PET, without statistical significance.

Conclusions: HT peritoneal membrane confers a risk for hypoaluminaemia and inflammatory state in CKD patients on automated peritoneal dialysis. HT patients are at an increased risk of PD-PEW. Intervention studies to elucidate the best nutritional approach should be designed to improve nutritional status in this population.

PO1274

Monitoring for Early Signs of Peritonitis in Patients Undergoing Peritoneal Dialysis

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Background: In the 2019 United States Department of Health and Human Services (HHS) established the “Advancing American Kidney Health” initiative, with a goal of increasing home-based dialysis from 12% to over 50% by 2025. To meet this goal, healthcare providers must address the common complications of peritoneal dialysis (PD) that contribute to modality failure and reluctance to opt for PD when starting dialysis. A sharp increase in PD utilization will require new approaches to reducing peritonitis and infection-related hospitalization.

Methods: Current strategies to detect peritonitis rely on crude signs and symptoms – predominantly cloudy spent dialysate and abdominal pain – an insensitive and non-specific approach. With the CloudCath monitoring system, the intent is to automatically and quantitively monitor the turbidity of the effluent fluid. We evaluated the CloudCath monitoring device which includes a cloud-based algorithmic solution for early detection of the patient condition associated with peritonitis.

Results: The device and algorithm were tested in a proof of concept clinical study (Troidle 2003). Using international multicenter PDOPPS data, we investigated the association of peritonitis with reported symptoms of depression via the Center for Epidemiologic Studies Depression Scale (CES-D) and quality of life (QoL) measures.

Methods: We used Peritoneal Dialysis Outcomes and Practice Patterns Study phase 1 (2014-2018) data from Australia and New Zealand (A/NZ), Canada (CA), Japan (JP), Thailand (TH), the UK and US in cause-specific recurring-event survival models on peritonitis outcomes, stratified by previous episodes. Patient QoL was estimated using the SF-12 Physical and Mental Health Composite Scores (PCS, MCS), and CES-D. Analyses were adjusted for age, years on PD, serum albumin level, residual urine, black race, sex, heart disease, diabetes, GI bleed, country, and prior peritonitis events.

Results: Peritonitis risk was associated with higher CES-D scores (p<0.05). Patients who reported CES-D scores ≥ 15 had 27% higher peritonitis risk compared to patients who reported scores < 10. While associations were weaker for MCS (p=0.69) and PCS (p=0.40), scores that indicated the lowest tertile of QoL in these areas were associated with 6-7% higher peritonitis risk than scores in the highest tertile (table).

Conclusions: While the association between poorer QoL and peritonitis risk was weak and non-significant, the association between having greater symptoms of depression (per CES-D) and future peritonitis risk warrants further investigation, as depression may be a modifiable risk factor.

Funding: Other NIH Support - Agency for Healthcare Research and Quality (AHRQ)

PO1275

Patient-Reported Factors and Peritonitis Risk: Results from the Optimizing Prevention of Peritoneal Dialysis-Associated Peritonitis in the US Study (OPPUS)

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Background: Peritoneal dialysis (PD)-associated peritonitis has been found to be associated with depression in a single-center study (Troidle 2003). Using international multicenter PDOPPS data, we investigated the association of peritonitis with reported symptoms of depression via the Center for Epidemiologic Studies Depression Scale (CES-D) and quality of life (QoL) measures.

Methods: We used Peritoneal Dialysis Outcomes and Practice Patterns Study phase 1 (2014-2018) data from Australia and New Zealand (A/NZ), Canada (CA), Japan (JP), Thailand (TH), the UK and US in cause-specific recurring-event survival models on peritonitis outcomes, stratified by previous episodes. Patient QoL was estimated using the SF-12 Physical and Mental Health Composite Scores (PCS, MCS), and CES-D. Analyses were adjusted for age, years on PD, serum albumin level, residual urine, black race, sex, heart disease, diabetes, GI bleed, country, and prior peritonitis events.

Results: Peritonitis risk was associated with higher CES-D scores (p<0.05). Patients who reported CES-D scores ≥ 15 had 27% higher peritonitis risk compared to patients who reported scores < 10. While associations were weaker for MCS (p=0.69) and PCS (p=0.40), scores that indicated the lowest tertile of QoL in these areas were associated with 6-7% higher peritonitis risk than scores in the highest tertile (table).

Conclusions: While the association between poorer QoL and peritonitis risk was weak and non-significant, the association between having greater symptoms of depression (per CES-D) and future peritonitis risk warrants further investigation, as depression may be a modifiable risk factor.

Funding: Other NIH Support - Agency for Healthcare Research and Quality (AHRQ)

PO1276

Image-Guided Percutaneous Peritoneal Dialysis Catheters: Greater Than the Sum of Their Parts

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Background: Peritoneal Dialysis (PD) is a favored treatment modality for patients with end-stage kidney disease. PD catheter Composix is a sterile and timely insertion of PD catheter. Most centers rely on laparoscopic insertion of PD catheters for PD initiation. Small studies indicate that image guided percutaneous (IGP) PD catheter insertion by interventional radiology (IR) may be non-inferior to laparoscopic catheters. However, there are limited data to compare IGP PD catheters to those inserted with laparoscopic technique. Hence, there are no definitive evidence based recommendations to support which technique may be superior. We conducted a retrospective analysis to compare complication rates and catheter survival in laparoscopic versus IGP PD catheter insertions.

Methods: Patients who underwent laparoscopic or IGP PD catheter placement from Jan 2014 to Aug 2019 were included in the analysis. IGP placement physicians are employed.
both fluoroscopic and ultrasound guidance. Primary outcome was rate of mechanical complications. Secondary outcome was death and transplant censored complication free catheter survival at 1 year. Results: 244 PD catheters were placed at our institution during the study time period by laparoscopic surgical technique and 188 by IGP technique. Baseline characteristics included gender, age, and BMI were similar in both groups. Surgical group consisted of 60% of patients with prior abdominal surgery as compared to 24% in the IR group OR 4.62 (2.35 – 9.09), P <0.0001. Mechanical complication rates were higher in the surgical group 29.6 % (18.0 – 43.6) versus 13.4 % (8.9 – 19.2) in the IR group (p 0.02). Death and transplant censored complication free catheter survival rate at one year was 87.8% (79.6 – 93.5) in the IR group and 73.3% (54.1 – 87.7) in the surgical group, P=0.063. In the surgical group, patients with higher BMI (> 35) had higher rate of complications 83.3% (79.6 – 93.5) or <35 group, OR 16.82 (1.77 – 159.58) P 0.014. In the IR group, patients with higher BMI (> 35) had higher rate of complications 83.3% (79.6 – 93.5) versus 22.9% in the low BMI (<35) group, OR 16.82 (1.77 – 159.58) P 0.014. In the IR group, patients with BMI > 35 had higher rate of complications 83.3% (79.6 – 93.5) versus 22.9% in the low BMI (<35) group, OR 16.82 (1.77 – 159.58) P 0.014. In the IR group, patients with BMI > 35 had higher rate of complications 83.3% (79.6 – 93.5) versus 22.9% in the low BMI (<35) group, OR 16.82 (1.77 – 159.58) P 0.014.

Conclusions: Our findings suggest IGP PD catheter is an effective option for PD initiation even in patients with high BMI and offers several advantages including ease of placement and lower recovery time.

PO1277
Repeat Peritonitis: A New Reality After Staphylococcus aureus Carriage Surveillance Implementation
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Background: Peritonitis is one of the major peritoneal dialysis complications and an important cause of technique failure. Notably, repeat peritonitis (RP) have substantial risk of developing further infection episodes that perpetuate peritoneal membrane damage. As Staphylococcus aureus (SA) is a major causative of RP, strategies such as staphylococcus aureus carriage surveillance (SACS) were implemented to decolonization of carriers in order to decrease SA infections. This study aims to describe repeat peritonitis clinical behavior and SACS influence on repeat peritonitis.

Methods: We developed one center retrospective study from 1998 to 2019 that compared RP episodes with a control group in terms of causative microorganisms, cure rate, catheter removal and permanent and temporary transfer to hemodialysis. We also compared the same data in RP episodes before and after SACS.

Results: Overall, RP were caused by gram positive microorganisms and had a significantly higher cure rate (97,1% versus 67,3%, p=0.001) and lower rate of hospitalization (11% versus 30,8%) than control group. After SACS, global peritonitis rate decreased (0,54 versus 0,35 episodes per patient-year), and RP rate increased (37,5% versus 7,4%, p=0.01) as Strepptococci became more frequent (56,7% versus 0,0% p=0,007) and SA less frequent (3,5% versus 60,0% p=0.001). Also, RP cure rate increased (100% versus 80,0% p=0.03) and permanent transfer to hemodialysis decreased (6,7% versus 40,0% , p=0.03).

Conclusions: RP Group have more favorable results than control group that presented higher gram-negative peritonitis rate. After SACS, Strepptococci became more frequent than SA in repeat group, peritonitis outcomes became more favorable but repeat peritonitis rate increased. We believe that in measures to prevent SA infections are implemented more programs will face this reality.

Repeat Peritonitis Causative Microorganisms

PO1278
Strategies to Prevent Infection-Related Losses in US Peritoneal Dialysis Programs by More Actionable Predictive Data Reporting
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Background: Peritoneal dialysis (PD)-associated peritonitis (PTN) accounts for a significant percentage of patients who transition to hemodialysis due to infection-related technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure. Data reporting to individual PD home programs on PTN rates is designed to drive a proactive approach for optimizing infection rates in PD programs and identify technique failure.

Methods: Between 2016 and 2020, a standardized reporting of PD-related PTN was carried out for 1487 affiliated PD programs across the United States (66,687 patients). Currently, PTN is reported on a 3-month rolling average for each program, with an annual analysis of the PTN rate of 1 event/66 patient-months; 32% of PTN events fall into the hospitalization criterion bucket, with 3% already having cultures drawn prior to admission. Among all episodes with an associated hospitalization, 90% have an associated culture. For non-hospitalization events, 64% had an associated culture among others, and 36% had an associated culture among others. We included cases of ESI and technique failure with PTN rates in PD programs.

Conclusions: In conclusion, smoking and constellation are significant independent risk factors of endogenous peritonitis in PD patients. The management of constellation and discontinuation of smoking may lower the risk of endogenous peritonitis in PD patients.

PO1279
Smoking Is a Risk Factor for Endogenous Peritonitis in Peritoneal Dialysis Patients
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Background: Peritonitis is one of the most common complications observed in patients who are undergoing peritoneal dialysis (PD). PD-related peritonitis is associated with total mortality and transfer from PD to hemodialysis. Therefore, the prediction and prevention of peritonitis are important in PD patients. Exit-site infection (ESI) is an important risk factor for peritonitis. Whereas, there exists peritonitis without ESI and technical failure such as endogenous peritonitis in patients on PD. However, it is unclear that the prevention and prediction of endogenous peritonitis. Therefore, we investigated the risk of endogenous peritonitis in PD patients in this study.

Methods: We investigated the patients who were undergoing PD at our hospital and attended our hospital regularly from April 2015 to March 2020. We treated 22 cases of peritonitis in these patients; there were 18 cases of endogenous peritonitis without ESI and technical failure. We considered older age, female sex, obesity, diabetes mellitus, diverticulosis, and constipation as the important risk factors for endogenous peritonitis in patients undergoing PD. Therefore, we added these six factors as confounding factors with current and previous smoking history in the univariate logistic regression models. P values <0.05 were considered statistically significant.

Results: We used univariate logistic regression models for the above-mentioned seven factors. Then, we defined age > 65 years as older age and body mass index > 25 as obesity. We defined patients who received purgative medication as having constipation. We found that diabetes mellitus (p = 0.0106), former or current smoking (p = 0.0065), and constipation (p = 0.0065) were statistically significant risk factors of endogenous peritonitis. Moreover, smoking and constipation were the most significant independent risk factors for endogenous peritonitis (p = 0.036) in our multivariate logistic regression model.

Conclusions: In conclusion, smoking and constellation are significant independent risk factors of endogenous peritonitis in PD patients. The management of constellation and discontinuation of smoking may lower the risk of endogenous peritonitis in PD patients.

Impact of Performing Cultures of Peritoneal Fluid Correctly on the Reduction of False-Positive and False-Negative Culture Rates in Patients on Peritoneal Dialysis (PD) Presenting with Peritonitis
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Background: Peritonitis is feared complication of PD and reason for loss of peritoneal membrane function. It negatively impacts the Quality metrics of home program performance. Preliminary observations in 2013 showed a high failure rate for treating culture negative peritonitis. Intervention based on our root cause analysis from 07/30/2013 to 12/31/2019 done to address disparities in performing proper culture techniques within hospital systems and outpatient home dialysis ambulatory clinics.

Methods: Prior to 07/30/2013 (5-10 ml) of a cloudy PD fluid was injected into an aerobic and anaerobic blood culture bottle. After 07/30/2013 we implemented a policy whereby 50 ml of PD effluent was used for centrifugation and the pellet was injected into culture bottles to preferentially concentrate the inoculum. We queried our EMR after 7 years of peritonitis were low across programs. Data was extracted using diagnostic codes and laboratory report. Data was analyzed using student’s 2 sample t test, Kruskall-Wallis and Wilcoxon analysis

Results: Total of 41 observations met our inclusion criteria for retrospective analysis. We had 26 observations before and 15 observations after the policy implementation. Mean number of tests ordered after 07/30/2013 declined. Number of false positive tests declined and number of true negative tests and true positive tests increased (p=0.02), indicating increasing specificity and a more targeted antibiotic regimen rescuing peritoneal membrane function early. No direct impact on survival nor any impact on technique failure was observed.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: A gap in proper collection of PD fluid was identified. We educated all residents, renal fellows, nursing staff and microbiology laboratory staff across the entire health care systems, and created an order set within EMR systems to close this gap.

ultrafiltration. Repeat microbiology studies showed fungal elements in the PD fluid, later identified as Candida albicans. Patient was not started on Steroids and Tamoxifen due to underlying fungal peritonitis. He was transitioned to hemodialysis and treated with a prolonged course of amphotericin. Subsequent peritoneal studies showed increasing burden of mold despite intraperitoneal drains. His course was further complicated by nephrotic GI bleed and inability to tolerate hemodialysis due to hypotension. Patient was eventually transitioned to comfort measures.

Discussion: The pathogenesis of EPS is poorly understood. Some of the risk factors include use of PD for > 5 yrs, high dialysate glucose concentrations, repeated episodes of peritonitis, which can lead to peritonitis scars and decreased macrophage activity. Diagnosis of M A PDAl is often delayed, as it presents as a culture -ve peritonitis. Successful treatment requires a PD catheter (PDC) removal in addition to multiple anti-microbial therapies and results in a permanent switch to haemodialfiltration (HDF).

Case Description: A 50-yr-old ♂, presented with fever, abdominal pain and cloudy PD fluid (PF) after returning from a holiday. He was systemically well apart from a tender abdomen. PD exit site and tunnel appeared normal. CRP was 80.7 mg/L (0.5 mg/L) and WCC was 6.0 x 10^9/L. Empirical treatment for PDAl was commenced with intraperitoneal Vancomycin + Gentamicin. Microscopy of the PF showed a WCC of 155/μL and -ve Gram stain. MA was cultured and confirmed by whole-genome sequencing. Amikacin, Imipenem & Clastatin and Tigecycline were commenced. Emergency PDC removal with a peritoneal washout was performed. He was switched to HDF. Day 16, Clarithromycin was stopped due to a prolonged QTc interval. Day 26, he developed hepatopathy that resolved after cessation of Tigecycline. Amikacin + Imipenem was continued for 5 months and switched to Amikacin + Linezolid. He developed Amikacin-induced tinnitus despite therapeutic dose monitoring. He completed 20 weeks of therapy and remains free of infection.

Discussion: M A is an environmental M that is found in water, soil, dust and is related to M causing tuberculosis and leprosy. It is known to contaminate devices and medical products. It causes lung infections in the immunocompromised. Our patient had no such history. The duration between PDC insertion and this episode was 2 yrs, making this an unlikely cause. The history did not reveal any reason for contracting this organism. The optimum treatment duration and selection of anti-microbial therapy in the management of M A PDA is unclear, primarily due to the paucity of confirmed cases and variability of the treatment regimens. PDC removal and peritoneal washout remain the mainstay of treatment. Our case highlights M A as an emerging organism in PDA and physicians should be aware of it.

PO1284

Polymicrobial Peritoneal Dialysis Peritonitis due to Eggertella lenta, Parabacteroides Species, and Bacteroides distasonis

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Introduction: Peritonitis is a severe and common infectious complication among patients on peritoneal dialysis (PD). Most cases are due to Coagulase negative staphylococcus. Anaerobic bacteria constitute < 0.5% of the peritonitis in PD patients. This is a case of anaerobic polymicrobial PD peritonitis of rare pathogens without a clear intestinal source.

Case Description: 92 year old man with end stage renal disease who had a failed deceased donor renal transplant and was started on peritoneal dialysis 6 months ago was admitted for abdominal pain with cloudy peritoneal fluid for 3 days. Peritoneal fluid had cells 22,000 cells/μL. He was treated with intraperitoneal taudolidine-urokinase PD catheter lock with good outcome. In 2018 she had an episode of ESI against Pseudomonas aeruginosa solved after a course of topical antibiotics as well as external cuff shaving. In 2019 she developed again ESI with Pseudomonas aeruginosa, and despite topical treatment as per antibiogram exit site cultures remained positive. One month later she presented a spontaneous expulsion of the PC. A contralateral PC was placed and she started PD. 2 months later she presented a spontaneous PC expulsion with evidence of ESI with Candida parapsilosis that was adequately treated. After infection resolved, a contralateral PC was placed with no complications. CASE2: 68-year-old woman with CKD secondary to type 2 cardiac syndrome. She started on PD because of diuretic-resistant heart failure (straight Tenckhoff PC 2 cuffs). She had no signs of ESI and denied using any topical medication. A contralateral PC was inserted with no complications. She had two episodes of exit site infection (ESI) secondary to Corynebacterium spp, recovered in 2017 and 2018. She was treated with intraperitoneal Vancomycin + Gentamicin. Microscopy of the PF showed a WCC of 155/μL and -ve Gram stain. MA was cultured and confirmed by whole-genome sequencing. Amikacin, Imipenem & Clastatin and Tigecycline were commenced. Emergency PDC removal with a peritoneal washout was performed. He was switched to HDF. Day 16, Clarithromycin was stopped due to a prolonged QTc interval. Day 26, he developed hepatopathy that resolved after cessation of Tigecycline. Amikacin + Imipenem was continued for 5 months and switched to Amikacin + Linezolid. He developed Amikacin-induced tinnitus despite therapeutic dose monitoring. He completed 20 weeks of therapy and remains free of infection.

Discussion: We present an atypical complication in PD. Triggers for PC extrusion in our cases appear to be related to peritoneal leak in the first case, and to ESI in the remaining two cases. Staphylococci are likely disrupting exit site healing and fibrosis formation around the cuff, contributing to this infrequent complication. These risk factors should be identified and kept in mind to prevent the catheter extrusion.

PO1285

A Rare Cause of Peritoneal Dialysis-Associated Peritonitis

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Introduction: Peritoneal dialysis (PD)-associated peritonitis (PDAl) caused by the non-tuberculous mycobacterium (M) species Mycobacterium abscessus (MA) is emerging as a severe and often resistant infection. MA causes disseminated infection in immunocompromised individuals and is resistant to classical anti-tuberculous drugs and antibiotics. Diagnosis of MA PDA is often delayed, as it presents as a culture -ve peritonitis. Successful treatment requires a PD catheter (PDC) removal in addition to multiple anti-microbial therapies and results in a permanent switch to haemodialfiltration (HDF).

Case Description: A 70-year-old woman, presented with fever, abdominal pain and cloudy PD fluid (PF) after returning from a holiday. She had a 5-yr history of PDAl with oral Vancomycin. Despite completing a course of antibiotics, she had persistent episodes of peritonitis. Successful treatment requires a PD catheter (PDC) removal in addition to multiple anti-microbial therapies and results in a permanent switch to haemodialfiltration (HDF).

Discussion: We present an atypical complication in PD. Triggers for PC extrusion in our cases appear to be related to peritoneal leak in the first case, and to ESI in the remaining two cases. Staphylococci are likely disrupting exit site healing and fibrosis formation around the cuff, contributing to this infrequent complication. These risk factors should be identified and kept in mind to prevent the catheter extrusion.

PO1286

A Unique Case of Encapsulated Peritoneal Sclerosis

Sumanth Kacharam, Jie Tang. Brown University, Providence, RI.

Introduction: Encapsulating peritoneal sclerosis (EPS) is a rare but devastating sequela of chronic inflammation in patients on peritoneal dialysis (PD). EPS is classically associated with filtration failure and can lead to recurrent abdominal pain and obstruction due to encasement of small and large bowel.

Case Description: A 45-year-old Cambodian male with a past medical history of ESRD secondary to IgA nephropathy on PD for 10 years presented with loose stools and hypotension after dialysis. His medical history included CML complicated by spinal choroma, paraplegic, neurogenic bladder and PVD with osteomyelitis resulting in bilateral AKA. He was previously admitted 14 days prior for culture negative (including fungal) peritonitis treated with intraperitoneal cefepime and C difficile colitis treated with oral Vancomycin. Despite completing a course of antibiotics, he had persistent abdominal pain and inability to tolerate PO intake. Repeat diagnostic paracentesis on this presentation revealed a total cell count of 2519 with 98% PMN. But culture remained negative. CT of abdomen showed global thickening and calcification of his peritoneal membranes. Ex laparotomy was performed with biopsies confirming EPS. At the time of diagnosis, he did not exhibit signs or symptoms of dialysis failure with excellent Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.

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PO1285
A Rare Case of Trichodermia-Related Peritonitis in a Patient on Peritoneal Dialysis
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Introduction: Trichodermia spp are saprophytic fungi commonly found in the soil, decaying wood and humid environments. They are known to cause infections in immunocompromised hosts but rarely in peritoneal dialysis (PD) patients. Cases are infrequently reported in the literature and are associated with high morbidity and mortality.

Case Description: A 65yo male with DM, HTN, HLD, ESRD on PD, was admitted with worsening abdominal pain for 4 weeks with low grade fever, chills, nausea and vomiting. His vitals were stable. Significant findings were a diffusely tender abdomen with peritonitis, rigidity on rebound tenderness. His PD effluent was cloudy. Labs were unremarkable. CT abdomen was negative for acute pathology. He was started on intraperitoneal vancomycin and cefazidime as an outpatient as he had two earlier bacterial peritonitis episodes in the year. However, preliminary cultures from his clinic grew fungal elements. This prompted urgent PD catheter removal and conversion to hemodialysis. The fungus identified was Trichodermia and he was started on IV Anidulafungin. Repeat PD cultures were negative and he was discharged on oral Voriconazole with follow up in ID clinic. Over the course of 2 weeks, he was readmitted twice with worsening abdominal pain. On the third admission, he had exploratory laparoscopy and found to have diffuse peritonitis. The PD catheter was removed and the Foley was placed. He was discharged on oral V oriconazole with follow up in ID clinic.

Discussion: Diagnosis of fungal peritonitis in PD is challenging and oftentimes delayed. Occurrences usually follow treatment of bacterial peritonitis and mimics its clinical features. Most isolates of Trichodermia spp have shown resistance to fluconazole and 5- Fluorocytosine but show intermediate susceptibility to Amphotericin B, Itraconazole, Ketoconazole and Miconazole. Therefore, it is important to perform antifungal susceptibility tests and then adjust the final treatment. In conclusion, Physicians who treat patients on PD should be aware of the possibility of this opportunistic infection. Prompt antifungal treatment should be considered in cases of recurring peritonitis in the apparent absence of bacterial organisms. More research is needed to guide early diagnosis and guide effective treatment of this rare fungal disease with high mortality.

PO1286
Streptococcus oralis Peritonitis in Peritoneal Dialysis
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Introduction: Peritonitis is the most common complication seen in peritoneal dialysis (PD). Although staphylococcal infections are the most common, Streptococci are rare causes of ambulatory peritoneal dialysis (APD) peritonitis. We report a case of APD peritonitis due to Streptococcus oralis (also known as mitis) in a patient who habitually engaged in nail-biting.

Case Description: A 57-year-old male with end-stage renal disease due to biopsy proven focal segmental glomerulosclerosis on PD since 2018 presented with 1 day of severe diffuse abdominal cramps. He has no known history of peritonitis. Vital signs were stable, and examination was notable for diffuse abdominal pain without rebound tenderness. Laboratory evaluation showed clean and dry fluid on CT scan did not show any acute intra-abdominal pathology. PD fluid was sent for cell count and culture. PD fluid was cloudy in appearance and amber in color. Due to concern for peritonitis, he was started on intraperitoneal vancomycin and tobramycin. Final fluid cell count was 20,900 WBCs/mm3 and final fluid culture was positive for Streptococcus mitis. He was treated with intraperitoneal vancomycin and cefazidime as an outpatient as he had two earlier bacterial peritonitis episodes in the year. However, preliminary cultures from his clinic grew fungal elements. This prompted urgent PD catheter removal and conversion to hemodialysis. The fungus identified was Trichodermia and he was started on IV Anidulafungin. Repeat PD cultures were negative and he was discharged on oral Voriconazole with follow up in ID clinic.

Discussion: Diagnosis of fungal peritonitis in PD is challenging and oftentimes delayed. Occurrences usually follow treatment of bacterial peritonitis and mimics its clinical features. Most isolates of Trichodermia spp have shown resistance to fluconazole and 5- Fluorocytosine but show intermediate susceptibility to Amphotericin B, Itraconazole, Ketoconazole and Miconazole. Therefore, it is important to perform antifungal susceptibility tests and then adjust the final treatment. In conclusion, Physicians who treat patients on PD should be aware of the possibility of this opportunistic infection. Prompt antifungal treatment should be considered in cases of recurring peritonitis in the apparently absence of bacterial organisms. More research is needed to guide early diagnosis and guide effective treatment of this rare fungal disease with high mortality.

PO1287
Effect of N-Acetylcysteine on Nontraditional Cardiovascular Risk Factors and Carotid Intimal Medial Thickness in Chronic Peritoneal Dialysis Patients
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Background: Accelerated atherosclerosis increases morbidity and mortality among PD patients. Various non-traditional risk factors (NTRFs) like oxidative stress (OS), impaired endothelial function (EF), micro-inflammation and increased homocysteine (HCS) have been implicated. N-acetyl cysteine (NAC) is an antioxidant, reduces HCS and ameliorates endothelial dysfunction. The aim was to determine the effect of NTRFs in chronic peritoneal dialysis (PD) patients. NTRFs have been studied in PD patients & its effect on structural atherosclerosis.

Methods: Stable consenting patients on chronic PD (PD duration >3 months) were given oral NAC (600 mg twice daily) for 3 months. No changes were made in PD prescription. Demographic data, clinical, biochemical profile, EF, OS, HCS, highly-sensitive C-Reactive protein (Hs-CP) and Carotid intimal medial thickness (CIMT, marker of structural atherosclerosis) were noted before and after 3 months. OS was measured by total anti-oxidant capacity (TAC) and thiobarbituric acid reactive substances (TBARS). EF was assessed by brachial artery flow-mediated dilatation (FMD) subsequent to occlusion. CIMT of both carotids at 8 sites was assessed by high-resolution ultrasonography.

Results: Of 80 patients approached by convenience sampling, 73 who completed study were analysed (2 refused consent, 5 did not follow-up at desired time). None of the patients reported any adverse events or discontinued the drug. In these patients, 28 were diabetics; 50 were males. Mean age, duration of PD and urine output: were 51.6±11.1 years, 13 months and 487.4±341.9 ml/day respectively. Table shows study parameters before and after NAC.

Conclusions: In our open-label study NAC effectively reduced multiple NTRFs and atherosclerotic burden in PD patients.

PO1288
Outcomes of Cardiac Surgery in ESKD Patients on Hemodialysis (HD) vs. Peritoneal Dialysis (PD)
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Background: Patients with ESKD have worse outcomes following major cardiac surgery compared to those without ESKD. However, the outcomes of cardiac surgery in PD patients vs. HD patients are not well studied.

Methods: Using our EHR-based Cardio-Thoracic Surgery (CTS) registry, we compared the outcomes of 590 patients with ESKD on HD and PD undergoing Coronary Bypass Graft (CABG) and/or valvular cardiac surgery. We compared baseline demographics and comorbidities between patients on PD and HD using Chi-square and t-tests for categorical and continuous variables respectively. We compared Length of Stay (LOS), days in the ICU, number of transfusions, and post surgical complications: (pericardial effusion, gastrointestinal (GI) bleed, cardiac arrest, and in-hospital death) using Kruskal-Wallis test, Chi-square and Fisher’s exact tests.

Results: Among 590 patients undergoing cardiac surgery, 62 (11%) were on PD, and 528 (89%) were on HD. PD patients had a lower proportion of heart failure (50% vs. 72%), lower median Cardio-Pulmonary Bypass (CPB) time (106 vs. 122 minutes), and a higher proportion of dyslipidemia (92% vs. 79%) at baseline. PD and HD patients had no significant differences in post-operative length of stay, number of ICU days, and postoperative complications including GI bleed, pericardial effusion, and cardiac arrest (table 1). There was also no difference in mortality between the two groups. Out of 62 PD patients, 15 (24%) were converted to HD.

Conclusions: There were no significant differences in the measured outcomes between patients on HD vs. patients on PD post cardiac surgery and or valvular surgery.

Post-operative outcomes of HD vs. PD

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Underline represents presenting author.

Statistics presented as Median [P25, P75], or N (column %).

NAC-N-acetyl cystein ; HCS-homocysteine; HsCRP-highly-sensitive C-Reactive protein; FMD-brachial artery flow-mediated dilatation; TBARS-thiobarbituric acid reactive substances; TAC-total anti-oxidant capacity; CIMT-Carotid intimal medial thickness.
the identification of novel molecular biomarkers of peritoneal EMT may facilitate the diagnosis of peritoneal disease allowing early initiation of treatment targeting peritoneal fibrosis. Hyaluronan (HA) is a glycosaminoglycan component of the extracellular matrix, produced by three members of HA synthase (HAS1, HAS2 and HAS3). HAS are known to be involved in EMT of cancer cells, however there is no information on the association of HAS with peritoneal EMT. 

Methods: Peritoneal MCs isolated from overnight dwell dialisates from 16 PD patients (PD_MC) at 2 [baseline peritoneal equilibration test (PET)] and 6 (follow-up PET) months of the PD initiation. We divided PD patients into two groups based on the alteration of baseline and follow-up PD MC morphology (Group 1 epithelial and Group 2 epithelial-mesenchymal). RNA-seq analysis (Ebiogen, Korea) was performed in order to detect baseline molecular markers predicting mesenchymal phenotype in follow-up. Based on RNA-seq analysis, the expressions of HAS isoforms were evaluated. HAS1 and HAS3 were isolated from omentum (OM_MC) with an exploration of the role of HAS on TGFβ-induced EMT. 

Results: RNA-seq analysis demonstrated the difference of gene expression related to EMT (27.6%), angiogenesis (30.2%), cell migration (27.4%), and extracellular matrix remodeling (26.3%). Among them, HAS2 expression in baseline analysis showed the highest fold difference (28.5-folds) between group 1 and 2. In OM-MC, HAS1, HAS2 and HAS3 were constitutively expressed whereas only HAS1 and HAS2 were upregulated by TGFβ. TGFβ-induced changes in cell morphology and the expression of E-cadherin, α-HA and fibronectin were ameliorated by siHAS2, but not by siHAS1. HAS1 inhibits (4-methylumbelliferyl; 4-MU) also alleviated TGFβ-induced EMT.

Conclusions: This data suggest HAS2 plays a role in TGFβ-induced EMT of peritoneal mesothelial cells and modulation of HAS2 can protect the peritoneal fibrosis in PD patients. Both HA or HAS2 in peritoneal effluent of baseline PET also can be the markers predicting peritoneal EMT and fibrosis.

PO1290
Am80, a Synthetic Retinoic Acid Receptor α-Specific Agonist, Suppresses Peritoneal Fibrosis via Inhibition of Krüppel-Like Transcription Factor 5 (KLF5) in Mice
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Background: We presented previously that Am80, a synthetic retinoic acid receptor α-specific agonist, inhibited the expression of Krüppel-like transcription factor 5 (KLF5) and reduced peritoneal fibrosis in mice. Now, we examined further detail about the mechanism of Am80 in inhibiting peritoneal fibrosis.

Methods: Peritoneal fibrosis was induced by intraperitoneal injection of chlorhexidine gluconate (CG) into peritoneal cavity of ICR mice. Am80 was administered orally for every day from the start of CG injection. After 3 weeks of treatment, peritoneal tissues were examined using serial sections by immunohistochemistry to identify what kind of cells expressed KLF5. Am80 was given in mouse fibroblasts stimulated by transforming growth factor β1 (TGF-β1) and the expression of KLF5 was assessed by Western blotting.

Results: While KLF5 was expressed in the thickened submesothelial area of CG injected mice, Am80 reduced peritoneal fibrosis in mice. Now, we examined further detail about the mechanism of Am80 in inhibiting peritoneal fibrosis.

Conclusions: These results indicate the KLF5 might not only associate phenotypical differentiation from fibroblasts to myofibroblasts but also regulate inflammatory responses and angiogenesis in the peritoneal fibrosis model. Am80 can suppress peritoneal fibrosis through inhibiting these mechanisms.

PO1291
Peritoneal Protein Clearance and Lean Body Mass Index: Relationship in Peritoneal Dialysis Patients
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Background: An important feature of Peritoneal Dialysis (PD) is peritoneal protein loss (PLL) during dialysis. Peritoneal Protein Clearance (PPC) is considered a better index as it reflects the individual differences of PPL and membrane function of both small and large pores. Higher PPC has been reported to be associated with hypoalbuminemia and malnutrition, with some authors stating higher overall mortality. However, new studies failed to draw similar conclusions, arousing new insights on the peritoneal protein metabolism. Lean body mass index (LBMI) has been used as a useful marker of nutritional status in PD patients. The aim of this study was to evaluate the relationship between PPC and LBMI.

Methods: Prevalent PD patients with peritoneal equilibration test and multi-frequency bioelectrical impedance analysis (BIA) were enrolled in the cross-sectional study. The study was performed from January 2014 to December 2019. PPC was calculated by dividing 24h dialysate protein loss by serum total protein. LBMI was assessed by BIA and LBMI was calculated dividing LBMI by body height squared. Spearman correlation test was performed to examine the association between body indexes and PPC. Multiple regression linear model was used for exploring the associated factors of PPC.

Results: We included 67 PD patients (54.1±17.3 years, 59.7% male; 31.3% diabetic). The mean evaluated parameters were: total Kt/V 2.5±0.6, nGFR 6.7±4.1 ml/min/1.73m2 and D/P creatinine ratio 0.65±0.01. The median PPL and PPCi were 5.2 (3.6-7.6) g/day and 1.94 (1.5-2.3) l/week, respectively. PPCi was significantly positively associated with LBMI (ρ=0.401, P=0.001) and BSA (ρ=0.327, P=0.007), but not with BMI (ρ=0.109, P=0.381). Compared with conventional body indexes, LBMI had better performance in predicting higher PPCi. Multiple linear regression model, when adjusted for gender, nGFR (GFR and diabetes), showed that older age (ρ=0.288, P=0.018), higher D/P creatinine ratio (ρ=0.232, P=0.050) and higher LBMI (ρ=0.334, P=0.014) were independent predictors of PPCi.

Conclusions: Higher LBMI is a marker of better nutritional state, which is associated with better survival in PD patients. In this study, higher LBMI was independently associated with higher PPCi, possibly explaining conflicting results on the impact of higher PPCi on mortality.

PO1292
Burden of Dialysis, Health-Related Quality of Life, and Employment Comparisons Between Peritoneal Dialysis and In-Center Hemodialysis: Findings from the DOPPS Program
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Background: The Dialysis Outcomes and Practice Patterns Study (DOPPS) and the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) collect information annually about quality of life, including employment and functional status. Differences in these domains by dialysis modality (PD vs. center-based hemodialysis) may inform individuals in choosing a dialysis modality.

Methods: PD and HD patients with comparable characteristics were analyzed. For baseline patient questionnaire, we used logistic regression to analyze binary outcomes employment (full- or part-time versus unemployed), depression (CES-D ≥10 vs. <10), and functional status (≥11 vs. <11), and used linear mixed models to analyze continuous outcomes (PCS, MCS, and burden of kidney disease score). Change of outcomes were described descriptively.

Results: There were 3227 PD and 4544 HD patients at baseline. Burden of kidney disease scores were better for PD compared to HD (overall 9-point adjusted difference, [95%CI 7.1-11]) with a higher proportion of patients on PD in the lowest burden range (10%-37%) compared to 8%-24% on HD, depending on country. PD patients also had better PCS and MCS, though these were less marked (overall adjusted difference of 0.9 [0.2-1.6] for PCS, 1.0 [0.2-1.9] for MCS). HD patients had worse functional status scores (adjusted OR HD vs. PD 0.6, [0.5, 0.8] for score ≥11); were less likely employed (OR=0.6, 0.5, 0.8); and had worse CES-D scores (OR=0.8, [0.7, 1.0] for CES-D ≥10). In Australia/New Zealand, HD patients had better MCS and CES-D scores and a higher proportion being employed than PD patients. 174 PD patients and 254 HD patients died within one year of the baseline patients and 53 patients died within six months. Changes over time in the continuous measures were small. Trends in employment, CES-D score, and functional status were small and not statistically significant.

Conclusions: Compared to HD patients, PD patients reported a lower burden of kidney disease score and among survivors, remains stable in either PD or HD over 12 months. This information, when shared with patients choosing a dialysis modality, could result in an increased uptake of PD.

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PO1293
H2S May Inhibit Peritoneal Dialysis-Related Fibrosis Through the Sulphhydration Regulation of PSMA?
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Background: Peritoneal dialysis (PD) is one of the first treatment methods for patients with end-stage renal disease, which has advantages on cardiovascular system protection, large toxin clearance and patients’ life quality improvement. But statistics shows that the 5-year withdrawal rate of PD patients was around 50%, and ultrafiltration failure caused by peritoneal fibrosis is the main reason, and there is no effective clinical prevention and treatment. In our previous study, we found that the flora of PD patients was obviously maladjusted, and the production of H2S in the intestine was significantly reduced. Some evidences showed that H2S may alleviate PD-related fibrosis, suggesting H2S may affect the fibrosis by regulating the level of sulphhydration, but the mechanism is not clear.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: Rat peritoneal mesothelial cells were randomly assigned into different groups. 4.5% peritoneal dialysate group (PD group), PD+H2S supplement GYY4137 group and PD+H2S+enalapril PAG group. The expression of pyroptosis associated proteins, inflammatory factors and fibrosis related pathways in different groups were compared. The changes of protein sulfhydril sulfhydration level were analyzed by HPLC/MS/MS. The target protein expression and downstream pathways expression were observed by PCR and Western blot.

Results: GYY4137 significantly reduced the expression of pyroptosis proteins (NLRP3, cas-1, gsdmd-n), inflammatory factors (IL-6, IL-8, TNF - α) and fibrosis related proteins (p-smad). Smad, TGF-β, VEGF response to high glucose PD fluid. We found that the level of PSAM-7 sulfhydration in the PD group decreased significantly, but in GYY4137 group, the level of PSAM7 sulfhydration increased significantly. The expression of pyroptosis proteins, inflammatory factors and fibrosis related proteins were significantly increased after PSAM7 sulfhydration was interfered by mutant plasmid. The expression level of NLRP3 was downregulated by siRNA. The expression of downstream inflammatory factors and fibrosis-related proteins were significantly increased/decreased.

Conclusions: H2S has a protective effect on PD-related fibrosis through the PSAM7 sulfhydration regulation, and further break the pathological changes of “pyroptosis- inflammation-fibrosis” axis and avoid the occurrence of inflammatory cascade reaction.

PO1294
Fatigue Predicts Higher Risk of Mortality in Peritoneal Dialysis Patients: A BRAZPD Analysis
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Background: End-stage kidney disease (ESKD) patients are often burdened by fatigue. Fatigue is a core outcome to peritoneal dialysis (PD) patients and providers, but its associations with clinical outcomes are unknown. We analyzed a nationally representative cohort of PD patients to test the hypothesis that higher fatigue independently associates with higher mortality risk.

Methods: We analyzed data from adult patients in BRAZPD, a nationwide Brazilian cohort across 122 PD centers. Patients incident to PD with complete KDQOL-SF survey in the first 90 days of dialysis were included. Fatigue was defined by the vitality cohort across 122 PD centers. Patients incident to PD with complete KDQOL-SF survey in the first 90 days of dialysis were included. Fatigue was defined by the vitality survey. We included data from 1,388 PD patients (mean age 58.5 ± 15.47 years, 64% male, 66% Caucasian). Proportions of patients with high vitality, moderate vitality, moderate fatigue, and high fatigue were 21%, 38%, 15% and 26%, respectively. Hazard-ratios (95% CI) for mortality estimated for the high vitality group (compared to high fatigue) were 0.39 (0.23-0.65), 0.41 (0.24-0.68) and 0.39 (0.22-0.68) for Cox, competitive risk and multilevel models, respectively. Results from the smoothing spline regression are shown in the Figure (B).

Conclusions: Higher fatigue in the initial months of PD was independently associated with 12-month mortality risk. Potential interventions targeting ESKD fatigue in PD patients may not only yield benefits in patient-reported outcomes but possibly also improve survival.

PO1295
Urgent-Start Peritoneal Dialysis: Experience in Mechanically Ventilated Prone Patients
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Background: Patients with respiratory failure who require prone positioning are not considered good candidates for PD due to the concerns for increased intra-abdominal pressure, impaired diaphragmatic movement, and leaking of peritoneal fluid. We addressed the COVID-related AKI (CRAKI) surge for renal replacement therapy (RRT) by initiating an acute PD program at Bellevue Hospital including prone patients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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POI1297
Peritoneal Dialysis (PD) Technique Training: What Features Influence Learning Time?
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Background: The adequate training of patients started on PD is an essential issue for technique success and basic to avoid and/or reduce complications. However, features affecting training duration have not been sufficiently studied so far. AIM: Identify features influencing PD training duration and their relation to first peritonitis episodes timing and permanence on PD.

Methods: We retrospectively analysed all training sessions done with first time PD starters in our Unit (January 2001–December 2018). Demographic data on age, gender, end ESRD cause, Charlson morbidity index (CCI), number of training sessions, type of PD start, employment and education status, derivation and PD technique were recorded.

Results: 188 patients were trained, 72% male. Median age 55.49 yr, 25% were diabetic. Mean CCI 4.9. Our patients required a median of 10 sessions (range 2-28) to gain sufficient skills performing the PD technique and feel confident, with a median of 19 days. Number of training sessions required increased with higher age (p = 0.05), higher CCI (p = 0.05) and diabetics (p = 0.05). Neither gender, cohabitation, type of PD start, education level, derivation type nor employment status were statistically significant factors affecting PD training. Assisted PD patients were older (54 vs 71 yo, p=0.00) and they required a higher number of training sessions (10 vs 15.7 sessions). Patients requiring longer training (>23 days) had more peritonitis episodes (p<0.05), the first peritonitis episode happened sooner (15.7 vs 17.4 months, p<NS) and they remained less time on PD (32.57 vs 27.7 months, p = 0.01).

Conclusions: The PD training time needed depends on patient’s age, diabetic status and comorbidities but does not relate to social, educational nor employment status. Patient’s requiring less training sessions have less peritonitis episodes and it happens later, remaining longer on PD technique.

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POI1298
Clinical Outcomes of Infection-Related Hospitalization in Incident Peritoneal Dialysis Patients
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Background: Infection is the second leading cause of death in patients undergoing long-term dialysis. Peritoneal dialysis (PD) is associated with an increased risk of infection-related hospitalization (IRH) when compared with hemodialysis. However, the effects of IRH on clinical outcomes in PD patients have not been established. In this study, we investigated the influence of IRH on clinical outcomes in incident PD patients.

Methods: In total, 583 incident PD patients were selected from the Clinical Research Center Registry for End/Stage Renal Disease, a nationwide multicenter prospective observational cohort study in Korea. Incident PD patients who had been hospitalized for infection-related diseases were categorized as the IRH group. The primary outcome was all-cause mortality and the secondary outcome was technical failure. The median follow-up period was 29 months.

Results: Seventy-three PD patients (13%) were categorized as the IRH group. Multivariate logistic regression analysis showed that diabetes mellitus was a significant independent predictor for IRH (odds ratio: 2.43, 95% confidence interval [CI]: 1.12–5.29, p=0.007). The most common causes of IRH were peritonitis (64.9%) and respiratory tract infection (11.9%). Multivariable Cox proportional hazard model analysis showed that IRH was a significant independent risk factor for all-cause mortality (hazard ratio [HR]: 2.51, 95% CI: 1.12–5.62, p=0.026) and for the technical failure of PD (HR: 3.23, 95% CI: 1.90–5.51, p<0.001).

Conclusions: Our data showed that after initiation of PD, IRH was significantly associated with higher risk of all-cause mortality and technical failure. Careful consideration of infection-related disease is needed in incident PD patients.

POI1299
Fluoroscopic-Guided Peritoneal Catheter Insertion: Radiology Anthropometric Analysis for Determining Optimal Catheter Position
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Background: Placement of a functioning peritoneal catheter requires optimal catheter positioning. Traditionally the pubic symphysis has been used as a landmark for the true pelvis and referenced for catheter-tip positioning. This practice is based on physical-exam methods without the benefit of fluoroscopic imaging.

Methods: Retrospective cohort of adult, peritoneal dialysis patients in London, Ontario, who underwent percutaneous peritoneal catheter insertion using fluoroscopy spanning Feb 1, 2013 - Aug 1, 2017. Pre-specified anthropometric measures: 1) distance between deep pelvic space (outlined by caudal border of pooled radiocontrast injected intra-procedure) and cranial border of pubis symphysis; 2) distance between catheter-tip and cranial border of pubis symphysis - were measured using Citrix software of stored images. Anthropometric measures were contrasted according to sex via t-tests (p<0.05) and multivariable regression analyses, assessing relationships of potential predictors (age, BMI, prior abdominal surgery).

Results: 295 patients (69% male) underwent fluoroscopic catheter insertion during the study period. Average age was 60 ± 16 years (std. dev.), BMI 28 ± 5 kg/m². 52% of patients had no prior surgical history, 30% had 1 prior abdominal surgery, 18% had ≥2 prior surgeries. Average distance between deep pelvic space and pubis symphysis was 2.9 ± 1.5 cm, with females having a larger distance (3.4 ± 1.7 cm) compared to males (2.5 ± 1.4 cm; P<0.001); Female sex being associated with a 0.6 ± 0.2 cm, (P=0.03) increase in distance between the pubis symphysis and deep pelvic space as compared to males, adjusted for age, BMI, and number of prior abdominal surgeries. Stratified by sex: age, BMI, number of prior abdominal surgeries was not associated with distance between the pubis symphysis and deep pelvic space. Catheter-tip to pubis symphysis distance was 3.8 ± 1.7 cm and similar across sexes.

Conclusions: Fluoroscopic methods of outlining the deep pelvic space for peritoneal catheter positioning approximate traditional methods. Differences observed in the distance between the pubis symphysis and deep pelvic space according to sex may reflect the impact of anatomical differences and/or type of abdominal surgeries. However, catheter tip positioning remained unaffected.

POI1300
Blood Pressure Telemonitoring in a Large US Peritoneal Dialysis Population
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Background: Home remote monitoring (HRM) is a telehealth strategy that utilizes cellular technology to transmit patients’ biometric data collected at home to the electronic health record of their dialysis provider. In April 2017, a HRM program was launched nationwide for peritoneal dialysis (PD) patients at a US large dialysis organization (LDO). Here, we report longitudinal trends in blood pressure (BP) control among PD patients participating in the HRM program.

Methods: Data for this analysis were abstracted from LDO electronic medical records. Patients included were dialyzing with PD and participating in the HRM program from Apr 2017-Jan 2020. The following outcomes were tracked monthly for all patients: mean BP, mean arterial BP (MAPB), number of transmitted BP measurements, number of BP alerts, and number of antihypertensive (anti-HTN) medications prescribed. BP alert thresholds were determined on a patient-by-patient basis by the treating physician.

Results: We identified 21,081 eligible patients (average age 59 years old; 57% male) from which >3.5 million individual BP measurements were transmitted. On average, there were 170 readings transmitted per-patient over the monitoring period of 43 months; in total, 764,658 total BP alerts occurred (36 BP alerts/patient). Only 34% of patients achieved the target BP of <130/80 mm Hg. We observed 30%, 23%, and 47%, of patients were prescribed 0, 1-3, and >3 anti-HTN medications, respectively. The most common action responding to BP alerts included changes in medications and prescribed ultrafiltration volume. However, a significant percentage of PD patients did not see an improvement in MABP [Figure].

Conclusions: HRM identified a significant percentage of PD patients with uncontrolled BP. HRM could be a useful component of clinical programs designed to improve BP control and cardiovascular outcomes.
PO1301
Plasmatic Magnesium as a Marker of Nutrition and Inflammation in Peritoneal Dialysis?

Background: There’s an important prevalence of hypomagnesemia (hypoMg) in Peritoneal Dialysis (PD), namely due to magnesium (Mg²⁺) losses in the dialysate. HypoMg has recently been associated with increased mortality in PD, a clearer fact in Hemodialysis. Processes involved seem to include alterations in body composition (BC) and inflammation, known as predictors of mortality in PD, beyond the risks immediately associated with hypoMg such as cardiac arrhythmias. The aim of this study was to evaluate the correlations between plasmatic Mg²⁺ (pMg), BC, inflammation and nutrition in PD.

Methods: A prospective study included patients admitted at our Unit between 2010 and 2019, with simultaneous acquisition of bioelectrical impedance analysis (BIA) and pMg levels. Clinical and biochemical data were collected from clinical records. Spearman rank-correlation coefficient was used to report correlations.

Results: 54 patients were enrolled (mean age of 54.2±17.6 years, 61% men, 86.3% hypertensive and 33.3% diabetic). Mean pMg was 2.10±0.37 mg/dL and high-sensitivity C-reactive protein (hs-CRP) 10.8±6 mg/L. Inverse correlations were found between pMg and fat mass (rs=−0.356, p=0.009), body mass index (BMI) (rs=−0.414, p=0.002) and hs-CRP (rs=−0.334, p=0.014). Regarding serum markers of nutrition, a correlation with pre-albumin (rs=0.297, p=0.036) was found. No correlations with phase angle, ratio of extracellular mass to body cell mass, lean body mass index, serum albumin, creatinine, total protein, total cholesterol or transferrin were found. hs-CRP in turn correlates with BMI (rs=0.309, p=0.023), inversely with pre-albumin (rs=−0.353, p=0.012) and has a tendency to correlation with fat mass (rs=0.254, p=0.052) and albumin (rs=−0.267, p=0.051).

Conclusions: Lower pMg is associated with increased fat mass and higher BMI. No correlations were found with other nutrition markers. The obesity paradox is still controversial in PD and some authors defend that an elevated BMI is associated with neutral to deleterious impact on PD outcomes, fact explained by fat mass. Proinflammatory effects are also well described in relation to obesity in PD. In conclusion, hypoMg seems associated with poorer nutrition, increased fat mass and inflammation. Dietary interventions with Mg²⁺ supplementation could address this problem and should be a target of interventional studies.

PO1302
Feasibility of Using Platelet PGDprime® Rapid Assay as a Peritonitis Screen for Peritoneal Dialysis Patients
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Background: Peritoneal Dialysis (PD) patients carry the risk of bacterial infection via the catheter access site and the exit site. Peritonitis is suspected based on patient symptoms and the visual quality of effluent, but may not be confirmed until a sample of the effluent is tested at a central lab via culture. A result may take several days to generate. The Platelet PGDprime® rapid test is a multiplexed immunoassay used to detect Gram-positive (GP) and Gram-negative (GN) bacteria in platelet units prior to transfusion. The utility of this rapid test for detection of bacteria in PD effluent was evaluated.

Methods: A sample (600 mL) of PD effluent from an asymptomatic patient was obtained and confirmed to be negative for bacteria by aerobic and anaerobic cell culture. Eight bacteria (5 GN & 3 GP) were grown in RPMI media and individually spiked at initially high levels into aliquots of the PD effluent, then serially diluted with the unspiked effluent in tenfold series. The CFU/mL of each starting spiking stock was quantified by OD at 620 nm. Each dilution was tested with PGDprime® to determine the lowest detectable level of bacterial contamination by ten-fold dilution.

Results: The lowest detectable concentrations of bacteria were summarized in Table 1. The true Limit of Detection (LoD) for each species is the lowest detectable concentration shown and the next lower logfold dilution level. Total test time was 25-35 minutes.

Conclusions: The PGDprime® rapid test for bacteria in plateletks can detect bacteria in PD effluent and may be useful for early detection of peritonitis in PD patients. Additional optimization to further adapt the test for PD effluent testing is underway.

Funding: Commercial Support - Verax Biomedical Incorporated

Table 1. Detection of Bacteria in PD Effluent by the PGDprime® Rapid Test

PO1303
Omentectomy Reduces the Need for Peritoneal Dialysis Catheter Revision in Children: A Study from the Pediatric Nephrology Research Consortium
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Background: There are no recommended guidelines for performing omentectomy at the time of peritoneal dialysis (PD) catheter placement in the pediatric population. There are no multi-center studies investigating omentectomy and PD catheter revision in the pediatric dialysis population.

Methods: A multi-center, retrospective study was performed through the Pediatric Nephrology Research Consortium (PNRC). Data review included all incident tunneled PD catheters placed between 1/1/2011 – 12/31/2016 for first-time PD patients (ages 0-20). The primary outcome was the need for catheter revision and/or replacement following initial placement. Multivariable logistic regression was used to determine the independent association of omentectomy with catheter revision/replacement.

Results: Data from 184 patients (62.5 % male; 35.4 % glomerulonephritis) from 8 centers were analyzed. Median age at PD catheter insertion was 7.4 years. Omentectomy was performed in 67 children at the time of catheter placement (36.4%). Revision or replacement was required in 63 children (52.2%); median time to revision/replacement was 38.5 days (IQR 20.5, 109) after catheter insertion. Revision/replacement of the catheter occurred in 23.9% who had an omentectomy, compared to 52.2% without omentectomy (p=0.0005). Compared to younger children, those ≥ 6 years of age at the time of PD catheter placement had decreased risk of catheter revision/replacement (18.2% age ≥ 6 vs 56.5% age < 6, p <0.001). After adjusting for all clinical and surgical covariates, omentectomy reduced need for revision by almost 70%, and revision was 4x more likely in those ≤ 6 years of age.

Conclusions: This multi-center study is the first to show that omentectomy at the time of PD catheter placement in pediatric patients is associated with decreased PD catheter revisions. Omentectomy should be strongly considered at the time of PD catheter placement, especially in children < 6 years of age who are at high risk for PD catheter malfunction.

Funding: Commercial Support - Verax Biomedical Incorporated

PO1304
Quality Improvement Initiative: Suboptimal Utilization of Loop Diuretics in Peritoneal Dialysis Patients
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Background: The prescription of high dose loop diuretics is safe and beneficial for PD patients to increase urine output, control of volume status, and decrease the need for high PD fluid glucose concentrations. The aim of this study is to assess the current state and develop an algorithm for rational diuretic use in PD pts to optimize dose, frequency, and reduce pill count in patients with urine output while reducing diuretics in anuric patients.

Methods: This was a prospective cohort QI initiative in prevalent PD pts. The algorithm considered PD fluid glucose > 1.5 % used, the volume status, current and historical urine volume trend, and clinical assessment. The dosing of loop diuretics was increased in pts with residual urine output > 200 ml/day when increased ultrafiltration was needed, while diuretics were stopped in anuric pts. The outcomes were the proportion of pts on loop diuretic in those with and without urine, the dose (median total daily,

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frequency) and the pill count before and 3 months after the intervention. In the algorithm, Furosemide prescription of 40 mg tablets was converted to 500 mg tablets divided as needed where possible.

Results: The study included 91 pts, mean age 63 yrs, 45% female, 75% Caucasian, 64% with DM, median time on PD of 1.58 yrs. Furosemide was the only loop diuretic used. At baseline, median total daily dose was 120 mg, BID 77%, OD 73%, and mean pill count was 3.6 pills/day. The proportions of patients prescribed diuretics among those with and without urine output were 54/84 (63%) and 8/17 (47%) respectively. Three months after the intervention the median total daily dose was 240 mg, BID 53% and OD 47%, mean pill count was 2.96 pills/day, and the proportions of pts on Furosemide for those with and without urine output improved to 85% and 27% respectively (all changes p < 0.05).

Conclusions: This short-term study suggests that QI intervention using an algorithm aimed at optimizing loop diuretic use in PD patients based on PD fluid glucose concentration used, and urine volume can increase the prevalence of diuretic use, increase the single and total daily dose, improve dosing frequency, and reduce pill burden in patients with urine output while reducing unnecessary use in anuric pts. This study is ongoing to examine outcomes of urine volume, glucose load of PD fluid, and electrolytes with the intervention.

POI1305
Assessing Fluid Status of Peritoneal Dialysis Patients with Assistance of Lung Ultrasound (Fluid-PLUS)
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Background: Fluid overload (FO) is common in patients on dialysis, and is associated with increased cardiovascular morbidity and mortality. Clinical examination is limited in detecting FO. Lung ultrasound (US) is a portable and relatively inexpensive objective measure of FO. In this study, we aimed to evaluate the potential utility of lung US for evaluation of FO in patients on peritoneal dialysis (PD) in the ambulatory setting.

Methods: This is a cross-sectional, observational study at 4 home dialysis clinics in Northern California. Adult patients on PD attending routine outpatient visits were asked to participate. Patients on PD for less than 3 months or endorsing new or worsening shortness of breath were excluded. Participants underwent lung US examination. Based on the total number of B-lines, patients were classified as no US-fluid overload (< 16 lines), or US FO (≥ 16 lines). Independently, nurses clinically evaluated patients’ fluid status and determined if a patient had clinical FO or no clinical FO.

Results: 43 patients underwent full evaluation. Mean age was 55 ± 15, 28% were female. 4% of patients had diabetes mellitus, and median PD vintage was 19 (IQR 10-37) months. Clinically, 13 (30%) of patients had FO. Lung US identified 15 patients (35%) as having FO. Clinical and US findings were congruent in 35 (81%) patients, but discordant in 8 (19%) of patients. Of the 30 patients without clinical FO, 5 (17%) were identified with US FO. On the other hand, of the 13 patients with clinical FO, 3 (23%) had no US FO. – Figure 1. Agreement between clinical examination and lung US was moderate (kappa 0.58, 95% CI 0.32 to 0.84).

Conclusions: Lung US may identify a subset of patients with FO missed by clinical examination. Further studies are required to evaluate the impact of managing patients according to lung US findings on clinical outcomes.

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POI1306
Use of Incremental Peritoneal Dialysis: Impact on Clinical Outcomes and Quality-of-Life Measures
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Background: Incremental peritoneal dialysis (PD), defined as a PD prescription that is less than the standard, full-dose prescription, has been suggested as a means of preserving residual kidney function and offering better quality of life; however, published evidence is limited.

Methods: We considered adult patients initiating PD between 31 Jul 2015 and 31 May 2019. Patients with body weight ≤ 40 kg, limb amputation, or estimated glomerular filtration rate (eGFR) >20 mL/min during first 4 weeks on PD were excluded. Exposure group was ascribed (incremental vs full PD) based on PD prescription during dialysis weeks 5 to 8. Incremental PD was defined by treatment frequency, exchanges/day, and exchange volume (for continuous ambulatory PD [CAPD] patients) or by treatment frequency and presence/absence of last fill (for automated PD [APD] patients). Analyses were performed separately for CAPD and APD patients: for each, incremental PD patients were propensity score matched to eligible full PD patients. Patients were followed for up to 12 months until censoring for loss to follow-up or study end. Outcomes were compared using Poisson models (mortality, hospitalization, PD failure), linear mixed models (eGFR), and paired t-tests (Kidney Disease Quality of Life [KDQOL] domain scores).

Results: Among CAPD patients, compared to those on full PD, incremental PD use was associated with better KDQOL scores on 3 domains: physical composite score (42.5 vs 37.7, P=0.03), burden of kidney disease (60.2 vs 45.6, P=0.003), and effects of kidney disease (79.4 vs 72.3, P=0.05). Hospitalization and mortality rates were numerically lower (0.77 vs 1.12 admits/patient-year, P=0.09 and 5.0 vs 10.2 deaths/100 patient-years, P=0.22); there was no association with residual eGFR or PD failure rate. Use of incremental PD was not differentially associated with any outcome among APD patients.

Conclusions: These results suggest that it may be beneficial to use incremental PD in the context of CAPD, particularly with respect to quality of life. No significant benefits were detected among patients initiating APD. No detrimental effects of using incremental PD were observed for either PD type.

POI1307
Combination of Hypertension and Preexisting Cardiovascular Disease and Mortality in Patients on Continuous Ambulatory Peritoneal Dialysis
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Background: Little is known about whether combination of hypertension and pre-existing cardiovascular disease (CVD) is more strongly associated with outcomes compared with either comorbidity alone in patients on continuous ambulatory peritoneal dialysis (CAPD).

Methods: We conducted a retrospective study of 3073 incident Chinese patients on CAPD from five dialysis centers between January 1, 2005 and December 31, 2018 in a real-world setting. All patients were divided four groups: group 1 (patients without either hypertension or pre-existing CVD); group 2 (patients with only hypertension); group 3 (patients with only pre-existing CVD); group 4 (patients with both hypertension and pre-existing CVD). The association between interesting comorbidities and mortality was analyzed using Cox regression models.

Results: Over a median of 33.7 months of follow-up, 581 (18.6%) patients died, with 286 (9.3%) CVD mortality. The incidence of all-cause mortality was 32.2, 56.1, 74.4, and 131.0/1000 patient-years, and the incidence of CVD mortality was 3.2, 8.4, 13.1, and 28.2/1000 patient-years in group 1, 2, 3, and 4, respectively. Cumulative survival and CVD mortality-free survival were lowest in those with both hypertension and pre-existing CVD (Figure 1). After adjusting for the demographic characteristics and laboratory parameters, group 4, 3, and 2 had 3.07 (95% CI 2.23 to 4.22), 2.05 (95% CI 1.11 to 3.80), and 1.38 (95% CI 1.08 to 1.77) of hazard ratios for all-cause mortality, and 3.20 (95% CI 2.04 to 5.03), 2.09 (95% CI 0.85 to 5.15), and 1.56 (95% CI 1.09 to 2.23) of hazard ratios for CVD mortality, respectively, compared to the group 1.

Conclusions: Combination of hypertension and pre-existing CVD was more strongly associated with mortality compared to either comorbidity alone in CAPD patients.

POI1308
Returning to Peritoneal Dialysis After Kidney Transplant Failure Is a Valuable Option

Background: The prognosis for patients returning to peritoneal dialysis (PD) after a failed transplant is poor and associated with peritonitis and transfer to hemodialysis. PD has an advantage over hemodialysis in preserving residual renal function, which is associated with better outcomes, including survival. Maintaining immunosuppression after starting PD can preserve transplant function but can also increase the risk for infection, and therefore is still arguable.
Methods: We have reviewed electronic charts of patients on PD in the last 8 years in our hospital. We computed survival, residual diuresis and reasons to discontinue PD in 2 groups: patients with graft failure that returned to PD (PD-Ktx, N=17) and other clinical conditions (PD-other, N=153). Reasons for stopping PD therapy included: dialysis inadequacy, kidney transplant, death, transfer to another center, and pertinent patient reasons.

Results: The median follow-up was 36 (12,71) months, which was similar between groups [45 (18,96) in PD-Ktx vs. 35 (12,70) months in PD-other, p=0.403]. Patients from PD-Ktx group were lighter than those from PD-other (57.2 ± 14.7 vs. 66.1 ± 16.1kg, p=0.02) and final diuresis volumes were similar among groups (p=0.879 and p=0.698, respectively). Reasons for stopping PD therapy in PD-Ktx and PD-other groups were dialysis inadequacy (17.6% and 20.9%, respectively), kidney transplant (17.6% and 15.7%), death (5.9% and 12.4%), transfer to another center (17.6% and 20.9%), and patient reasons (15% and 14.6%). These outcomes were not significantly different between groups (p=0.921). Four out of 17 patients from PD-Ktx maintained immunosuppression and none of those had peritonitis. Kaplan Meier survival comparing PD-Ktx and PD-other showed there is no difference in stopping PD due to peritonitis (log-rank 0.543), which was confirmed in a Cox regression adjusted for weight, diabetes, residual diuresis and age (p=0.493).

Conclusions: Clinicians should leverage the risk of peritonitis versus extend PD technique by preserving residual diuresis in patients with allograft failure returning to PD. We have found similar outcomes in the current study. However, whether withdrawal immunosuppression is needed for these patients requires further investigation.

PO1309
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Background: Decision-Making Tools (DMTs) are still not widely used but are considered gold standard to ensure patients are well informed to choose renal replacement therapy (RRT) modality. OBJECTIVE: To analyze the impact of a structured modality information program (via DMTs) on RRT modality choice and start.

Methods: All 2014-2017 predialysis patients (pts) with CKD G4-G5 and those starting unplanned dialysis without a prior information process underwent a DMTs program. Use of DMTs was followed up to Dec 31st 2018. DMTs included values evaluation, RRT information with different tools, staff deliberation support and patient modality choice. Results shown as percentage of pts who reached a certain stage over the total number of pts under evaluation.

Results: 2012 pts (mean age 61 ± 11 y.) from 48 clinics (cl.) in Poland (PL, 19 cl., 980 pts), Romania (RO, 12 cl., 351 pts), Hungary (HU, 10 cl., 341 pts), Germany (DE, 6 cl., 292 pts) and Argentina (AR, 1 cl., 48 pts) underwent DMTs. Staff considered PD contraindicated in 29% of pts, hence optimal candidates for HD/PD were 1408 pts. (mean age 62 ± 16 y., 96% male). HD patients had higher mean kidney size and mean body weight ratio compared to PD patients. The median survival of those on PD (36.3 months) and HD (77.2 years) were not significantly different. Among 948 pts who had started dialysis by study closure (n=948), PD choice (35%) varied among countries: 15% (RO), 30% (PL), 36% (HU), 62% (DE) and 98% (AR). For pts who had started dialysis by study closure (n=948), PD choice (35%) varied among countries: 15% (RO), 30% (PL), 36% (HU), 62% (DE) and 98% (AR). For pts who had started dialysis by study closure (n=948), PD choice (35%) varied among countries: 15% (RO), 30% (PL), 36% (HU), 62% (DE) and 98% (AR).

Conclusions: Physicians should leverage the risk of peritonitis versus extend PD technique by preserving residual diuresis in patients with allograft failure returning to PD. We have found similar outcomes in the current study. However, whether withdrawal immunosuppression is needed for these patients requires further investigation.

PO1311
Peritoneal Dialysis in the Setting of Acute Brain Injury, an Underappreciated Modality
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Introduction: Dialysis is complicated in the setting of acute brain injury due to a number of factors including acute shifts of solute, acute acid base shifts, need for anticoagulation, and changes in intracranial pressure. For these reasons, CRRT is the modality of choice when renal replacement therapy is needed. PD is less discussed but shares many of the benefits often attributed to CRRT. We describe a case successfully managed with PD.

Case Description: A 25-year-old male with history of ESRD secondary to FSGS on CCPOD for 5 years presented to the hospital with headache and altered mental status. He was in his usual state of health until the day prior to admission. Initial imaging revealed a large intraventricular hemorrhage extending to the 4th ventricle. He underwent an emergent right depressive hemicraniectomy and clot evacuation. Patient was admitted to NCCU. Post-operative imaging revealed worsening cerebral edema, intraventricular hemorrhage, and hydrocephalus. As the patient had a functioning tenckhoff catheter, peritoneal dialysis was made to continue peritoneal dialysis, which he tolerated well, until the need for a percutaneous gastrostomy tube arose. He was transitioned to hemodialysis transiently but returned to peritoneal dialysis once he was able to tolerate oral food. He has now continued on PD for 1 year.

Discussion: In the dialytic management of patients with acute brain injury, a number of considerations must be undertaken including the avoidance of hypotension to minimize ischemia reperfusion injury and maintain cerebral perfusion pressure, avoidance of anticoagulants that can precipitate or worsen bleeding, the potential for the precipitation of cerebral edema by rapid solute clearance and osmotic dissipation of therapeutic hypernatremia, and the mitigation of intracellular acidosis from bicarbonate delivery. Peritoneal dialysis is an ideal but underreported modality as evidenced by the case presented.

PO1312
Peritoneal Ultrafiltration Is Associated with Improvement of Functional Class in Patients with Congestive Heart Failure
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Introduction: Congestion is considered an integral component of heart failure syndrome and is a key driver of adverse outcomes. Peritoneal ultrafiltration (PUF) has emerged as an efficient therapeutic modality for management of fluid overload in patients with congestive heart failure (CHF) without end-stage kidney disease (ESKD). The efficacy of therapies of CHF are conventionally assessed through their effect on New York Heart Association (NYHA) classification. We sought to explore the reported impact of PUF on functional class of these patients.

Case Description: Class in Patients with Congestive Heart Failure
PO1310
Peritoneal Dialysis or Haemodialysis for Polycystic Kidney Disease? Ten Years’ Experience in a Single Centre
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Background: When polycystic kidney disease (PKD) progresses into end-stage renal disease (ESRD), the choice of dialysis modality is not straightforward. PKD may increase the risk of complication and technique failure (TF) in peritoneal dialysis (PD). We looked at the long-term outcomes of PKD patients put on either PD or haemodialysis (HD).

Methods: New cases of ESRD due to PKD entered into dialysis program of a tertiary hospital in Hong Kong from December 2009 to November 2019 were identified. Their baseline demographics, mean kidney size and clinical outcomes were recorded. Hong Kong has a “PD first” policy. But for PKD patients, the decision to start PD or HD is by the nephrologists’ clinical judgment. For statistical analysis, chi-square test and t-test were used for categorical and continuous variables respectively. Kaplan-Meier curve was used to analyse survival.

Results: A total of 45 patients were identified, 31 were put on PD, 14 were put on HD. Their baseline characteristics were shown in Table 1. HD patients had higher mean kidney size to body weight ratio compared to PD patients. The median survival of those on PD (36.3 months) and HD (77.2 years) were not significantly different. Among 948 pts who had started dialysis by study closure (n=948), PD choice (35%) varied among countries: 15% (RO), 30% (PL), 36% (HU), 62% (DE) and 98% (AR).

Conclusions: This study showed that for PKD patients with moderate enlarged kidneys, PD could be a reasonable choice. However, for patients with very large kidneys, early TF rate with PD was high, HD would be a better choice for these patients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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Methods: Articles cited in PubMed database using keywords “heart failure”, “peritoneal ultrafiltration”, and “peritoneal dialysis” were searched. Available data from contemporary clinical trials of PUF in patients with CHF (without ESKD) that were performed between January 2010 and August 2019, and included more than 20 patients were selected and reviewed. Those trials evaluating the impact of PUF on NYHA functional class were included. Pertinent data were extracted and recorded.

Results: Out of 10 clinical studies meeting the criteria, 4 did not have the needed data on NYHA class; 6 studies (3 retrospective and 3 prospective) with a total of 408 participants and a mean age of 71.9 were included. The pre-PUF mean left ventricular ejection fraction and weight were 34.6% and 78.6 Kg respectively. The median follow up was 13.7 months. There was substantial variation in the reporting of time point for various endpoints. These studies unanimously reported improvement in NYHA functional class, which was close to -1 class for those that assessed the entire study population.

Conclusions: Available data based on contemporary clinical trials suggests that PUF, when used for management of patients with CHF, is associated with improvement of functional class. This finding is in keeping with our previous report on the salutary impact of PUF on volume status of these patients. Future controlled studies are needed to explore whether these benefits would translate into improved survival.

PO1313
Blood Urea Nitrogen/Creatinine Ratio and Mortality in Patients on Continuous Ambulatory Peritoneal Dialysis

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Background: Little is known about the association between the Nitrogen/Creatinine (BUN/Cr) ratio and mortality in continuous ambulatory peritoneal dialysis (CAPD) patients.

Methods: We conducted a retrospective study of eligible 2837 patients on CAPD from five dialysis centers in Chinese between January 1, 2005 and December 31, 2018. We calculated baseline BUN/Cr ratio, and then estimated the hazard ratio (HR) of BUN/Cr ratio for all-cause mortality using Cox hazard regression models, and used the restricted cubic spline curve to evaluate the association between the BUN/Cr ratio and mortality, with adjusting for confounding factors.

Results: The median age of at baseline was 50.0 years (39.0-61.0) and the baseline median BUN/Cr ratio was 7.62 (5.43-9.13). The median observational period was 35.3 (18.3-61.9) months. During this period, 509 (17.9%, 95% CI 16.5 to 19.4%) of 2837 patients died, with 253 (8.9%, 95% CI 7.9% to 9.9%) CVD mortality. The incidence of all-cause mortality and 1.66 (95% confidence interval, 1.15 to 2.40) of HR for CVD mortality, after BUN/Cr ratio ≥ 5.43 as a reference, those with BUN/Cr was 19.0, 26.0, 28.1, 30.9/1000 patient-years among quartile 1, quartile 2, quartile 3, and quartile 4, respectively. When using BUN/Cr ratio of ≤ 5.43 as a reference, those with BUN/Cr ratio ≥ 5.43 had 1.72 (95% confidence interval, 1.34 to 2.22) of HR for all-cause mortality and 1.66 (95% confidence interval, 1.15 to 2.40) of HR for CVD mortality, after adjusting for baseline characteristics and laboratory variables. Cubic spline showed there was a linear association between the baseline BUN/Cr ratio and the risk of all-cause and CVD mortality, with a higher risk of mortality at a higher BUN/Cr ratio (Figure 1).

Conclusions: In conclusion, the BUN/Cr ratio at the start of dialysis therapy was independently associated with all-cause and CVD mortality among CAPD patients, with a higher risk of mortality at a higher BUN/Cr ratio.

PO1314
Abstract Withdrawn

PO1315
Between Gradients and Ratios

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Introduction: Hydrothorax due to peritoneal dialysis is a rare but known outcome from dialysis mainly in continuous ambulatory peritoneal dialysis [CAPD]. Around 80% cases are due to a pleuroperitoneal fistula (PPF), an abnormal communication between the pleural and peritoneal space allowing leak of dialysate. A pleural fluid glucose to serum glucose gradient of >50 mg/dl is 100% specific for detecting the leak of glucose rich dialysate via the fistula.

Case Description: A 63-year-old man with history of heart failure with reduced ejection fraction and end stage renal disease [ESRD] on continuous cyclic peritoneal dialysis [CCPD] for 3 months, presented with recurrent hydrothorax. CXR showed worsening right sided hydrothorax despite a recent paracentesis. He continued CCPD as his initial pleural to serum [PF-S] glucose gradient was normal at 21 mg/dl. However, PF-S glucose ratio was >1 raising the clinical suspicion. For confirmation, a peritoneal scintigraphy with nuclear technetium 99 scan was performed that revealed a pleuroperitoneal fistula as the source of the recurrent hydrothorax.

Discussion: Peritoneal dialysis can be complicated by development of a hydrothorax in both CAPD and CCPD. Hydrothorax development is often attributed to a pleuroperitoneal leak which can be congenital or acquired. Initial diagnosis can be supported by increased PF-S glucose gradient >50mg/dl, but in our case, this did not prove to be a reliable indicator. Literature suggests that the pleural effusion is unlikely to be due to a pleuroperitoneal communication with a low PF-S glucose gradient of <50 mg/dl. However, there is also evidence that supports that peritoneal leak as the only cause for pleural glucose to be higher than the serum, i.e. a PF-S glucose ratio >1.0. The PF-S glucose > 1.0 in our case also supports the higher sensitivity of this approach.

PO1316
Impact of Obesity on Success of Peritoneal Dialysis in ESRD Patients

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Background: Obesity rate is rising in the US and 1 in 4 adults are projected to have severe obesity by 2030. Prevalence of obesity in ESRD patients is also rising. Higher BMI has been shown to be associated with better survival in HD patients. However, data is inconsistent for PD patients. We examine the impact of different BMI classes on PD outcomes

Methods: This is a single center retrospective cohort study. Inclusion criteria includes patients >18 yrs, > 3 month PD vintage and patients who received PD from 2014-2018. Exclusion criteria includes patients with BMI <20, patients with no Kt/V data or missing BMI. SAS statistical software was used for data analysis

Results: 181 total patients are divided into 4 groups. Baseline characteristics were similar in all groups (fig 1). Outcomes include transition from PD to HD, transplantation rate, mortality rate, number of hospitalizations, PD vintage and catheter-related infections. Our data showed that there is no difference in outcomes among different BMI groups (tab1, fig 2)
Conclusions: Our single study shows that obesity is not associated with poor peritoneal dialysis outcomes. People with high BMI should still be offered PD as a modality.

Discussion: This case demonstrates a rare complication of PD. Hydrothorax can occur due to increased intra-abdominal pressure causing migration of dialysis fluid from the peritoneal cavity into the pleural space by opening of defects in the diaphragm communicating the two cavities; negative intrathoracic pressure and transiently increased hydrostatic pressure of the dialysate may cause dialysate leak. This phenomenon typically occurs more frequently in women with polycystic kidney disease due to reduced abdominal capacity. Increased glucose in pleural fluid, CT peritoneography and NM scintigraphy are methods of confirming diagnosis. Transition to HD with monitoring for spontaneous closure of the pleuro-peritoneal leak is first line conservative treatment. If the leak persists, surgical repair of the diaphragmatic defect is definitive treatment to resume PD.

PO1318
Ochrobactrum Peritonitis in Peritoneal Dialysis: A Rare Case and Literature Review
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Introduction: Ochrobactrum are gram-negative, non-fastidious, motile bacilli typically isolated in aqueous environments. Reports of infections by this pathogen primarily occur in immunocompromised hosts from environmental exposure, nosocomial contamination of sterile fluids and/or indwelling catheter use. Due to impaired immunity and exposure to exogenous microbes, peritonitis is a common and feared complication of peritoneal dialysis. We present a case of Ochrobactrum anthropi peritonitis and review the literature of similar case.

Case Description: A 67-year-old male with history of ESRD secondary to IgA nephropathy on CCPD for 4 years presented to the hospital with fevers, nausea, abdominal pain and generalized weakness. He experienced an episode of acute bacterial peritonitis 1-month prior to this hospitalization secondary to Pseudomonas aeruginosa treated with ciprofloxacin and fluconazole, and he completed the antibiotic course with resolution of peritonitis, which is a risk factor for hospitalizations, mortality and is the most common cause of transition to hemodialysis. The diagnosis of PD-related peritonitis requires the presence of white blood cell count of >100/μL or positive culture from the effluent dialysate in the setting of abdominal pain and cloudy effluent dialysate. This method requires time and access to a diagnostic facility, which may not be easily available to all dialysis patients to achieve a power of 80% to be able to obtain a 95% specificity. We are including patients on PD. Point-of-care strips that utilize colorimetric changes in leukocyte esterase to detect the presence of white blood cells are available. Three of eight published cases were associated with bacteremia. Antimicrobials treatments have typically included carbapenems, piperacillin/tazobactam, and fluoroquinolones. Three of eight cases required removal of the Tenckhoff catheter. Peritonitis related mortality was zero percent. This case and review of the literature can serve to inform future occurrences.

PO1319
The Utility of Point-of-Care Reagent Strips for Rapid Rule out of Peritonitis in Patients on Peritoneal Dialysis

Background: 10% of all end stage renal disease (ESRD) patients in the United States use peritoneal dialysis (PD). An important complication in this population is PD-related peritonitis, which is a risk factor for hospitalizations, mortality and is the most common cause of transition to hemodialysis. The diagnosis of PD-related peritonitis requires the presence of white blood cell count of >100/μL or positive culture from the effluent dialysate in the setting of abdominal pain and cloudy effluent dialysate. This method requires time and access to a diagnostic facility, which may not be easily available to all patients on PD. Point-of-care strips that utilize colorimetric changes in leukocyte esterase reagent can be used to provide a quick, presumptive diagnosis of peritonitis. We evaluate the specificity or true negative rate of two reagent strips – PeriScreen and Multistix 10 SG.

Methods: We are conducting a diagnostic test study in a prospective cohort at the home dialysis clinic at Washington University in Saint Louis. We plan to include 100 patients to achieve a power of 80% to be able to obtain a 95% specificity. We are including

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patients who are asymptomatic i.e. without abdominal pain or cloudy dialysate effluent. We will be able to detect, by direct analysis of their effluent dialysate, if the timing of their dialysis kinetics are being measured. Two samples will be sent to the laboratory to obtain white blood cell count, and bacterial culture. PeriScreen and Multistix 10 SG reagent strips will then be dipped in the remaining two samples. The results from all four scores are reported as positive or negative, and the results of the reagent strips will be compared to the gold standard of white blood cell count and culture. Specificity will then be calculated.

Results: Data from 10 patients has been obtained to-date. The average age of these patients was 60.1 (±1.47) years, with 50% of them being females, and 50% of them were Caucasians. In these patients, the PeriScreen was found to have specificity of 100% and the Multistix 10 SG was found to have specificity of 100%.

Conclusions: Based on preliminary results, both PeriScreen and Multistix 10 SG reagent strips appear to have specificity >95%. Using this data, we aim to create a protocol for patients to use these strips at home to help rule out PD-related peritonitis in a more efficient manner.

PO1320

Acyclovir for Herpes Zoster Encephalitis: Panacea or Problem?
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Introduction: Herpes zoster, which is the reactivation of varicella-zoster virus (VZV), is more common in immunocompromised patients, with a higher incidence of encephalitis. The treatment of choice is intravenous acyclovir, with one of its adverse effects being neurotoxicity. We present a case where the disease effects and the medication side effects were difficult to distinguish.

Case Description: A 59-year-old man with ESKD and a history of failed allograft on peritoneal dialysis (PD) presented with one day of acute onset headache, confusion and ataxia. Two days prior, he was diagnosed with dermatomal zoster and was treated with valacyclovir 1000 mg thrice daily. Lumbar puncture showed no pleocytosis, but protein elevation at 90 mg/dL. EEG showed no epileptiform activity and MRI and MRA brain were normal. Because his symptoms started after the initiation of overdosed valacyclovir, medication toxicity was considered more likely than VZV encephalitis. PD was continued, but he deteriorated with worsening mental and pulmonary status after aspiration, requiring intubation. Subsequently, he underwent 3 daily hemodialysis (HD) treatments without improvement. On the 3rd day post-intubation, the CSF VZV PCR returned positive prompting intravenous acyclovir at 5mg/kg/day. Over the next day, he showed marked mental status improvement and got extubated. The serum VZV PCR also resulted positive which was diagnostic of disseminated herpes zoster with encephalitis. After 6 days of intravenous acyclovir therapy, he was discharged on valacyclovir 500mg twice daily to complete 21 days of therapy.

Discussion: Herpes zoster encephalitis and valacyclovir neurotoxicity can lead to similar presentations and pose a diagnostic challenge. Due to low volume of distribution and low protein binding, valacyclovir is highly dialyzable. Hemodialysis can be helpful for patients to use these strips at home to help rule out PD-related peritonitis in a more efficient manner.

POI321

Pittsburgh Sleep Quality Index Score Predicts All-Cause Mortality Independently in Chinese Dialysis Patients
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Background: Poor sleep quality (SQ) is common in dialysis patients. The Pittsburgh Sleep Quality Index Score (PSQI) is a standard tool for evaluating SQ with high validity and reliability. The relationship of PSQI score to survival in dialysis patients has not been well studied. Less was reported in China. The aim of this study was to explore the association between PSQI score and all-cause mortality in Chinese dialysis patients.

Methods: 109 patients who were treated for more than 3 months in Sun Yat-sen Memorial Hospital of Sun Yat-sen University between April 1, 2006 and Aug 1, 2017 and completed questionnaires on SQ were enrolled in this retrospective study. The PSQI was used to evaluate SQ. PSQI score >5 or ≤2 were considered to indicate “poor sleepers” or “good sleepers” respectively. The primary outcomes was all-cause mortality. Restrictive cubic spline (RCS) regression models were used to examine the dose-response relationship between PSQI score and all-cause mortality. Cox proportional hazards regression analysis was performed.

Results: 109 patients were included, composed of 51 hemodialysis and 58 peritoneal dialysis patients. Mean follow-up time was 69.1 ± 29.9 months, during which 21 deaths occurred. 67 (61.5%) patients had poor SQ. Compared with poor sleepers, good sleepers had significantly higher levels of hemoglobin [78.0 (68.0, 97.0) vs. 74.0 (61.0, 85.0), P = 0.02]; leukocyte count [9.7 (8.0, 11.7) vs. 8.4 (7.0, 10.2), P = 0.002]; and serum albumin [4.1 (3.5, 4.6) vs. 4.3 (3.7, 4.5), P = 0.022]; RSC analysis showed that 7 was the cutoff value at which the effect of PSQI score on mortality changed. More than 7 of PSQI score increased the risk on all-cause mortality. When PSQI score was analyzed as a continuous variable in the multivariate Cox proportional hazards model, it was associated significantly with all-cause mortality (hazard ratio [HR] = 1.20, 95% confidence interval [95% CI] 1.05, 1.36, P = 0.007). While a threshold of 7 on the PSQI score was found in an additional adjusted model, a PSQI score > 7 was associated with a 2.96 times increase in the hazard for all-cause mortality (HR = 2.96, 95% CI 1.15, 7.61, P = 0.025).

Conclusions: PSQI score > 7 predicted all-cause mortality independently in Chinese dialysis patients. Further studies are needed to confirm decreasing PSQI score less than 7 in Chinese dialysis patients will improve survival.

PO1322

Patient Characteristics and Frequency of Prescription (Rx) Alterations in Automated Peritoneal Dialysis (APD)
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Background: APD provides the flexibility to adapt PD Rx to the needs, lifestyle, and health status of a patient (e.g. residual renal function [Kru], volume and transport status). The alterations may include changes in dwell volumes, dwell times, or number of exchanges. The current analysis aims to describe frequency of APD Rx alterations and patient (pt) characteristics associated with these alterations.

Methods: All de-identified demographic, lab, and Rx data were extracted from Fresenius Kidney Care clinical data warehouse. Adults who were incident to APD from 01/01/2015 to 12/31/2019, completed APD training and ≥1 treatments, and had no change in PD modality or data quality issues with their records were included. Any change in dwell volumes, dwell times, or number of exchanges was considered an alteration. Characteristics of the pts in the month leading up to their most recent alteration were described and stratified by the number of Rx alterations they received at follow-up.

Results: 15,237 pts were eligible for inclusion. The majority (72.7%) of pts had ≥1 PD Rx alterations during a mean follow-up time of 418 days (compared to 201-day follow-up for pts with 0 alterations). Most pts (53%) had dwell volumes adjusted, with 52%, 4%, and 44% having increases, decreases, or both increases and decreases in dwell volume, respectively. The table details pt characteristics prior to alteration by frequency of Rx alterations.

Comparisons: Compared to pts with no Rx alterations, pts with more Rx alterations were heavier, had higher serum phosphorus, lower PD Kt/V, and lower Kru. The number of alterations along with the timing and direction of these changes need to be further studied to help determine if a pattern of changes is associated with risk of PD technique failure and switch to HD.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

POI123

Mitochondric Acid 5 Alleviates Chlorhexidine Gluconate-Induced Peritoneal Fibrosis in Mice
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Background: Peritoneal fibrosis is one of important complications induced by long-term peritoneal dialysis. Mitochondrial dysfunction causes an increase of oxidative stress and depletion of ATP. Thus, it may be associated with fibrosis and other diseases in several organs, especially, mitochondrial acidosis (MA-5), which is a derivative of the plant hormone indole-3-acetic acid, was synthesized and its therapeutic potential for mitochondrial dysfunction in kidney disease models has been reported. In this study, we investigated the effect of MA-5 for peritoneal fibrosis in mice.

Methods: Peritoneal fibrosis was induced by intraperitoneal injection of chlorhexidine gluconate (CG) every other day for 3 weeks in C57BL/6J mice. MA-5 was administered at 2 mg/kg by gavage every day. Control mice received only a vehicle
Vascular Access Type and Risk of Mortality and Hospitalization Among Elderly Hemodialysis Patients: A Target Trial Emulation Approach
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Background: Evidence is mixed regarding optimal choices of incident vascular access type for elderly patients on hemodialysis (HD). Prior studies have primarily compared functioning arteriovenous fistula (AVF) to arteriovenous graft (AVG) and been limited to survival outcome. We used a target trial emulation approach and intention to treat (ITT) analyses to compare AVF versus AVG placement among elderly patients on HD.

Methods: Patients eligible for the target trial were those ≥67 years old at HD initiation, with no AVF/AVG placed before HD initiation, referred for AVF/AVG placement, and had AVF/AVG within 1 year after HD initiation. Patients would be randomly assigned to AVF or AVG and be followed right after AVF/AVG placement for 5 years. Outcomes including mortality, all-cause hospitalization, and cause-specific hospitalization (infection, cardiovascular disease, and vascular access (VA)) related were assessed within 6 months, 1 year, 3 years, and 5 years would be assessed. ITT analysis based on patients’ first AVF or AVG placement would be applied. We used USRDS data from 2010-2016 to emulate the target trial and propensity score (PS) matching to balance the groups’ characteristics.

Results: A total of 37,890 (out of 47,912) patients who had AVF/AVG placed within 1 year after HD initiation were included after PS matching. Among them, 28,847 (76.5%) had AVF placed and 9,043 (23.5%) had AVG placed. AVF was associated with lower risk of mortality over follow-up. Within 6 months after AVF/AVG placement, incidence of all-cause and VA-related hospitalization was significantly lower in the AVF group (HR 0.82; 95% CI: 0.78-0.86) for all-cause hospitalization; RR 0.68 (0.62-0.74) for VA hospitalization, but not infection- or CVD-related hospitalization. AVF was associated with significantly lower incidence of all-cause and VA-, infection-, and CVD-related hospitalizations in longer follow-up time (RR 0.84 (0.82-0.87) for all-cause hospitalization within 3 years; RR 0.63 (0.59-0.67) for VA-related hospitalization within 3 years).

Conclusions: Our primary analyses found elderly patients on HD may benefit from getting an AVF compared to an AVG. We will further test whether these results hold true in patients within strata of age group, comorbidities, probabilities of AVF maturation, and life expectancy.

PO1325
Implementing Multidisciplinary Pre-ESRD Program to Improve Vascular Access in New-Start Dialysis Patients
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Background: Tumneled dialysis catheters (TDC’s) are associated with morbidity and mortality in dialysis patients. In the U.S., more than 80% of patients start dialysis with a TDC and even higher rates for ethnic minorities. As part of the Santa Clara County healthcare system, we care for an underserved population, predominately of ethnic minorities. To reduce our TDC rates, we implemented a Pre-ESRD program that encompasses a multidisciplinary team, EMR tracking, access referral guidelines, and culturally relevant patient education. We assessed whether this program reduced the proportion of patients starting dialysis with a TDC and no other vascular access (TDC-Only).

Methods: We performed a retrospective chart review of new start dialysis patients in 2014 (before program implementation) and in 2017 (after program implementation). Patients must have been seen in renal clinic for at least 3 months before starting dialysis. We compared the proportion of TDC-Only between the two groups using the Chi-Square Test. We also compared the type of vascular access placed between the two groups.

Results: 87 patients started dialysis in 2014 and in 2017. There was no difference in age (58 vs 56 years) or diabetes (61% vs 70%) between the two groups. The two groups consisted mostly of minorities (Hispanic: 52% vs 55%, Asian: 31% vs 26%, Black: 7% vs 3%, and White: 10% vs 14%) and non-English speakers (44% vs 46%). The type of access at dialysis start is summarized in the table. The proportion of TDC-Only reduced by 21% after program implementation but did not reach statistical significance: 62% of patients started with TDC-Only in 2014 compared to 49% in 2017 (p=0.09). In addition, AVF placement more than doubled after program implementation (19% vs 42%; p<0.001).

Conclusions: Implementation of a multidisciplinary Pre-ESRD program reduced the number of TDC-Only and increased the number of AVF’s in new dialysis start patients. Our study is unique due to our patient population of predominantly minorities and non-English speakers.
PO1327

Conversion to Arteriovenous Fistula but Not Arteriovenous Graft Is Associated with Improved Hemodialysis Efficacy Markers in Children: Pediatric Nephrology Research Consortium Study

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Background: Arteriovenous fistulae (AVF) and arteriovenous grafts (AVG) are preferred vascular access for chronic hemodialysis (HD) patients. Our objective was to investigate the impact of switching from tunneled cuffed catheters (TCC) to AVF or AVG on HD efficacy markers in pediatric HD patients.

Methods: Retrospective chart reviews were completed on individual patients from 20 pediatric HD centers. All the patients used TCC prior to AVF/AVG and each patient acted as his/her own control. Data on dialysis efficacy markers were collected at creation of AVF/AVG and for two years follow-up, along with patient demographics and clinical information. Statistical methods used included hypothesis testing and statistical modeling after adjusting for relevant demographic variables.

Results: First PVA was created in 98 individual children: 87 (89%) were AVF and 11 (11%) were AVG. The mean TCC vintage prior to AVF/AVG was 10.4 ± 17.3 months. At one-year follow-up, AVF patients improved the Kt/V by 0.23 (p=0.008) and URR by 5.4% (P<0.001). At second year follow-up, both Kt/V and URR remained higher than values at creation (p=0.02, p=0.0001, respectively), being similar to first year’s values (p=0.57, p=0.36, respectively). Furthermore, AVG patients improved serum albumin by 0.33 gram/dl (p=0.0001) and serum hematocrit by 2.94% (p=0.0001) at one-year and maintained similar improved values at second year follow-up (p=0.001, p=0.003, respectively). These observations were further supported by the adjusted models. Children with AVG did not demonstrate any statistically significant change in Kt/V, URR, serum albumin or hematocrit at either one-year or second year follow-ups.

Conclusions: Switching to AVF was associated with improved HD efficacy markers (Kt/V, URR, serum albumin and hematocrit). Surprisingly, conversion to AVG was not associated with a similar positive impact for the above markers.

PO1328

Study of Impact of Preoperative Venography as an Adjunct to Doppler Imaging in Difficult Vascular Access

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Background: As the number and complexity of patients on dialysis increases, this presents an increasing challenge for vascular access. Successful renal access surgery requires both careful planning and technical skill. Venography offers direct imaging of both peripheral and central veins in the upper limb.

Methods: Venography was done at our institute prospectively for difficult vascular access cases between Oct 2019 & Mar 2020. All patients who had prior 2 failed AVF surgeries were included in study and were evaluated with physical examination, Doppler imaging and Venography. We prospectively analysed venograms and also compared the outcomes before and after venography based on historic control before venogram with same inclusion criteria. Both groups were compared with respect to vascular access type, patency, complications.

Results: During the study period, venography prior to surgery was performed in 30 patients. Venography of one upper limb (right/left: 6/30) was performed in 6 patients(20%). The remaining 80% patients underwent bilateral venography, resulting in a total of 54 upper limb venograms. 9 patients(30%) were considered unsuitable for native AVF creation on the venograms, 4 underwent a haemodialysis AV-graft (AVG) creation (2 autologous saphenous vein AVG grafts, 1 synthetic graft), two opted for CAPD, remaining 4 surgery was not done.

Conclusions: Venography is a useful imaging modality for preoperative venous mapping prior to difficult vascular access surgery along with preoperative Doppler imaging, resulting in increased patency rates. In our study, preoperative venous imaging in adjunct with color Doppler imaging helped in choice of AVF site planning and avoiding complications and ruling out central venous obstruction and a better patency rates although limited by shorter follow up and small size.

PO1329

Analysis of Vascular Distensibility Measured by Ultrasound Speckle Tracking

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Background: We have developed a novel open source ultrasound software program that measures vascular strain and distensibility using conventional ultrasound Digital Imaging and Communications in Medicine (DICOM) data for use in the dialysis vascular access setting. In this study, we evaluated the variation in measurement from operator point selection and physiologic beat to beat variation of the arterial wall.

Methods: Ten subjects scheduled for arteriovenous fistula (AVF) creation were enrolled in the study. Ultrasound scanning of the brachial/radial arteries was performed. Ten users were prompted to select two points of interest at the top and bottom of the arterial vessel wall in each of the ten subjects. These points were tracked using the Kanade-Lucas-Tomasi (KLT) tracking algorithm.

Results: Sub-millimeter resolution (less than 100 micron) measurements were obtained. We found variation point selection by the users for the ten cine loops to be up to 120 pixels for the top and up to 140 pixels for the bottom of the vessel wall. The range in measured variation attributable to user point selection was 5.79% to 47.29% and inter-cardiac (physiologic) variation was 6.41% to 17.68%.

Conclusions: Despite the low resolution of conventional DICOM images, we are able to measure sub-millimeter distensibility. In order to better understand the physiologic variation in vascular wall compliance, a formalized approach to point selection is needed. We are evaluating algorithms and statistical ensemble methods for use in studies to predict AVF maturation.

Funding: Veterans Affairs Support
From image cine loop (A), a single frame (B) is used to select vessel wall edge points, for image tracking (C), to determine sub-millimeter resolution wall strain and distensibility (D) showing beat to beat variation.

POI1330

Relationship of Vascular Access Flow and Stenosis Detected by Frequency Domain Analysis of Videos Taken with a Smartphone

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Background: We developed a video image processing (VIP) technique with frequency domain analysis to assess arteriovenous fistula (AVF) blood flow. This study aimed to investigate the relationship of heart rate and access blood flow rate (Qa) represented by the frequency signals at maximum (FMax, Hz) and minimum (FMin, Hz) of magnitude in frequency domain analysis.

Methods: We employed VIP pre- and post-endovascular interventions in 90 hemodialysis patients (age 63.3 ± 14.3, 41 females, weight 78.6 ± 21.5 kg). FMax and FMin pre- and post-intervention were recorded. ΔF was defined as FMax - FMin for each video. Qa was measured pre- and post-intervention by HVT100 endovascular flowmeter (Transonic Systems Inc., Ithaca, NY, USA). The degree of stenosis (%) was quantitated by angiography. Heart rate (HR, beats/min) was expressed as a frequency (FHR, Hz).

Results: The pre- and post-intervention differences between FMax and FMin were 1.14 ± 0.74 Hz and 1.38 ± 1.44 Hz, respectively. ΔF increased with Qa pre- and post-intervention (Fig 1(a)) and post-intervention (Fig 1(b)). ΔF increased most when Qa increased from pre-intervention range of 300 to 600 ml/min to post-intervention 600 to 900 ml/min. Fig 1(c) shows the relationship between % stenosis and the change in ΔF between pre- and post-intervention. The difference between FMax and FMin was associated with % stenosis pre-intervention (Fig 1(d)).

Conclusions: The relationship between FMax and FMin suggests that the signal of FMax represents an important hemodynamic component of Qa. ΔF may be used as an index to predict low levels of stenosis. The use of frequency domain analysis from video image data provides a contact-free method to ascertain Qa and to indirectly indicate the degree of stenosis. Further study is needed to standardize the quality of video and streamline the methodology.

POI332

The Effect of Nitrate as a Vasodilator to Vascular Access Patency in Patients Undergoing Hemodialysis

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Background: Maintaining the patency of vascular access (VA) is very important to achieve adequate hemodialysis (HD) dose in HD patients. Failure of vascular access is associated with morbidity and mortality. Thus, maintaining the patency of VA is challenging. In this study, we investigated the effects of nitrate as a vasodilator on VA patency in HD patients.

Methods: We investigated study on the Korean insurance claims data of the HD patients between January 2012 and December 2017. All patients divided into nitrate treatment group and no therapy group depending on whether nitrate was administered. The nitrate therapy group included only patients who received the drug for 30 days or more. The primary outcome was the primary patency of AVF. Effect of nitrate treatment was examined using Kaplan Meier analysis and Cox proportional hazard, after adjusting for covariates.

Results: The use of portable US devices for assessment of maturity and cannulation guidance is feasible even in busy HD units. We were able to reduce the infiltration rate with the use of US guidance in combination with physical examination. We plan to expand ultrasound education to include all members of the dialysis staff involved with cannulation within our dialysis units. Regular competency checks are essential to identify and supplement gaps in knowledge.
**PO1333 Influence of CKD on In Situ Tissue Formation in Biodegradable Vascular Grafts**

Paul J. Besseling, Merle M. Krebbel,1 Joost O. Flodderus,1 Martin Teraa,1 Carlijn V. Bouter,2 Martijn Cox,3 Marianne C. Verhaar.1 InteStiVex’s; 1University Medical Centre Utrecht, Utrecht, Netherlands; 2Eindhoven University of Technology, Eindhoven, Netherlands; 3Xelts bv, Eindhoven, Netherlands.

**Background:** Vascular access is considered the Achilles’ heel of hemodialysis, requiring frequent interventions to maintain patency. One proposed solution is a self-healing in situ tissue engineered vascular access graft. This requires the presence of a functional wound healing response capable of initiating tissue formation. However, it is unknown whether tissue formation is negatively affected by chronic kidney disease (CKD). In this study, we aim to investigate the effect of CKD on in situ tissue formation in vascular grafts in a rat model.

**Methods:** To mimic the effect of CKD in humans, a rat 5/6th nephrectomy model was used. Control animals underwent a sham operation. When CKD animal reached a threshold of 50mg/24h proteinuria an electrospun biodegradable vascular graft, made from supramolecular polymers, was implanted in the abdominal aorta. Explantation was performed at 2, 4, 8, and 12 weeks, to follow the different phases of wound healing and early tissue formation. Each group was examined for cell infiltration and proliferation, presence of immune, endothelial, smooth muscle cells, and extracellular matrix components.

**Results:** Cytometry of circulating immune cells shows an increase in monocytes (CD11b+) and macrophages (CD68+) in CKD animals. Histological analysis indicates that all implanted grafts contain infiltrated cells throughout the material with a non-significant increase over time in both groups. Both groups show a peak in proliferating cells at week 8, with virtually no proliferating cells at 12 weeks. Infiltrated macrophages (CD68+ & CD163+) show no significant difference between sham and CKD and peak at week 8 followed by a decline. Masson trichrome and Sirius red staining show an increase in ECM formation over time with no significant difference between groups. Mature vascular cells such as smooth muscle cells and endothelial cells are found from week 8 onward, indicating a shift from a proliferative phase to a remodeling stage.

**Conclusions:** The found difference in circulating immune cells this did not translate in a significant difference in tissue build up, cell type, ECM production, scaffold breakdown and patency between sham and CKD animals. Our data suggests that uremic conditions have a limited effect on tissue formation in vascular grafts in a rat model.

**PO1335 The Integrated Program of Needle Dislodgement Bleeding Alarm System Is Associated with a Decreased Incident of Venous Needle Dislodgement or Bleeding**

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**Background:** A puncture of vascular access is commonly used in clinical treatment, such as hemodialysis or central venous catheters. There are some devices for detecting the presence of needle dislodgement in the market. Still, there are no large-scale reports for the integrated program for nursing training and device implantation. This study aims to conduct a program for an integrated training course and the VND device. We hope to reduce the incidence of needle removal and blood leakage.

**Methods:** This study was divided into two phases, the control period, and the study period. In the control period, the abnormal events of venous needle dislodgement and blood leakage was recorded in the hemodialysis unit room during the first three months. Before the study period, we introduced an integrated program, including the standard process of fistula puncture, care during hemodialysis, an inspection of the venous puncture site and an alarm system. In the study period, we also conducted the standard program and collected the data of the events of venous dislodgement or bleeding.

**Results:** The control period was conducted from July 2019 to September 2019, and the study period was performed in November 2019. A total of 62 patients completed the study. During the control period, there were a total of 2087 dialysis treatments, of which 80 needle dislodgement was recorded in the hemodialysis unit room during the first three months.

**Conclusions:** This study introduced venous needle dislodgement or bleeding alarm system and training program in the hemodialysis unit. The incidence of venous needle dislodgement or bleeding was lower after the program. The incidence rate in the moderate and severe groups was also decreased. This program can improve the quality of patient care.

**Funding:** Commercial Support - Acusense

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**PO1334 Use of Ticagrelor to Preserve Hemodialysis Vascular Access**

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**Background:** Hemodialysis (HD) is the main renal replacement therapy for end stage renal disease (ESRD) patients in the USA. Arteriovenous fistulas (AVF) remain the access of choice due to their superior patency and infection risk when compared to other accesses. AVF complications are a significant contributor to increased morbidity and hospitalizations in HD patients. There is currently no consensus as to whether thrombo-prophylaxis is warranted. Multiple studies have looked at various antiplatelet agents; however, none have looked at Ticagrelor, a newer antiplatelet that may have a beneficial effect for maintaining vascular access.

**Objective:** The objective of this study was to evaluate the efficacy and safety of Ticagrelor in HD patients with AVF. 33 HD patients aged 18 to 35 years old with AVF were randomized to receive either Ticagrelor 90 mg twice daily or placebo. The main outcome measure was the presence of needle dislodgement in the market. Still, there are no large-scale reports for the integrated program for nursing training and device implantation. This study aims to conduct a program for an integrated training course and the VND device. We hope to reduce the incidence of needle removal and blood leakage.

**Methods:** This study was divided into two phases, the control period, and the study period. In the control period, the abnormal events of venous needle dislodgement and blood leakage was recorded in the hemodialysis unit room during the first three months. Before the study period, we introduced an integrated program, including the standard process of fistula puncture, care during hemodialysis, an inspection of the venous puncture site and an alarm system. In the study period, we also conducted the standard program and collected the data of the events of venous dislodgement or bleeding.

**Results:** The control period was conducted from July 2019 to September 2019, and the study period was performed in November 2019. A total of 62 patients completed the study. During the control period, there were a total of 2087 dialysis treatments, of which 80 needle dislodgement was recorded in the hemodialysis unit room during the first three months.

**Conclusions:** This study introduced venous needle dislodgement or bleeding alarm system and training program in the hemodialysis unit. The incidence of venous needle dislodgement or bleeding was lower after the program. The incidence rate in the moderate and severe groups was also decreased. This program can improve the quality of patient care.

**Funding:** Commercial Support - Acusense

**PO1336 Evaluation of Stable Permanent Hemodialysis Access Bleeding Time After Dialysis Needle Removal**

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**Background:** Prolonged bleeding time (BT) after dialysis needle removal may signify permanent hemodialysis access (PHA) dysfunction but “normal” BT is not well defined. We hypothesized that the presence of needle dislodgement in the market. Still, there are no large-scale reports for the integrated program for nursing training and device implantation. This study aims to conduct a program for an integrated training course and the VND device. We hope to reduce the incidence of needle removal and blood leakage.

**Methods:** This was an observational study examining 35 patients receiving chronic hemodialysis with PHA using 15-g needles for ≥3 months. Patients included in the analysis were required to have a stable AVF and have no evidence of needle dislodgement or bleeding, and the incidence rate was 3.3 events per 100 sessions. There were a total of 682 dialysis sessions and 15 events of venous needle dislodgement or bleeding during the study period. The incidence rate was 2.1 events per 100 sessions. The incidence rate of moderate and severe cases was 1.1 events per 100 sessions in the control period and 0.3 events per 100 sessions in the study period.

**Conclusions:** This study introduced venous needle dislodgement or bleeding alarm system and training program in the hemodialysis unit. The incidence of venous needle dislodgement or bleeding was lower after the program. The incidence rate in the moderate and severe groups was also decreased. This program can improve the quality of patient care.

**Funding:** Commercial Support - Acusense

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**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

**Underline represents presenting author.**

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PO1337
Natural Vascular Scaffolding Therapy for Arteriovenous Fistula Development in Rats
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Background: Arteriovenous fistula (AVF) maturation failure results from insufficient lumen dilation and progressive inward neointimal hyperplasia (NH). Vascular wall distention is likely affected by the integrity of vascular extracellular matrix (ECM). We hypothesized that preserving ECM integrity at the time of AVF creation surgery could improve AVF maturation. Natural Vascular Scaffolding (NVS) Therapy is known to interlink collagen and elastin, the most abundant vascular ECM components, by covalently linking these proteins via photoactivation. We investigated the effect of NVS treatment on AVF development in a rat model.

Methods: Femoral AVFs were created in young Wistar male rats as an end-to-side anastomosis. Immediately after the blood flow was restored to dilate the femoral vein by arterial pressure, a 10-μl-drop of the NVS compound (2 mg/ml in phosphate buffered saline (PBS)) was placed at the anastomosis perivascularly and incubated for 5 minutes to allow full vessel wall penetration, followed with 1-min illumination of the anastomosis area by 450-nm light. The control group received a 10-μl-drop of PBS and the same light activation. The skin was closed immediately after light activation. Each group had 10 rats. Rats were euthanized 4 weeks post-AVF creation for histology, morphometry, immunohistochemistry of interleukin-6 (IL-6, an inflammation marker), and second-harmonic-generation evaluation by multiphoton microscopy of collagen fibers.

Results: Rats tolerated the NVS treatment well. The NH area was similar in both groups. The AVF vein’s open lumen area and % open lumen area in treated rats were significantly larger than in control rats (4.18-fold p=0.014 and 1.98-fold p=0.009, respectively). IL-6 intensity was significantly smaller in the NVS group than the PBS group (p=0.027). Collagen fibers in the NVS-treated AVFs trended towards perpendicular alignment with respect to the lumen circumference, with greater roundness, roughness, and eccentricity than in the PBS-treated AVF vessels.

Conclusions: Our studies showed that the NVS treatment significantly increased the AVF open lumen area, without significantly affecting the NH area. This suggests that NVS treatment may have therapeutic potential by facilitating lumen expansion while allowing a concomitant outward remodeling of the veins potentially leading to enhanced AVF maturation in patients.

Funding: Commercial Support - Alucent Biomedical Inc., Salt Lake City, UT, United States

PO1339
Longitudinal Geometry of Pig Arteriovenous Fistulas (AVFs)
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Background: Hemodynamics has been postulated to be an important factor contributing to successful versus failed AVF maturation. Pigs, in general, have hemodynamic features that are similar to those in humans, and thus are an attractive animal model for investigating the mechanisms underlying and the interventions for promoting AVF maturation. A few earlier small clinical studies found associations between AVF geometry and maturation. Since geometry is a critical determinant of hemodynamics, we investigated the geometry of pig AVFs using magnetic resonance imaging (MRI) technology.

Methods: Carotid (side)-jugular (end) AVFs were created in female Yorkshire cross domestic pigs. Non-contrast black-blood MRIs were obtained at 1, 2, and 6-10 weeks (wks) post-AVF creation (n=3 per time point) and used to reconstruct AVF lumen geometries. Lumen area, anastomosis angle, venous tortuosity, and nonplanarity angle magnitude were quantified.

Results: The non-surgery lumen area of the external jugular vein was ~7 mm². The AVF vein lumen area (mean ± standard deviation) significantly (p=0.0370) increased from 25.3 ± 11.1 mm² in wk 1, to 32.3 ± 4.3 mm² in wk 2, then to 62.7 ± 21.3 mm² in wks 6-10 suggesting that our pig AVF is a model for successful AVF maturation. Importantly, we also observed an increasing trend in the lumen areas from wk 1 to wks 6-10 of the proximal artery (24.0 ± 17.3 mm² vs. 28.0 ± 6.60 mm²) and the distal artery (24.5 ± 16.1 mm² vs. 34.8 ± 13.9 mm²). The anastomosis angles were similar in wk 1 and 2 (51.6 ± 23.2° vs 50.2 ± 21.0°) then decreased to 25.8 ± 17.3° in wks 6-10. Venous tortuosity slightly increased from 0.13 ± 0.05 in wk 1 to 0.15 ± 0.05 in wk 2 then to 0.17 ± 0.06 in wks 6-10. Non-planarity angle magnitude was 14.9 ± 8.9° in wk 1 then decreased to 10.7 ± 8.5 in wk 2 then increased to 24.6 ± 9.4° in wks 6-10.

Conclusions: This is the first serial and detailed study of pig AVF geometric parameters. The anastomosis angles of our pig AVFs were in line with human radiopaque AVFs in the literature (~30-60°). Our study sets the stage for examining the role of geometry in alterations in hemodynamic forces and in AVF maturation processes.

Funding: NIDDK Support, Other NIH Support - NHLBI, Veterans Affairs Support

PO1340
To Study Real-World Effectiveness of Paclitaxel Drug-Coated Balloon Angioplasty in Hemodialysis Patients

Background: A large, multicenter randomized study has shown that use of drug coated balloon (DCB) in angioplasty improves vascular access patency trend over control at 9-month during 2-year study period. We have conducted a retrospective study to see if there is a real-world effectiveness of DCB angioplasty in maintaining vascular access patency in hemodialysis patients.

Methods: We retrospectively reviewed 83 drug coated balloon angioplasties performed in our hospital from April 2018 to April 2020 and compared them with a control group of 83 angioplasties done by non-drug coated balloon matched by the date

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
of procedure. Target lesions were categorized as central, peripheral, anastomotic and in-stent for both arteriovenous fistula (A VF) and arteriovenous grafts (AVG). Patient demographics (Age, Sex) and risk factors (Hypertension, Hyperlipidemia, Vascular Disease, Diabetes Mellitus) were also compared. The duration of target lesion patency (in days) before and after the DCB interventions were compared with date matched non-DCB interventions (control group).

Results: There are 83 angioplasties in each group (DCB versus control group). The average duration of target lesion patency (in days) before intervention in DCB and control group were 152 versus 137 (P value = 0.57) for A VF and 163.3 versus 191.3 (P value = 0.70) for AVG respectively. The average duration of target lesion patency (in days) after intervention in DCB group and control group were 114.8 versus 161.7 (P value = 0.03) for A VF and 177.9 versus 221.5 (P value = 0.5) for AVG respectively.

Conclusions: As opposed to the randomized controlled trial, our study shows that the average duration of target lesion patency of AVG after drug coated balloon angioplasty was significantly shorter than non-drug coated balloon. Greater severity of lesions in the DCB group could be the reason for this observation.

Target Lesion Patency Outcomes

<table>
<thead>
<tr>
<th>Type of Access</th>
<th>Duration of Patency (Days)</th>
<th>Drug-Coated Balloon (DCB)</th>
<th>No Drug Coated Balloon (NDCB)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A VF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-intervention</td>
<td>152.5</td>
<td>157.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Post-intervention</td>
<td>165.3</td>
<td>157.5</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>AVG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-intervention</td>
<td>65.3</td>
<td>191.3</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>Post-intervention</td>
<td>177.9</td>
<td>221.5</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>

PO1341

Estimated Upper-Body Blood Flow and Central-Venous Oxygen Saturation Before and After Percutaneous Transluminal Angioplasty in Newly Created Vascular Access

Laura Rosales, Hanjie Zhang, Marilou Mateo, Brenda K. Chan, Seth Johnson, Stephijn Thijszen, Peter Kotanko. Renal Research Institute, New York, NY.

Background: Arterio-venous fistula (AVF) is the most effective vascular access in hemodialysis (HD) patients and, assessing AVF maturation is critical to initiate its timely use. Previously we have demonstrated that central-venous oxygen saturation (ScvO2) and estimated upper-body blood flow (eUBBF) increase during AVF maturation. We assessed ScvO2 and eUBBF before and after percutaneous transluminal angioplasty (PTA).

Methods: We studied HD patients from an ongoing AVF quality improvement project. ScvO2 and hematocrit were measured with Crit-Line (FMC, Waltham, MA) between minutes 5 and 20 into HD. eUBBF was computed and described previously (Rosales, Blood Purif, 2019). Five out of 19 patients underwent PTA during AVF maturation and subsequent successful cannulation.

Results: Three of five patients (mean age 71±11) were males two were incident patients. Four interventions were due to venous stenosis and one was due to arterial anastomosis stenosis. Two patients underwent PTA 2.2 ± 0.3 weeks after AVF creation and the remaining 3 patients within 11.2 ± 4 weeks. Following PTA ScvO2 increased in all, except in patient #1, eUBBF increased in every patient (Table 1).

Conclusions: Our preliminary results indicate that ScvO2 and eUBBF provide functional information that can be obtained non-invasively. These point-of-care bio-signals reflect hemodynamic cardiovascular adaptation following successful PTA. Future studies are warranted if knowledge of ScvO2 and of eUBBBF shorten catheter residence time.

Table 1: ScvO2 and eUBBF before and after percutaneous transluminal angioplasty

<table>
<thead>
<tr>
<th>N</th>
<th>Time to Intervention (Weeks)</th>
<th>Before Intervention</th>
<th>After Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td></td>
<td>ScvO2 (%)</td>
<td>eUBBF (L/min)</td>
</tr>
<tr>
<td>Patient 1</td>
<td>2.0</td>
<td>65.4±1.5 [63.7, 69.9]</td>
<td>1.2±0.9 [1.2, 1.4]</td>
</tr>
<tr>
<td>Patient 2</td>
<td>2.4</td>
<td>63.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Patient 3</td>
<td>7.0</td>
<td>71.8±0.4 [71.5, 72.1]</td>
<td>1.8±0.1 [1.8, 1.9]</td>
</tr>
<tr>
<td>Patient 4</td>
<td>13.6</td>
<td>68.8±0.8 [66.5, 70.7]</td>
<td>1.8±0.1 [1.8, 1.9]</td>
</tr>
<tr>
<td>Patient 5</td>
<td>13.7</td>
<td>64.6±0.6 [61.4, 67.9]</td>
<td>1.0±0.2 [1.0, 1.2]</td>
</tr>
</tbody>
</table>

*Patient 2 had only one of the 1-week assessments prior intervention. Data are expressed as mean, standard deviation, minimum and maximum values.

PO1342

Association Between FGF-23 Serum Levels with the Maturation Process of a Native Arteriovenous Fistula in Patients with End-Stage CKD

Juan Reyna-Blanco, L. M. Perez-Navarro, Rafael Valdez-Ortiz. Hospital General de Mexico Dr Eduardo Liceaga, Ciudad de Mexico, Mexico.

Background: The process of maturation of an arteriovenous fistula (AVF) is complex and difficult to predict. It is known that high levels of fibroblast growth factor 23 (FGF-23) could be related to endothelial dysfunction, which could also influence the maturation of an AVF. Our goal is to know the association between serum levels of FGF-23 and the maturation of an AVF.

Methods: This is a prospective cohort study with patients who underwent an AVF. The primary outcome was ultrasonic maturation at 6 weeks defined by the Birmingham criteria (diameter >0.4 cm and blood flow more than 500 ml/min).

Results: Forty-nine patients with a mean age of 48 ±14 years were included and 24% were women. The most common cause of CKD was diabetic nephropathy (55%), 25%, 10% and 16% were brachycephalic, brachymedian, brachybasylic and other AVF respectively. Thirty nine percent of AVFs did not mature at 6 weeks. No significant differences were identified when comparing the agreement with maturation or not of the AVF in age, comorbidities, BMI, previous number of hemodialysis catheters, history of thrombosed catheter or catheter infection, hemodialysis vintage, residual diuresis, surgical time, hemoglobin, creatinine and serum calcium or phosphorus. However, the length of the arteriotomy was greater in the fistulas that do not mature with respect to the mature fistulas (7 mm vs. 6 mm p = 0.03). Likewise, the use of loop diuretics was more prevalent in AVF that did not mature (without maturation: 74% vs. maturation: 43%, p = 0.03). None of the distal radiocephalic AVF reached maturity. There were no association between serum levels of cFGF-23 and maturation of AVF, nor was the correlation between serum levels of cFGF-23 and the diameter or flow of the fistulas at six weeks.

Conclusions: The prevalence of maturation failure in AVFs was 39% according to Birmingham criteria. There is no correlation between serum levels of cFGF-23 and the flow or diameter of the AVF at six weeks. A larger population is required to corroborate these results.

PO1343

Effect of Hemodialysis Vascular Access Type on Serum Interleukin-6 (IL-6) Levels in ESRD

Monika Aggarwal, George M. Feldman, Naveen Samuel, Reuben P. Retnam, Dipankar Bandyopadhyay, Shobha Ghosh, Hunter Holmes McGuire VA Medical Center, Richmond, VA; Virginia Commonwealth University, Richmond, VA.

Background: Chronic inflammation is prevalent and associated with poor outcomes in end stage renal disease (ESRD), and may be related to underlying comorbid conditions like diabetes mellitus. It is unclear if dialysis vascular access type may affect inflammation. We evaluated the effect of hemodialysis vascular access type on serum IL-6 level.

Methods: 15 patients with ESRD on chronic maintenance hemodialysis at McGuire Hunter Holmes VAMC were enrolled. Blood samples were drawn at 0, 30, 60, 90, 120, 180, and 240 minutes after starting dialysis. Serum IL-6 was measured using ELISA. Data were analyzed using t-test and is presented as Mean±SD.

Results: 6 patients had catheter (mean age 71.3±3.3 years), and 9 (mean age 64.5±4.4 years) had AV access. All were male. 5 patients in each group were African-American. 2 patients with catheter and 7 patients with AV access had diabetes. IL-6 level was higher at all time points(statistically significant) in patients with catheter compared to patients with AV access (Fig 1. and Table 1.)

Conclusions: ESRD patients with catheters had higher serum IL-6 levels compared to AV access inspite of lower proportion of diabetics. Catheters may contribute to inflammation, which may partly explain worse outcomes seen with catheters.

Funding: Veterans Affairs Support

Table 1: IL-6 Level at different time points (Mean±SD)

<table>
<thead>
<tr>
<th>Time Point (Minutes)</th>
<th>AV access</th>
<th>Catheters</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.85±1.2</td>
<td>10.06±4.97</td>
<td>0.017</td>
</tr>
<tr>
<td>30</td>
<td>2.16±1.18</td>
<td>6.18±0.29</td>
<td>0.011</td>
</tr>
<tr>
<td>60</td>
<td>2.93±4.23</td>
<td>11.8±3.82</td>
<td>0.004</td>
</tr>
<tr>
<td>90</td>
<td>3.15±4.51</td>
<td>12.22±4.92</td>
<td>0.006</td>
</tr>
<tr>
<td>120</td>
<td>3.34±4.82</td>
<td>13.1±4.52</td>
<td>0.001</td>
</tr>
<tr>
<td>180</td>
<td>3.82±4.17</td>
<td>15.9±3.75</td>
<td>0.001</td>
</tr>
<tr>
<td>240</td>
<td>3.72±1.96</td>
<td>18.0±1.188</td>
<td>0.003</td>
</tr>
</tbody>
</table>

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Underline represents presenting author.
Assessment of Arteriovenous Fistula Dysfunction with Access Stenosis in Hemodialysis Patients Using Smartphone Videos
Lin-Chun Wang,1 Fausan Zhu,1 Ohmmar Thwin,1 Lela Tisdale,1 Xia Tao,1 Vaibhav Maheshwari,1 Alhaji Cherif,1 Norbert Shtaynberg,2 Dean C. Preddie,2 Stephan Thijssen,1 Peter Kotanko,1,3 Renal Research Institute, New York, NY; 2Azura Vascular Care, New York, NY; 3Icahn School of Medicine at Mount Sinai, New York, NY.

Background: Hemodynamically relevant stenoses in arteriovenous fistulas (AVF) lead to a reduction in access flow rate (Qa). We hypothesized that these changes in blood flow patterns may be detectable in video recordings done with commercially available smartphones.

Methods: We studied HD patients with AVF dysfunction requiring balloon angioplasty. One-minute video recordings of the skin above the AVF and Qa measurements were conducted before and after the intervention by an iPhone 6S. Qa was measured by HVIT100 Transonic flowmeter. Degree of stenosis was assessed by angiography. Frame-to-frame pixel changes in video images were amplified; time-domain data were transformed into the frequency-domain signals. Fifty random 10-second segments were sampled per one-minute video, and the frequency with the lowest magnitude ($F_{min}$) was determined in each sample (Fig. 1). The average $F_{min}$ was assessed for its association with the degree of stenosis.

Results: Ninety subjects were studied (63±6 years, HD vintage 4.1±3.5 years). Post-intervention Qa (1638±714 ml/min) was on average 1.23-fold higher than pre-intervention Qa (1373±684 ml/min; P=0.01, paired t-test). Subjects were grouped by degree of stenosis, and the number of subjects in each category is shown in Fig. 1B. Higher degrees of stenosis were associated with greater increases in Qa from before to after the intervention (Fig. 1C). Interestingly, the degree of AVF stenosis was also positively related with the change in $F_{min}$ from before to after the intervention (Fig. 1D).

Conclusions: Smartphone video recordings of AVF appear to contain frequency-domain information that correlates with hemodynamic changes caused by AVF stenoses. While the $F_{min}$ metric employed in our analysis is not ideal, these results should encourage the quest for other parameters that exhibit higher correlations with vascular access dysfunction, allowing timely referrals and avoidance of emergency interventions.

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Underline represents presenting author.
PO1346
Efficacy and Long-Term Patency of Kissing Stent Technique for Endovascular Reconstruction of the Axillary Vein: A Case Report with Long-Term Follow-Up
Samir M. Akram, Khurram Saleem, Mohamed A. Rahman. Nephrology Associates of Northern Illinois and Indiana, Oak Brook, IL.

Background: Purpose: to report the endovascular reconstruction (EVR) of axillary vein (AXV) with kissing stent technique (KST) following AXV obstruction due to proximal stent migration (PSM) from the cephalic arch (CA). We suggest a strategy to minimize this problem. PSM in venous system is rare but dreadful complication of EVR. Increasing venous sizes towards the heart predisposes to PSM. We report a case of AXV obstruction due to stent migration into subclavian vein (SCV). We describe the successful use of kissing stent technique (KST) to reconstruct the AXV.

Methods: Case report and review of literature.

Results: Case report: MS is an 81-yr-old female with right brachiocephalic arteriovenous fistula (R BCAVF) for chronic hemodialysis. She has recurrent cephalic arch stenosis (RCAS) (Fig1). A Viabhan 11 x 5 stent was placed which, partially migrated into the SCV, blocking the AXV (Fig2 & Fig3). The Basilisc vein (BV) was cannulated and a straight glide wire introduced. A Lumine 10 x 6 stent was delivered next to Viabhan stent in the AXV. Both stents were expanded with 10 x 4 angioplasty balloon restoring the forward flow in the AXV (Fig4). At 5-year follow up both stents were patent (Fig5) except for pre and post stent stenosis, successfully treated with angioplasty. Discussion: EVR is employed to treat RCAS. However, there is risk of PSM. A strategy we implement to reduce PSM is to avoid complete dilatation of lesion prior to stenting which, in this case prevented full migration of the stent. KST for EVR of superior vena cava and common iliac veins has been reported but not for EVR of AXV. We report the first case of utilizing KST for EVR of the AXV with 5-year follow up.

Conclusions: KST for EVR of the Axillary vein is technically feasible and has long-term efficacy.

Funding: Private Foundation Support

PO1347
Understanding the Transition to Standardized Fistula Rate (SFR) and Long-Term Catheter Rate (LTCR) Measures in the Medicare ESRD Quality Incentive Program (QIP)
Donnyu Wang, Alissa Kapke, Jeffrey Pearson, Adebola O. Adeleye, Delia Houseal, Eric W. Young, Arbor Research Collaborative for Health, Ann Arbor, MI; Centers for Medicare and Medicaid Services, Baltimore, MD.

Background: In ESRD QIP Payment Year (PY) 2021, vascular access measures change to the SFR and LTCR measures. The changes involve transition of the data source from Medicare claims (CLM) to CROWNWeb (CW), expansion from Medicare fee-for-service (M-FSS) to all ESRD patients, revised quality criteria (e.g. multiple access types), expanded patient exclusions (e.g. limited life expectancy), and case-mix adjustment for SFR.

Methods: The degree of concordance in reporting vascular access type reported in CLM and CW was assessed and trends in arteriovenous fistula use (AVF) and long-term catheter use (LTC) with the CLM-based and CW-based methods were evaluated from calendar year (CY) 2012-2019. Facilities’ performance rates for the CW-based measures were calculated using PY20 data and compared to their PY20 performance for the CLM-based measures.

Results: The degree of reporting concordance between CLM and CW was high for fistula use (κ=0.95; p<0.01) and slightly lower for catheter use (κ=0.76; p<0.01). The agreement of all access types increased from 90% in CY12 to 97% in CY18. National trends in vascular access were consistently worse for CW-based measures, although this gap narrowed over time (Figure). PY20 data indicate facilities achieved a lower median SFR (0.83% vs. CLM-based AVF rate) and higher median LTCR by 1.4% (vs. CLM-based LTCR); however, accompanying changes to performance standards (using baseline data) result in simulated ESRD QIP measure scores increasing by approximately 0.5 points.

Conclusions: Vascular access reporting concordance in CLM and CW improved considerably in CY 2018, which corresponds to the first year of use in the ESRD QIP. The CW-based vascular access performance rates were worse than CLM-based rates; these differences are primarily attributed to the poorer performance of non-FFS patients included in the CW-based measures. Whether new vascular access measures have worse performance rates, average ESRD QIP measure scores increase slightly.

Funding: Other U.S. Government Support

PO1348
Hemodialysis Access Surveillance Evaluation (HASE) Study

1 Albany Medical College, Albany, NY; 2 University of Miami School of Medicine, Miami, FL; 3 University of Miami School of Nursing and Health Studies, Coral Gables, FL; 4 California Kidney Specialists, San Dimas, CA; 5 Dialysis Clinic Inc, Nashville, TN; 6 Jersey Shore University Medical Center, Neptune City, NJ.

Background: Arteriovenous (AV) access thrombosis remains one of the most troubling AV access related complication affecting hemodialysis patients. It necessitates an urgent and occasionally complicated thrombectomy procedure and increases the risk AV access loss. The routine use of AV access surveillance for early detection and management of stenosis to reduce thrombosis remains controversial.

Methods: We conducted a multicenter, prospective, randomized clinical trial comparing standard of care with monthly Ultrasound Dilution Technique (UDT) flow surveillance using a Transonic flow measurement device (Transonic Systems Inc., 34 Dutch Mill Road, Ithaca, NY 14850, USA) to standard of care alone.

Results: We prospectively randomized 436 patients with end stage renal disease (ESRD) on hemodialysis with arteriovenous fistula (AVF) or graft (AVG) using cluster (i.e. dialysis shift) randomization to either standard of care with monthly blood flow surveillance between the two groups, irrespective of whether thrombectomy procedures were included or excluded. There was no statistically significant difference between the two groups in the rate of or the time to the first thrombotic event or number of catheters placed due to thrombosis.

Conclusions: The use of monthly AV access surveillance with UDT flow measurement in this multicenter randomized control trial reduced the per patient thrombotic events without significantly increasing the total number of angiographic procedures. Even though there is a trend, surveillance did not reduce the first thrombotic event rate. Funding Transonic Systems Inc., 34 Dutch Mill Road, Ithaca, NY 14850, USA

PO1349
Right Heart Dysfunction in Hemodialysis Patients

Background: Despite emerging evidence that right ventricular dysfunction (RVD) is a major determinant of outcome, previous studies have largely neglected the RV in ESRD patients.

Methods: We conducted a cross-sectional study on patients who received maintenance hemodialysis (HD) between Jan 1 - Dec 31, 2010 and were cared for by URMC nephrology faculty. For this cohort, all ambulatory trans-thoracic echocardiograms (TTEs) between Jan 1 2010 and Dec 31, 2018 were identified. Only TTEs with images of sufficient quality to assess the RV were included. Those with pre-existing congenital heart disease, atrial fibrillation, or prior valve surgery were excluded. Subjects might have more than one included TTE. Data from subject’s charts were extracted.

Results: The degree of reporting concordance between CLM and CW was high for fistula use (κ=0.95; p<0.01) and slightly lower for catheter use (κ=0.76; p<0.01). The agreement of all access types increased from 90% in CY12 to 97% in CY18. National trends in vascular access were consistently worse for CW-based measures, although this gap narrowed over time (Figure). PY20 data indicate facilities achieved a lower median SFR (0.83% vs. CLM-based AVF rate) and higher median LTCR by 1.4% (vs. CLM-based LTCR); however, accompanying changes to performance standards (using baseline data) result in simulated ESRD QIP measure scores increasing by approximately 0.5 points.

Conclusions: Vascular access reporting concordance in CLM and CW improved considerably in CY 2018, which corresponds to the first year of use in the ESRD QIP. The CW-based vascular access performance rates were worse than CLM-based rates; these differences are primarily attributed to the poorer performance of non-FFS patients included in the CW-based measures. Whether new vascular access measures have worse performance rates, average ESRD QIP measure scores increase slightly.

Funding: Other U.S. Government Support

AVF (Left) and LTC (Right) National Trends based on CW and CLM Reporting
Results: We identified 425 individuals on HD. Of these, there were 141 ambulatory TTs, of which 64 TTs met all inclusion criteria. RVD is defined as abnormality in any of the following echocardiographic parameters: S’ (< 9.5 cm/sec), TAPSE (< 17 mm), Free Wall Right Heart Strain (< -20%), or RV Fractional Area Change (< -35%). Of the 64 TTs, 19 had one or more parameters indicating RVD. Select findings with bivariate analysis are described in the Table 1. Continuous variables are expressed as means (S.D.) and analyzed by ANOVA. By multivariate logistic regression, diastolic vital age < 10 years, history of vascular disease, and absence of AVS were associated with RVD. There was a trend with OSA. Limitations include retrospective analysis, small numbers, and heterogeneity in patients with respect to history of dialysis access type prior to undergoing TTE.

Conclusions: RVD is common finding on TTs in HD patients, but is under recognized. A larger prospective study is needed to identify factors that are associated with development of RVD that could potentially be modifiable.

Table 1

PO1350 Catheter Care in a Hemodialysis Unit: “Do It Daily,” a Multimodal Patient Education Approach
Miten Dhruve, Michael Garron Hospital Foundation, Toronto, ON, Canada.

Background: Central venous catheters or CVLs are the leading cause of mortality and morbidity in the dialysis population. The HDI group wanted to empower the patients to manage and care for their catheters. We developed a standardized educational framework in collaboration with healthcare professionals and the Patient Experience Panel (PEP). Our ultimate goal was to reduce rates of catheter infections in our hemodialysis unit by improving patient’s knowledge, confidence, and skills related to catheter self-care. Our immediate goal was to improve patients’ catheter care knowledge and skills and to standardize and optimize nursing skills and knowledge.

Methods: The patients were given a pre-education survey to establish baseline knowledge, attitudes and skill levels. Educational materials were developed based on the knowledge, attitudes and skill levels. Educational materials included a video, posters, pamphlets and fridge magnets using the catchphrase “Do it Daily”. The acronym “DAILY” represents the following: D for “dressing, soiled wet or damaged”, A for “any rash, itching or broken skin”, I for “increased pain at catheter site”, L for “length of catheter changed” and Y for “you have redness, pus, fever”. Post education surveys were conducted to assess the patients’ knowledge and skill levels.

Results: Thirty-three patients completed baseline surveys, education programs and post education surveys. No significant difference in proportion of patients answering yes to Knowledge or Skill assessment pre- and post-education survey. Although, there was a trend of patients stating they had received enough teaching about catheter care, and the need for patients to do it for themselves. Eighty-nine percent of patients found the education/training easy to understand.

Conclusions: Use of Multi-Modal patient education material is an easy to understand and feasible tool to help patients understand proper care of their dialysis catheters.

PO1351 A Retrospective Study of Tunnelled Dialysis Catheters with Exposed Cuff and Risk of Subsequent Catheter-Related Bloodstream Infection
Zachary J. Bauer, Aecom Hana, Christopher Kassab, Amulya Rajagopal, Lalithaksha Murthy Kumbar. Henry Ford Hospital, Detroit, MI.

Background: Tunnelled dialysis catheters (TDC) are prevalent in patients with end stage renal disease (ESRD) on hemodialysis (HD). Exposure of catheter cuff leads to replacement of TDC over guidewire (TDCEx). It is unclear if exposed catheter cuff increases the risk of infection if exchanged over guidewire.

Methods: This single center retrospective study reviewed TDCEx procedures in patients with ESRD on HD using a TDC for at least 14 days. The primary endpoint was catheter related bloodstream infections within 30 days or within 90 days of catheter exchange. Infection rate (IR) were reported as total infections per 1000 catheter days.

Results: 1030 procedures were reviewed; 537 were indwelling TDC for mechanical dysfunction (n=305) and exposed cuff (n=130) were compared to TDC with infection (n=102). Catheters with infection were mainly treated with removal and delayed insertion. IR based on indications were, 0.78 (95% confidence interval (CI), 0.38-1.38) for infections, 0.64 (95% CI, 0.28-1.14) for exposed cuffs, 0.46 (95% CI, 0.25-0.76) for mechanical dysfunction. When comparing all TDCEx due to non-infectious reason to the catheters with infection, no significant difference was found for IR within 30 days [hazard ratio (HR), 0.78; 95% confidence interval (CI), 0.21-2.82; p-value 0.700] or within 90 days (HR, 0.51; 95% CI, 0.24-1.07; P=0.075). Comparing TDCEx due to exposed cuff with TDCEx for a mechanical dysfunction, a significant difference in IR was noted at 30 days [HR, 1.59; 95% CI, 0.45-5.63; P=0.474] and at 90 days (HR, 1.65; 95% CI, 0.71-3.87; P=0.246). No significant difference was seen in IR between catheters with infection and TDCEx for exposed cuffs at 30 days [HR, 0.95; 95% CI, 0.21-4.25; P=0.948] or at 90 days (HR, 1.42; 95% CI, 0.58-3.51; P=0.442). Catheters with infection compared to TDCEx for mechanical dysfunction had a significantly increased IR at 90H (2.36; 95% CI, 1.03-5.37; P=0.042) with no significant difference at 30 days [HR, 1.52; 95% CI, 0.38-6.06; P=0.556].

Conclusions: TDCEx for catheters with exposed cuff do not increase the risk for catheter related bloodstream infections at 30 or 90 days. Infected catheters continue to have a higher risk for CRBSI at 90 days even with removal and delayed insertion.

PO1352 Meta-Analysis of Antibiotic and Non-Antibiotic Lock Solutions for Prevention of Hemodialysis Catheter-Related Infections
Sohail Abdul Salim,1 Wisit Cheungpasut,2 Charat Thongprayoon,4 Karim Soliman,1 Michael B. Tapovalai,1 Lajos Zsom,1 Tibor Fquilop.4
1University of Mississippi Medical Center, Jackson, MS; 2-Cégél Hemodialysis Units, Cegedel, Hungary; 3Hatvan Hemodialysis Units, Hatvan, Hungary; 4Mayo Clinic Minnesota, Rochester, MN; 5Medical University of South Carolina, Charleston, SC.

Background: Catheter-related bloodstream infection (CRBSI) associated with hemodialysis catheters are associated with increased mortality and morbidity whilst posing a significant financial burden on health care. The effects of antibiotic and antimicrobial locking solutions on the risk of CRBSI are unclear.

Methods: From inception to April 2020, we looked for relevant clinical controlled trials in the following databases: EBSICO, PubMed, Cochrane CENTRAL, MEDLINE, EMBASE, clinicaltrial.gov, Google Scholar and performed a meta-analysis of the identified studies.

Results: 26 studies with 4,967 patients reported on the incidence of catheter-related bacteremia (CRBSI). The overall pooled Risk Ratio (RR) was lower in the intervention group signaling a 70% lower incidence of CRBSI compared with the heparin group (RR=0.30, 95% CI [0.25, 0.36], p=0.001). Group analysis showed that the administration of antibiotic regimens led to a 72% decrease in the risk of CRBSI episodes (RR=0.28, 95% CI [0.21, 0.37], p<0.0001), whereas non-antibiotic antimicrobial solutions reduced the risk of CRBSI by 68% (RR= 0.32, 95% CI [0.25, 0.41], p<0.0001). A test for subgroup differences revealed no significant difference favoring either of the two interventions.

Conclusions: Both antibiotic and antimicrobial solutions are effective in reducing CRBSI.

PO1353 The Catheter Tip Position as the Main Non-Infectious Cause of Catheter Replacement Survival
Jose G. Navarro Gallardo, Pablo Maggiani, Noe Martinez murillo, Jorge J. Font, Jonathan Chavez, Jose A. Torres, Christian P. Flores. Universidad de Guadalajara, Guadalajara, Mexico.

Background: Identify the risk factors associated with catheter (Cath) replacement (CR). Novanatomic variables analyzed

Methods: Our objectives: Identify risk factors associated with CR. The Cath were placed guided by ultrasound (US). We analyze age, gender, height, previous number of punctures, blood pressure, lab tests, anatomic position, extrasystoles, # of punctures, Jugular Vein (JV) collapsibility, Cath TUG, TIP and TOP, tunneled or not, Heparin, complications, Skin-JV Distance, Neck circumference, cath insertion to clavicula distance (UCD), JV and Carotid diameter and distance between JVN and Carotid.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Multivariable logistic regression model to determine the variables associated with catheter replacement during the 180 days follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter Insert to TVA/AV Distance (cm)</td>
<td>1.05</td>
<td>1.00 to 1.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Breathing/Choke Distance (cm)</td>
<td>1.52</td>
<td>1.50 to 1.52</td>
<td>&lt;0.001</td>
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<tr>
<td>Tunneled Catheter</td>
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<td>1.00 to 1.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Catheter-related bloodstream infection</td>
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<td>1.10 to 1.20</td>
<td>&lt;0.001</td>
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<tr>
<td>Neutrophil count (K/mm3)</td>
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<td>0.40 to 0.50</td>
<td>&lt;0.001</td>
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<tr>
<td>MPO</td>
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<td>1.00 to 1.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Anatomic Position</td>
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<td>1.00 to 1.00</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Results:** From Feb-Dec 2019 with a 180 days follow-up, 147 vascular Cath placements were analyzed. The CR was presented in 21 patients (14.2%) with a survival of 85.5% (95% CI 0.80 to 0.91) (figure 1). The correct position of the Cath TIP decreases the risk of CR (OR 0.81, 95% CI 0.73-0.90, p < 0.001). Cath-related bloodstream infection (CRBI) increases the risk of CR (OR 2.52, 95% CI 2.13-2.98, P < 0.001). CICD > 3.4 cm decrease risk of CR due to CRBI. (OR 0.89, 95% CI 0.81-0.97, P < 0.01)

**Conclusions:** Only the correct position of the Cath TIP protects vs CR while CRBI increases the risk. The shorter the CICD the less CR due to CRBI.

**Funding:** Other NIH Support - Universidad De Guadalajara Jalisco, Hospital Civil Fray Antonio Alcalde De Guadalajara

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**PO1354**

NitrilCap Hemodialysis Catheter Insert to Prevent Catheter-Related Bloodstream Infection

**Authors:** Alexander S. Yezzi,1 Karthik Ramanj,1 Maria Kim,2 Joshua Dooverspike,1,2 Faroug Sulieman,3 Marie Cornell,1 Alvaro Rojas-Pena,11 University of Michigan, Ann Arbor, MI; 1NOTA Labs, Ann Arbor, MI.

**Background:** Tunnelled dialysis catheters (TDCs) are associated with blood stream infections. We developed a novel nitric oxide (NO) eluting catheter insert and tested its effects in vitro and in sheep for two weeksto assess its bactericidal activity.

**Methods:** Two cm long inserts using S-nitrosothioglutathione (GSNO) as the NO donor and various other components were prepared and tested for their real-time NO release. In vitro studies were done to test the insert’s bactericidal effects in a real catheter hub antimicrobial model with S. aureus and P. aeruginosa. NO releasing inserts (NitrilCap) were compared to a control (without NO releasing). After 72 h of incubation at 24°C, the amount of viable bacteria in the fluid was quantified for each sample. Subsequently, the antimicrobial/anti-biofilm efficacy of NitriCap was tested in a 14-day ovine model of infections. We developed a novel nitric oxide (NO) eluting catheter insert and tested its antimicrobial/anti-biofilm effects during in vitro and in sheep for two weeks to assess itsbacteriocidal activity.

**Results:** A formulation was devised with an initial burst of NO (>100 flux), followed by sustained NO flux for 72 h duration (>20 flux). This formulation lead to a 6.6 log decreases in the amount of viable bacteria in the fluid was quantified for each sample. Subsequently, the antimicrobial/anti-biofilm efficacy of NitriCap was tested in a 14-day ovine model of microbe rich natural environment and compared to controls (without NO).

**Conclusions:** This data strongly suggests that the NitriCap displays significant antimicrobial/anti-biofilm effects during in vitro and large animal in vivo studies, demonstrating that its implementation could minimize catheter related bloodstream infections.

**PO1355**

Catheter Dependency After Vascular Access Placement Among Elderly Patients on Hemodialysis: An Intention-to-Treat Analysis

**Authors:** Beiji Lu,1 Micah R. Chan,2 Brad C. Astor,3 University of Wisconsin-Madison School of Medicine and Public Health, Madison, WI.

**Background:** Evidence is mixed regarding optimal choices of incident vascular access type for elderly patients on hemodialysis (HD). Arteriovenous fistula (AVF) may be desirable given its better long-term outcomes. However, many elderly patients have a lower probability of AVF maturation and limited life expectancy which may limit the potential long-term benefit of AVF. We aimed to use an intention-to-treat (ITT) analysis to assess catheter dependency after incident AVF/arteriovenous graft (AVG) placement among elderly patients on HD

**Methods:** Patients who were 66+ years old at HD initiation, with no AVF/AVG placed before HD initiation, and had a first AVF/AVG placed within 1 year after HD initiation between May 2012 and May 2017 in the USRDS were included. Patients were followed from the first AVF/AVG placement using ITT analysis principles. Vascular access in use for HD was assessed using CrownWeb data. Catheter dependency was defined as using catheter only or using AVF/AVG combined with a catheter for HD.

**Results:** A total of 39,036 patients were included. Among them, 31,190 (79.9%) had AVF and 7846 (21.1%) had AVG placed. A substantially lower proportion of patients in the AVG group relied on catheter for HD early after VA placement (88.2% vs 91.9% in AVG and AVF, respectively, at 1m after placement; 23.3% vs 64.3% at 3m; 16.4% vs 28.9% at 6m, Fig1). In longer follow-up, proportion of catheter among patients remaining on HD in both groups, with slightly higher proportion in the AVG group observed at 1 year and beyond (14.8% vs 12.3% at 12m; 14.6% vs 9.6% at 24m). Risk of mortality was high in both group (24.8% in AVG vs 28.7% in AVF by 12m; 42.4% in AVF vs 46.7% in AVG by 24m after VA placement).

**Conclusions:** AVG is associated with substantially less catheter dependency than AVF in the short-term and only slightly higher catheter dependency at one year and beyond. AVG placement may be beneficial in selected elderly patients to minimize catheter use.

**PO1356**

Detecting the Prevalence of Bacterial Colonization on Tunnelled Hemodialysis Catheters Using 16S rRNA Gene Sequencing and Scanning Electron Microscopy: Lack of Evidence for Universal Colonization

**Authors:** Ali Mirza Onder,1 Christopher F. Cuff,2 Anthony A. Billings,3 Songul Onder,2 Judy A. King,4 University of Mississippi Medical Center, Jackson, MS; 2The University of Tennessee Health Science Center College of Medicine, Memphis, TN; 3West Virginia University Health Sciences Center, Morgantown, WV; 4Louisiana State University Health Sciences Center Shreveport, Shreveport, LA.

**Background:** Tunneled cuffed hemodialysis catheters (TCC) are claimed to be free of bacterial colonization. However, there is contradicting evidence. Two methods were used for bacterial detection and classification: one is based on scanning electron microscopy (SEM) and the other one is based on 16S rRNA gene sequencing. The former method is quick, cheap and can be done in the dialysis unit. The latter one is slower, expensive and can be done in reference laboratories.

**Methods:** 45 TCC were investigated; 10 were removed due to CRB and 35 were removed for non-infectious reasons. 16S rRNA qPCR technique was used to detect intraluminal bacterial colonization after scraping the intraluminal biologic material. Proximal, middle and distal TCC were evaluated by scanning electron microscopy to qualitatively show the difference in bacterial/biofilm growth at four different regions of the catheter for NitriCap vs. control (Fig. 2).

**Conclusions:** This data strongly suggests that the NitriCap displays significant antimicrobial/anti-biofilm effects during in vitro and large animal in vivo studies, demonstrating that its implementation could minimize catheter related bloodstream infections.
determine the percentage (%) of intraluminal biofilm surface area coverage (BSA). All catheters were cultured for bacterial growth following sonication.

**Results:** Twenty-seven catheters were 16S rRNA qPCR (+) (60%). Eight of these catheters were removed due to CRB. 16S rRNA qPCR (+) results were associated with the absence of bacteremia (negative predictive value of 89% and Odds Ratio = 8.0). 16S rRNA qPCR (-) results were not predicted by catheter vintage or dialysis vintage. All catheter segments were covered by biofilm with a mean % BSA of 68.4 ± 26.1%. There was statistically significant difference between the % BSA of the three catheter segments (p=0.0344). The proximal catheter segments had larger % BSA compared to distal segments. The intraluminal % BSA was inversely correlated with dialysis vintage (p=0.031). There was no statistical difference for % BSA when catheters were compared according to their 16S rRNA qPCR, catheter culture, or blood culture results.

**Conclusions:** For this cohort, biofilm accumulation on TCCs was universal but bacterial colonization was not, as measured by three different methods, suggesting that biofilm may precede colonization of TCC by microorganisms. This piece of evidence may help to improve prophylactic strategies against CRB.

**PO1357**

Are Rescue Maneuvers More Efficient for Tunned Catheter Late Dysfunction Than Wire Guide Catheter Replacement?

**Methods:** On GB, a proactive step was taken to prevent catheter failure and to identify patients at risk for CRBC.

**Results:** Among the 16 patients who developed CRBC, 10 had infectious complications (62.5%). Of these, 4 had positive blood cultures (25%). The remaining 6 patients had non-infectious causes of CRBC: 2 had mechanical complications (12.5%), 2 had vascular anomalies (12.5%), 1 had an embolic event (6.25%), and 1 had no identifiable cause (6.25%). The median time to CRBC was 5 days (range 1-14 days). The median age of patients with CRBC was 12 years (range 5-18 years). The median body mass index (BMI) of patients with CRBC was 22.5 kg/m² (range 15.8-30.2 kg/m²). The median time on hemodialysis at the time of CRBC was 6 months (range 1-24 months). The median number of inserted dialysis catheters at the time of CRBC was 1 (range 1-3). The median number of rescue maneuvers performed at the time of CRBC was 1 (range 1-3). The median time to successful catheter insertion at the time of rescue was 10 minutes (range 5-15 minutes).

**Conclusions:** Rescue maneuvers are effective in treating CRBC and can be performed safely and efficiently. Further studies are needed to determine the optimal rescue maneuver and to assess the long-term outcomes of patients who undergo rescue maneuvers.

**PO1358**

Use of Diphenhydramine as Adjuvant to Conscious Sedation in Patients Undergoing Interventional Nephrology Procedures

**Methods:** We compared patients who received conscious sedation with IV midazolam and IV fentanyl and patients who received IV diphenhydramine preceded by IV midazolam and IV fentanyl. Level of sedation was managed per guidelines of moderate sedations. Data collected included baseline patient characteristics, dip of midazolam and fentanyl duration of the procedure, type of the procedure and incidence of bradycardia and hypoxia during procedure. We also looked at if sedation was administered by physician vs nurse.

**Results:** Out of total 407 patients included in the study, 225 patient received Diphenhydramine as adjuvant to conscious sedation. Diphenhydramine use significantly reduced midazolam (2.2 mg vs 2.88 mg, p value <0.001) and fentanyl (88.2 mcg vs 105.97 mcg, p value 0.04) without any difference in the rate of side effects, as compare to nurse administered sedation.

**Conclusions:** Our study indicates that the use of IV diphenhydramine is safe and effective as conscious sedation for patient undergoing Interventional Nephrology procedures and associated with reduction in benzodiazepine and opioid dose requirements.

**PO1359**

Perforation of Superior Vena Cava: A Rare Complication of Tunneled Hemodialysis Catheter Placement

**Introduction:** Placement of tunneled hemodialysis catheter (TDC) is a fairly common procedure performed in hospitals and outpatient vascular centers. It is considered a fairly simple and risk free procedure for most part. Perforation of SVC while passing guide wires or dilating the tract is very rare and has been reported only in a very few case reports in the literature. We report a case that highlights this rare but frightening complication. This case also highlights the risk of deep central vein thrombosis associated with dialysis catheters.

**Case Description:** A 40-year-old female had a left subclavian vein temporary HD catheter placed in ER for emergent HD for ethylene glycol poisoning related complications. After one week, the temporary HD catheter was exchanged for a TDC under fluoroscopy. Shortly after the procedure the patient became dyspneic, tachycardic, and hypotensive. Imaging revealed perforation of SVC by the catheter tip resulting in a large right hemothorax. Immediate chest tube was placed followed by Thoracotomy and repair of SVC perforation and removal of TDC. One week later she developed left arm swelling and was diagnosed with deep vein thrombosis of the left subclavian vein, left internal jugular vein and the left axillary vein. The patient continued HD through a femoral HD catheter. She was started on heparin drip and systemically anticoagulated. The renal functions eventually recovered and arm swelling resolved and she was able to be discharged from hospital.

**Conclusion:** Teaching Points: This case highlights rare but frightening complications of placement of a tunneled hemodialysis catheter, especially involving the left side neck veins. SVC perforation is a potentially fatal complication that can occur during placement of HD catheters. Immediate recognition, chest tube insertion for drainage, and/or pericardiocentesis along with emergent SVC repair are the key factors to management. Given the high frequency of HD catheter placements, providers should be aware and know how to treat and manage these complications in a timely manner.

**PO1360**

Unusual Dialysis Catheter Location in a Transplant Patient

**Introduction:** Persistent left superior vena cava (PLSVC) is the most common thoracic venous malformation, despite its low incidence. PLSVC is generally discovered fortuitously without clinical signs. Serious hemodynamic complications may occur during the implantation and the permanency of a hemodialysis vascular access on this vessel. Given the high frequency of HD catheter placements, providers should be aware and know how to treat and manage these complications in a timely manner.

**Case Description:** A 56-year-old woman, kidney transplant recipient 8 years ago, was admitted to the Intensive Care Unit with septic shock secondary to disseminated intravascular coagulation. Hemodialysis through a femoral HD catheter was placed on hemodialysis through this access uneventfully throughout the hospitalization period.

**Discussion:** PLSDV is a congenital malformation reported in 0.4-0.5% of the general population. Patients usually asymptomatic and the anomaly is infrequently diagnosed or only noticed incidentally during imaging studies. Some patients can present with arrhythmias and sudden death. Screening diagnostic studies include chest radiograph and echocardiography, confirmed by CTA, magnetic resonance and cardiac catheterization. The possibility of catheterization of PLSVC is uncertain. Some authors argue that if the vessel is too thin to catheterize a large-bore guide wire or catheter it should not be attempted. It is suggested that an accurate assessment of inner diameter of the vein can be performed before catheterization, it could be used as a site for conventional vascular access. However, there are reports of serious complications during catheterization such as pneumothorax, hemothorax, arrhythmias and cardiac arrest.
POI361

Percutaneous Thrombectomy of an Ipsilateral Arteriovenous Dialysis Graft in a Patient with Dextrocardia

Alexander Hlepas, Anna M. Zemke, Monnie Wasse. Interventional Nephrology Rush University Medical Center, Chicago, IL.

Introduction: Dextrocardia with situs solitus (DSS) and associated duplicated left superior vena cava (DLSVC) is a rare condition. In affected patients with end-stage kidney disease (ESKD) the preferred dialysis access type and site are unclear, however anatomical variations may impact feasibility and success of dialysis access related procedures. In the setting of the altered anatomy, drainage of an access to the right atrium takes an altered pathway with differing technical concerns for stent deployment and avoidance of thrombus propagation in a clotted AVG.

Case Description: We report a rare case of covered stent placement during thrombectomy of a clotted ipsilateral right forearm loop AVG in the setting of DSS in an ESRD female. Given a severe venous anastomotic lesion and severe draining brachial vein stenosis, a covered stent was placed across the length of the stenosis. However, a guidewire could not be parked in the IVC to safeguard against potential stent migration to the heart, given the presence of dextrocardia, and the procedure was associated with a high risk of thrombus migration. An associated DLSVC draining into the CS (Coronary Sinus) was present, thus creating a direct path from the AVG through the central veins and the CS down to the heart. A right brachiocephalic vein was not present, and the right subclavian vein drained directly into the persistent right SVC (right part of duplicated left). After repeating the angiogram, measuring the length and marking it on the imager, a 6.10 cm Viabahn stent graft was passed to the level of the stenosis bridging the lesion with 2 cm maintained in the Acuseal 6 mm AVG and deployed. Thrombus was cleared with a 4 French Fogarthy catheter and after installation of TPA and excellent flow return achieved.

Discussion: DSS is a rare malformation which may impact the preference of dialysis access site and type in ESRD patients. Possible complications due to the altered anatomy need to be further evaluated. Appropriate precautions to prevent thrombus migration from a clotted ipsilateral graft in the setting of dextrocardia need to be further discussed. This case shows the feasibility of stent placement in a clotted AVG despite the inability of placing a guidewire down the IVC due to dextrocardia.

POI362

Missed Central Venous Stenosis Causing Unilateral Arm Swelling

Sylvester Barnes. Loyola University Health System, Maywood, IL; Edward Hines Jr. VA Hospital, Hines, IL.

Introduction: The patient is a 67YOM with a history of ESRD, right mandible SCC treated with resection, chemotherapy, and radiation with a right sided PowerPort placed for chemo, removed after roughly 1 year. Prior to initiation of dialysis the patient had a right upper extremity brachiocephalic fistula created leading to unilateral right arm swelling shortly afterwards.

Case Description: Fistulogram was performed showing no significant stenosis. Persistent arm swelling continued. CT venogram showed no areas of central stenosis nor any external mass compression (figure 1). Repeat fistulogram showed similar findings; however, pressure wire measurement was obtained showing a gradient of 20 mmHg at the right innominate/SVC junction. Catheter directed injection revealed a near complete stenosis (figure 2). Angioplasty was performed with an 8 mm balloon. Repeat pressure measurements showed a decrease to 10 mmHg with angiogram demonstrating significant improvement in the lesion.

Discussion: Over two weeks he had swelling resolution. This case highlights physical exam findings of central vein stenosis. Despite being absent on multiple imaging modalities persistent physical exam findings necessitated continued evaluation. The validity of pressure wire measurements to help guide further imaging and treatment options is also highlighted.

POI363

Arterial Emboli in the Setting of Prolonged Dialysis Access Thrombosis

Alian Albalas, Sloan Almehmi. The University of Alabama at Birmingham, Birmingham, AL.

Introduction: Thrombosis of the dialysis access is a frequent complication that is encountered in dialysis patients and is associated with poor access outcomes. Delaying dialysis access thrombectomy decreases the chances of re-establishing the flow within the access circuit. However, it is unclear whether this delay would be associated with emboli of the arterial tree. Here we report on two patients in which the access declotting was delayed resulting in arterial emboli.

Case Description: Patient 1: A 32-year-old male with a history of end stage renal disease (ESRD) on hemodialysis via right upper arm HeRO graft who presented with clotted access and volume overload. Due to the severe respiratory distress, he underwent a temporary catheter insertion and urgent dialysis. He came back after 4 days for access declotting. Initial arteriogram revealed right axillary and brachial artery emboli that was removed successfully using tissue plasminogen activator (tPA) catheter infusion followed by and Fogarty balloon. Patient 2: A 65 yr. old male with ESRD on hemodialysis via right upper extremity AV graft who presented with clotted access for one week. The angiogram revealed total occlusion of the venous anastomosis that was treated with angioplasty. The arteriogram demonstrated an embolus within the brachial artery distal to the anastomosis and another embolus in the distal radial artery. Both emboli were treated successfully with selective tPA infusion using Kumpe catheter.
Discussion: These two cases showed that prolonged dialysis access thrombosis can be complicated with arterial embolic events that require high suspicion and immediate treatment.

PO1364
Associations Between Length of Dialysis Facility Ownership and Vascular Access
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Background: Length of dialysis facility ownership may be associated with facility performance in achieving guideline-recommended clinical indicators and outcomes measures. Using publicly available dialysis facility-level data, we sought to assess facility performance on 2 clinical indicators prior to and after facilities were acquired by a large dialysis organization (LDO).

Methods: Using data from Dialysis Facility Compare, we compared units that the LDO acquired during 2013 through 2016 to existing units by looking at 3 time frames: change from the year prior to acquisition, the year of acquisition, and the year following acquisition. These were compared to facilities under LDO ownership for at least 3 years and facilities not owned by the LDO. The measures assessed were percentage of patients with a catheter in use for more than 90 days and percentage of patients with an arteriovenous (AV) fistula in use.

Results: Sixty-seven units were acquired by the LDO during 2013 through 2016. Units acquired by the LDO had a higher percentage of patients with catheter use ≥90 days in the year prior to acquisition than units owned by the LDO for at least 3 years and units not owned by the LDO and improved during the year acquired and the year following acquisition (14.1%, 12.8%, 11.4%, respectively). Similar improvements were observed for AV fistula use (see Table).

Conclusions: Prior research has posited both positive and negative effects of acquisition on quality of patient care. The current results do not find negative effects and suggest possible improvements in care over the course of 1 to 2 years following acquisition, which suggests that implementation of LDO patient care protocols in newly acquired facilities may take time to unfold.

Funding: Commercial Support - DaVita

PO1365
Data-Backed Multidisciplinary Care Substantially Improves Renal Replacement Therapy Outcomes
Xiuyan Wang,1 Ollie Fielding,1 Jung Hoon Son,1 Edward M. Lee,1 Andrew Bohmert,1 Frank Liu,2 Jeffrey I. Silberzweig,2 The PEAK team 1pulsedata, New York, NY; 2The Rogosin Institute, New York, NY.

Background: The Rogosin Institute created the Program for Education in Advanced Kidney Disease (PEAK), a multidisciplinary care team that assists patients in making a smooth transition to renal replacement therapy (RRT) in 2015. In October 2018 the PEAK team transitioned to using a machine learning (ML) algorithm and care platform devised by pulsedata to identify their highest risk patients and increase the rate of optimal RRT starts and increase support for patients in choosing a home dialysis modality.

Methods: The ML model continually surveys the Electronic Health Record (EHR) to identify patients at risk of progression to an eGFR <10 or RRT start in the next six months for referral into the PEAK program. The patient review platform presents a longitudinal view of the patient’s data, allows for the documentation of the RRT care plan and is used to review the high risk patients at a weekly care planning session. The care team updates patient progress and the platform highlights patients who have had no recent care actions.

Results: Home dialysis rates increased 50% after the ML/platform deployment (30% vs 20%). Home dialysis rates among graduates of the PEAK program are now 10x the NYC average (27% since January 1, 2019 vs 2.5%). Patients who spend more time in the PEAK program are more likely to receive an optimal dialysis start (as an outpatient and with venous access) (p=0.00002, unequal variances t-test); the mean PEAK duration for an optimal start is 316 days vs. 196 for non-optimal starts. Optimal starts are also associated with a greater number of PEAK appointments (4.9 appointments vs 3.7; p=0.0004, unequal variances t-test). Further, of patients starting dialysis using a central venous catheter (CVC), PEAK program graduates remove them significantly sooner (mean 88.57 days for non-PEAK vs. 54.71 mean days for PEAK (p=0.02, unequal variances t-test).

Conclusions: The PEAK MDC-pulseData partnership has dramatically improved care coordination resulting in a substantial increase in home dialysis modality and optimal dialysis starts and reduced the amount of time dialysis patients spend using a CVC.

Funding: Commercial Support - pulseData

PO1366
Education and Experience Gained Through Nephrology Business Leadership University (NBLU) Provide Valuable Benefits to Graduating Nephrology Fellows: A Survey-Based Study
Diana Mahboob,1,2 Manasi Bapat,1 Samir Nangia,1,2 Dallas Renal Group, Dallas, TX; 3Texas Christian University, Fort Worth, TX; 4East Bay Nephrology, Berkeley, CA.

Background: Nephrology fellowship programs provide excellent clinical training but education regarding the economic, business, and leadership aspects of practicing as a nephrologist are lacking. Nephrology Business Leadership University (NBLU) addresses these needs in order to provide graduating fellows with practical tools for navigating their early private practice or academic careers.

Methods: We surveyed attendees of NBLU from each of the four years since the conference was created. An anonymous survey was sent to alumni electronically and focused on how the experiences and knowledge gained at NBLU have impacted their early careers.

Results: Seventy-one percent of fellows who were contacted responded to the survey. Respondents represented all four years of NBLU and all geographic areas of the U.S. All fellows indicated that they would recommend NBLU to other fellows, with 91% indicating that they would highly recommend it. Respondents reported that NBLU increased their knowledge about the nephrology job market, the economics of nephrology practice, and the various ways to engage in leadership opportunities in nephrology, including by using social media platforms for education and networking. Fellows reported enhanced knowledge regarding both private and academic nephrology careers and most established lasting relationships with colleagues from across the country which they intend to maintain throughout their careers.

Conclusions: Nephrology fellows report a significant need for business and leadership education which is currently lacking from fellowship programs. NBLU provides a week-long curriculum which has a lasting positive impact on graduating nephrology fellows. Empowering nephrology trainees on the verge of entering the workforce has the power to strengthen the field as these early career nephrologists inspire other trainees to join this challenging yet fulfilling field.

Funding: Commercial Support - pulseData
PO1367

Resident’s Perception of the Nephrology Specialty

Georges Naboulsi,1,2 Ali Mehdizadeh,1 Jonathan J. Taliercio,1,2 Patricia F. Kao,3 Grace Mcnutt,1 Jessica Greenfield,1 Abby L. Spencer,1 John F. O’Toole,1,2 Joseph V. Nally,1,2 John R. Sedor,1,2 S. Beth Bierr,1 1Cleveland Clinic, Cleveland, OH; 2Case Western Reserve University, Cleveland, OH; 3Washington University in Saint Louis, Saint Louis, MO.

Background: Interest in nephrology as a specialty has been declining among residents. As a result, more than half of the programs remain unfilled. The residents’ perceptions of the nephrology field that might account for this loss of interest are unknown. We aimed to identify factors influencing residents’ views on pursuing a career in nephrology.

Methods: We used the results of our previously published qualitative analysis on residents’ perception of nephrology to inform and design a survey of 60 questions. The survey was delivered using the secure application REDCap to 680 residents across eight medicine residency programs in different regions nationally.

Results: 184 residents (27%) responded to the survey. 56% (103) were male, 77% (142) were American graduates and 21% (42) were international graduates. Major positive perceptions of nephrology were: intellectually challenging, positively impacts patients’ lives, opportunity to obtain the job of choice with possibility to practice in an academic setting, and a good work-life balance (Fig. 1A). Those aligned well with the top factors influencing residents’ choice of specialty (Fig. 1B). The major negative perceptions included: inability to perform procedures, financial compensation, and patient population (Fig. 1A). Those aligned poorly with many of the key factors influencing residents’ choice of specialty (Fig. 1B).

Conclusions: Nephrology is well perceived in the top three categories of factors that influence residents’ specialty choices. This suggests that negative factors such as inadequate financial compensation, inability to perform procedures, lack of innovation, and a difficult patient population largely outweigh the positives. In order to attract more candidates, the nephrology community should highlight the innovations and policy initiatives such as the Kidney Precision Medicine Project, the Kidney Innovation Accelerator, and the Advancing American Kidney Health initiative. Nephrologists should also consider creating/expanding interventional nephrology programs and increasing resident exposure to outpatient nephrology.

Funding: Private Foundation Support

PO1368

Clinical Practice Guideline Adoption and Nephrologist Demand

Joseph Lanerva1, Kurtis Pivert,2 Stephen M. Sozio,2 (1American Society of Nephrology, Washington, DC; 2Johns Hopkins University, Baltimore, MD; 3Duke University, Durham, NC.

Background: It is unknown how clinical practice guidelines (CPGs) can affect subspecialty consult (and subspecialist) demand. This study sought to quantify how nationwide adoption of a CKD evaluation and management CPG could influence consult volume, nephrologist demand, and existing geographic maldistribution of nephrologists.

Methods: We projected the volume of nephrology consult based on KDIGO’s 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease recommendations for nephrology consultation. KDIGO’s CPG recommends a nephrology consult for patients with either a) eGFR <30 mL/min/1.73 m2; b) urine ACR >300 mg/g; or c) eGFR <60 mL/min/1.73 m2 and/or ACR >30 mg/g and refractory hypertension (BP =140/90 mmHg despite ≥4 antihypertensives). We used data from the National Health and Nutrition Examination Survey (NHANES) from 2011–2016 weighted equally across three survey periods, and disaggregated data at the Census Division level to capture geographic variation in potential demand. We calculated eGFR using the CKD-EPI formula and projected KDIGO-recommended nephrology consults as number of weighted individuals per Census Division meeting KDIGO criteria. We quantified nephrologist demand as a ratio of consult volume per nephrologist at the Census Division level using data from the 2014 American Medical Association Masterfile.

Results: Projected nephrologist demand varied geographically, from 1.67% in New England to 2.22% in the Pacific (4.51%) (Fig. 1A). Those aligned poorly with many of the key factors influencing residents’ choice of specialty (Fig. 1B).

Conclusions: Implementing a CKD CPG could lead to increased demand for nephrologists, which may exacerbate the suboptimal geographic distribution of kidney health specialists.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
9/17 (53%) responded to the survey. **Nephrologists.** 20/30 (25%) responded to the survey. Program Directors and Nephrologists agreed that Stones, C.K.D. Tubular disorders, and >0.26 extensive). The activity launched online on March 1, 2019, and data were received, and should be considered as an alternative training format, especially when in-person workshops cannot be conducted. Future trainings can incorporate communication challenges that arise during telemedicine video or telephone encounters.

**PO1373**

Dose Adjustment of Rheumatoid and Allergic Medications in CKD: Awareness and Knowledge Among Internal Medicine House Staff

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**Background:** Patients with chronic kidney disease (CKD) are at increased risk for adverse drug events due to medication dosing errors. We study the awareness and knowledge among Internal Medicine house-staff (IMHS) of proper dose adjustment of commonly used rheumatology and allergy/immunology medications for patients with CKD.

**Methods:** We surveyed 353 IMHS to evaluate their awareness of medication dose needs adjustment for patients with CKD and knowledge for medication adjustment by level of glomerular filtration rate for common rheumatology and allergy/immunology medications.

**Results:** There was lack of awareness and knowledge for both rheumatology and allergy/immunology medications. Not correct awareness and knowledge were: allopurinol (21.2%, 73.4%), colchicine (19.0%, 75.9%), diphenhydramine (34.3%, 34.3%), loratadine (82.2%, 93.2%), and montelukast (34.0%, 34.0%). Exploratory logistic regression analyses showed PGY1 residents had higher odds for lack of awareness for allopurinol (OR:2.57, 95% CI:4.69, 9.93, p<0.001), colchicine (OR:3.98, 95% CI:1.50, 10.51, p<0.01), diphenhydramine (OR:2.24, 95% CI:1.10, 4.54, p<0.04), and montelukast (OR:2.45, 95% CI:1.20, 5.00, p<0.05) compared to PGY3 residents. Nephrology rotation in medical school was associated with lower odds for incorrect knowledge for allopurinol (OR:0.46, 95% CI:0.25, 0.87, p<0.05) and montelukast (OR:0.50, 95% CI:0.27, 0.92, p<0.05).

**Conclusions:** Overall, awareness and knowledge was poor among IMHS for dose adjustments of rheumatology and allergy/immunology medications in patients with CKD. Proper education and exposure to nephrology during training may improve quality and safety of care for patients with CKD.

**PO1374**

Emerging Therapies for Managing Patients with Alport Syndrome: Online Medical Education Improves Knowledge and Confidence of Nephrologists

**Amy Larkin,^1 Donald Blatherwick,^1 George Boutsalis,^2 Ellie Klepecopuis.**^1 Medscape Education, New York, NY;^3 Drexel University College of Medicine, Philadelphia, PA.

**Background:** As new therapies for Alport syndrome continue to progress through development, nephrologists are encouraged to use updated understanding of these therapies to guide treatment. It is unknown if education online for nephrologists could improve clinical knowledge and confidence in managing patients with Alport syndrome with current and emerging treatment strategies.

**Methods:** The continuing medical education (CME) activity was an online video panel discussion among 3 faculty on current and emerging strategies for the management of Alport syndrome. Three multiple-choice knowledge questions and 1 self-reported confidence question were presented both before and immediately after the CME activity. A repeated pairs pre-post-assessment study design was used and a chi-square test (P<0.05 is considered significant) assessed educational effect for each activity. Cramer’s V was used to calculate the effect size (0.06-0.15 is a noticeable effect, 0.16-0.26 considerable, and >0.26 extraordinary). The activity launched online on March 1, 2019, and data were collected through April 3, 2019.

**Results:** Overall, knowledge and confidence improved among nephrologists (n = 71, V= 0.348, P<0.001) from pre- to post-assessment: 24% demonstrated improved understanding of important factors when prescribing renin-angiotensin-aldosterone system (RAAS) inhibitors in patients with Alport syndrome (V=216 (considerable educational impact), P<0.05) 32% demonstrated improved recognition of efficacy data for bardoxolone methyl in Alport syndrome increase in the number of nephrologists (V=297 (extensive educational impact), P<0.001) 63% demonstrated improved identification of adverse effects for emerging treatments for Alport syndrome (V=581 (extensive educational impact), P<0.001) 38% reported increased confidence in understanding of role that chronic renal inflammation plays in AS Continued educational goals: 41% failed to recognize impact of bardoxolone methyl on Alport syndrome 20% did not recognize important factors when prescribing RAAS inhibitors in patients with Alport syndrome.

**Conclusions:** The online video panel discussion CME activity demonstrated success in improving knowledge and confidence of nephrologists related to current and emerging therapies for the management of Alport syndrome. Continued knowledge gaps were identified for future educational targets.

**Funding:** Commercial Support - Reata
Online CME Effectively Improves Nephrologists’ Knowledge, Competence, and Confidence Related to Hyperkalemia Management

Background: To improve outcomes for patients, clinicians must be able to implement evolving standards of care and apply relevant data on hyperkalemia management. We sought to determine if a series of online continuing medical education (CME) activities could improve the clinical knowledge, competence, and confidence of nephrologists related to hyperkalemia management.

Methods: The curriculum consisted of 2 online, 30-minute activities related to new data and case-based application of data in common patient cases. The educational effects were assessed using a repeated pairs pre-assessment/post-assessment study design. For all questions combined, the McNemar’s chi-squared test assessed differences pre to post. P-values <.05 are statistically significant. Cramer’s V was used to calculate the effect size (0.06–0.13 is a noticeable effect, 0.16–0.26 considerable, and >0.26 extensive). The activities launched in March and June 2019, and data were collected for 4 weeks for each activity.

Results: Improved knowledge and competence was demonstrated among nephrologists (N= 371): 17% increase in selecting a treatment strategy when a patient becomes euvolemic but still shows slightly elevated potassium levels (N=188; V=191; P < .001) 24% increase in recognition of long-term data for newer potassium binders (N=183; V=193; P = .001) 26% (N=183) had a measurable increase in confidence in using a potassium binder to treat a patient hyperkalemia 34% (N=188) had a measurable increase in confidence in applying team-based strategies to better manage patients with HF who present with hyperkalemia Persistent knowledge/competence gaps remain: 56% of nephrologists (N=183) incorrectly identified incidence of hyperkalemia in patients with heart failure treated with renin-angiotensin-aldosterone system (RAAS) inhibitors 49% of nephrologists (N=183) could not recognize long-term efficacy data for newer potassium binders 74% of nephrologists (N=188) made an incorrect clinical decision in a patient who was euvolemic but had elevated potassium levels

Conclusions: This study demonstrates the success of an online curriculum with multiple educational components at improving knowledge, confidence, and competence of nephrologists related to hyperkalemia management. Persistent gaps were identified for future educational targets.

Funding: Commercial Support - independent educational grant from AstraZeneca

Case-Based, Interactive Medical Education Significantly Improves Management of Chronic Hyperkalemia in Complex Patients
Amy Larkin, Donald Blatherwick, George Boutsalis. Medscape LLC, New York, NY.

Background: We sought to determine if interactive, case-based online continuing medical education (CME) for nephrologists could improve clinical knowledge, competence, and performance in the area of chronic hyperkalemia management in complex patients.

Methods: The instructional method consisted of an online, case-based, interactive text activity. Clinicians were presented with 2 patient cases that included multiple-choice, multiple-true/false, and open-ended questions allowing them to make clinical decisions about treatment. Educational effect was assessed using a 4-question repeated paired post-assessment and McNemar’s chi-squared test. P values are shown as a measure of significance; P values <.05 are statistically significant. Cramer’s V determined the effect size (≥0.05 no effect; 0.06–0.15 small effect; 0.16–0.30 medium effect; >0.30 large effect).

The activity launched May 15, 2019; data were collected through June 24, 2019.

Results: Significant overall improvements were seen (n = 59; P = .003; V = 0.156) as a result of participation in the CME activity. Specific areas of improvements include: 8% of nephrologists (P = .05; V = 179) improved at using a loop diuretic when a low-potassium diet was unsuccessful at lowering potassium levels 25% of nephrologists (P =.008; V = 241) demonstrated improvement at prescribing a newer potassium binder in a patient with consistently elevated potassium despite a low potassium diet and loop diuretic 10% of nephrologists (P = .04; V = 0.076) improved at using a newer potassium binder in a patient on dialysis with hyperkalemia 36% of nephrologists reported increased confidence using potassium binders in patients on RAAS inhibitors Continued educational gaps: 29% of nephrologists did not initiate a newer potassium binder in an appropriate patient

Conclusions: This study demonstrates the success of an online, highly interactive, case-based educational intervention on improving knowledge, competence, and performance of nephrologists regarding complex management of chronic hyperkalemia.

Funding: Commercial Support - Relypsa, a Vifor Company

Curriculum-Based Online Education Effectively Improves Nephrologists’ Ability to Manage Hyperkalemia in Practice
Amy Larkin, Donald Blatherwick, George Boutsalis. Medscape LLC, New York, NY.

Background: The goal of continuing medical education (CME) is professional growth and improved patient care. We sought to determine if a series of online continuing medical education (CME) activities could improve the clinical knowledge, competence, and confidence of nephrologists related to hyperkalemia management.

Methods: The online CME curriculum consisted of 6 activities. Of these, 5 were video-based and used repeated pre-/post-assessment data gathering by 14% and performance by 150% (all relative improvements, P<.001) by nephrologists. Specific improvements: 22% relative increase in knowledge related to rationale for optimizing RAAS inhibitors in patients with chronic hyperkalemia (P<.001) 15% relative increase in confidence related to effective use of pharmacotherapy for hyperkalemia (P<.001) 441% and 231% relative increases in performance (2 patient simulation cases) related to effective use of pharmacotherapy for hyperkalemia (P<.001). Of the nephrologists who were included, 36% reported increased confidence in managing hyperkalemia, with the largest confidence gains being related to effective use of potassium binders

Conclusions: This curriculum demonstrates that by increasing knowledge and confidence related to hyperkalemia management in a curriculum approach, large improvements in performance can be achieved (over 90% were effectively using pharmacotherapy post-CG). Learners, on average, knew 70% of the information assessed and still require more education in optimizing RAAS inhibitors in patients with chronic hyperkalemia and use of diet to manage hyperkalemia. Among the learners, 36% gained confidence regarding hyperkalemia management in practice, but are still not fully confident. As such, further education is needed in these areas.

Funding: Commercial Support - Relypsa, a Vifor Company

An Analysis of Sciento-metrics and Social Media in Nephrology
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Background: In the past decade, the use of social media to disseminate scientific literature, particularly in the Nephrology community, has exponentially increased to educate, network, mentor. The hallmark of scientometrics has traditionally been based on Journal Impact Factor (JIF), calculated from the citations of each article. It has been previously demonstrated that twitter mentions of published works, correlate with citations, and therefore JIF, in the fields of Urology, Biomedical Science, and Ecology. However, this relationship has yet to be established in the field of Nephrology.

Methods: The top 5 journals in Nephrology, based on impact factor (Kidney International, Nature Reviews Nephrology, AJKD, JASN and CJASN), published 76 articles in January of 2018 in print. Altmetrics bookmarklet was used to collect twitter demographics on each article (number of tweets, by whom, and number of followers). Citation data was sourced from Web of Science’s InCites Journal Citation Reports. Articles were categorized as ‘highly cited or tweeted’ when they were ≥ 75 percentile of citations or tweets, and ‘less cited or tweeted’ at ≤ 25th percentile.

Results: Of the article cohort, the most common article types were clinical investigations (42%), followed by basic research (26%), and reviews (10%). The citation range was 0.29 ± 15.87 citations per article, while the twitter mentions mean was 28.38 ± 68.97 tweets. The Spearman correlation coefficient for Twitter mentions and citations was 0.25 (p = 0.026). The odds ratio of an article being both highly cited and highly tweeted was 3.6 (CI: 0.71 to 18.25). The relative risk showed that highly tweeted articles were 1.87 (CI: 0.83 to 4.19) University. It is likely to be highly cited than less cited. Finally, the peak tweets (279) occurred in October of 2017 while the peak in citations occurred in 2019.

Conclusions: The preliminary analysis showed a significant but weak correlation of twitter mentions and citations. This suggests that twitter increases an article’s reach, its likelihood of becoming cited, and therefore the JIF. Future directions will include exploring a larger sample size and confounding factors such as word count, number of authors, and number of citations.

Qualitative Interview Study on Advanced Care Planning for Patients with Advanced CKD and Their Families: The Impact of the MY WAY Advance Care Planning Intervention
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Background: Despite recommendations for shared decision-making approaches to advance care planning (ACP) for people with advanced chronic kidney disease (CKD), doctor-patient conversations about ACP are infrequent. The MY WAY educational and patient-coaching intervention aims to elicit patient values to increase rates of ACP. This qualitative sub-study sought to: (1) gain understanding of participant responses to MY WAY materials, and (2) learn about patients who did or did not engage in ACP.

Methods: We conducted semi-structured interviews with participants from the intervention arm of the MY WAY study. Fifteen people with CKD were queried about their experiences of the MY WAY print materials and coaching session. Interviews were recorded, transcribed for simultaneous coding by two researchers. Data were analyzed using thematic analysis.
Results: Fifteen intervention participants ages 59-87 were interviewed (10 women, 5 men). Five major themes emerged: participant advice for interventionists; experience with ACP before and after the intervention; participant experience of printed materials; participant response to coaching session; and chronic kidney disease thoughts and communication. Differences between participant experiences of general and CKD-specific ACP emerged, including willingness to discuss care wishes with family members and clinicians.

Conclusions: Participants perceived the coaching session to have high utility in facilitating ACP, but expressed less engagement with CKD-specific care plans. Findings suggest complexities of the coaches' instruction and problem-solving play a key role in participant comfort with ACP conversations, and that engagement with ACP may not correlate with engagement with CKD-specific care wishes. Notably, even participants who engaged actively with general ACP expressed that kidney-specific care would need to be addressed with their nephrologists if or when the need arose. Future studies should further explore the interrelation of general ACP and CKD-specific care planning.

Funding: Private Foundation Support

POI1380

Enhancing Patient Care by Partnering with Patients in Kidney Health Research


Background: Canada's Strategy for Patient-Oriented Research (SPOR) has raised awareness of the need to generate knowledge that is more relevant to patients and to accelerate the translation of evidence into clinical care. Members of the Canadian nephrology community have come together to develop a national patient-oriented research network, Can-SOLVE CKD, that is partnering with patients to close existing gaps in kidney disease knowledge in order to deliver better health outcomes. The Can-SOLVE CKD Network brings together patients and nephrology researchers to transform treatment and care for Canadians living with or at risk for chronic kidney disease.

Methods: The network’s 18 research projects are informed by two national priority-setting exercises conducted with patients, their families and care providers. As the network executes the projects, patients have been integrated into research teams, bringing an enhanced “patient lens” to bear on all aspects of the research life cycle: design, development, implementation, evaluation, and dissemination. Participants are also at the centre of the network’s governance model, which incorporates a Patient Governance Circle and an Indigenous Peoples’ Engagement and Research Council.

Results: Can-SOLVE CKD researchers have reported the positive impact of partnering with patients. “My research is better” is often cited as an outcome of patient engagement within the network. Patient partner involvement on the network’s Research Operations Committee has enriched the annual review of projects, resulting in valuable, real-world feedback to project teams. Respondents to the network’s patient engagement survey report feeling better informed about and having greater trust in kidney research as a result of their participation.

Conclusions: We have witnessed a shift in the culture of nephrology research in Canada paralleling the broader movement toward patient-oriented research. The traditional role of patients as research subjects has evolved to include patients as valuable and equal members of Can-SOLVE CKD’s research projects.

Funding: Government Support - Non-U.S.

POI1381

Online Patient/Caregiver Education on Hyperkalemia Can Improve Knowledge and Confidence as Well as Prompt Real-Life Changes

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Background: Managing hyperkalemia with a strict diet is limiting and difficult for patients. We sought to measure the impact of online education for patients/caregivers on knowledge and confidence as well as prompting change in daily life.

Methods: The patient/caregiver education was designed as 2 online, interactive activities. Both were comprised of text and integrated visuals, the second also included a patient commentary video. Demographic questions were asked prior to starting the education. A knowledge question was asked both before and after the activity to assess learning gains, as well as intent to change and confidence questions at the end. The activity was made available in English in March and May of 2019, and data was collected through September 2019.

Results: To date, 72,440 learners have participated in the patient/caregiver activity. Activity 1: Do You Have High Potassium? There are Some Tips for Managing Potassium in Your Diet Participants: 35, 889 Completers of all questions (in outcomes analysis: 4,305 Demographics: 63% female; 63% white, non-Hispanic; 67% age of 54; 45% have hyperkalemia, 42% were interested in learning more about the condition and 29% have this knowledge and confidence changes: 24% improvement in recognizing foods high in potassium (50% pre to 74% post) Intent-to-act: 81% plan to identify and avoid foods high in potassium Confidence changes: 79% reported increased confidence talking to their doctor about medicines that can treat hyperkalemia

Activity 2: Are Medicines That Lower Potassium Safe? Participants: 36, 551 Completers of all questions (included in outcomes analysis: 2, 987 Demographics: 59% female; 78% white, non-Hispanic; 82% over the age of 54; 58% were interested in learning more about the condition and 29% have this condition knowledge changes: 23% improvement in recognizing how potassium binders work to treat hyperkalemia (42% pre to 65% post) Intent-to-act: 69% plan to talk to their doctor about medicines that can treat hyperkalemia

Conclusions: The metrics and outcomes gathered in this assessment are a strong indicator that these patient/caregiver-focused online educational activities improved knowledge and confidence, and prompted intent to act by patients/caregivers related to hyperkalemia.

Funding: Commercial Support - Relysa, a Vilor Company

POI1382

Rethinking Renal Caregiving in Anthropological Terms: An Interdisciplinary Methodological Approach

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Background: Rethinking caregiving in nephrology through an anthropological lens may bring a new perspective to a holistic understanding of renal care by encouraging health professionals to reflect critically on the complex webs of care, culture, and ethics in which renal medicine is enmeshed.

Methods: This study draws on anthropological methodology and ethnographic research to develop a framework for reconceptualizing renal care. An extensive review of the anthropological literature on renal care is used to illustrate some of the multifaceted challenges of caregiving in nephrology and to develop a framework for use in the clinical encounter to better understand patients’ illness-related beliefs and their relevance for clinical practice.

Results: The key domains in renal care are framed by diverse cultural, societal, and individual beliefs regarding the organ’s function and the causes of kidney disease. Ethnographic data from dialysis and renal transplant patients in the United States, Europe, Mexico, and China show that diverse and controversial disease and treatment beliefs pose a different kind of challenge to the communication between health professionals and their patients. Based on these findings, a framework has been developed that can be integrated in medical education programs and provides a guide for health professionals to think through the complex psychological, ideological, and ethical underpinnings of nephrology’s central therapeutic modalities such as transplantation and dialysis.

Conclusions: Bringing an anthropological sensibility to the clinical care may help to understand the cultural and moral world in which the caregiver-patient relationship needs to be formed. The integration of the medical humanities into the educational programs of renal care caregivers can be used to develop a better understanding of patients’ diverse disease and treatment beliefs which will ultimately improve the caregiver-patient relationship.

Funding: Private Foundation Support

POI1383

WeChat Platform and Specialty Nursing Outpatient Clinics to Improve the Compliance of a High-Quality Low-Protein Diet in Patients with CKD Stage 3-5

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Background: Low protein diet (LPD) has become one of the important means to treat chronic kidney disease (CKD) patients. At present, the low protein diet compliance of CKD patients in China is not ideal, the compliance rate is only 48.3% - 54.5%. The dietary compliance of CKD patients is based on the knowledge of diet, and the survey shows that CKD patients and their families have a low level of knowledge of diet of kidney disease. Therefore, in order to improve the low protein diet compliance of CKD-5 patients and reduce the incidence of malnutrition, we set up a wechat group through the network platform to guide the low protein diet of ckd-5 patients. The nutrition team regularly issues the low protein diet knowledge, and makes an appointment for the follow-up of patients to the specialized nursing clinic every 1-3 months to provide one-to-one guidance services. To explore the effect of continuous care based on WeChat platform and Specialist Nursing Outpatient Clinics on the compliance of high-quality low-protein diet in patients with Chronic Kidney Disease (CKD) stage 3-5.

Methods: 46 cases of diagnosed CKD 3-5 patients were randomly divided into a control group (22 cases) and an observation group (24 cases). The control group conducted routine nursing outpatient clinic and diet counseling, while the observation group implemented a high-quality low-protein diet nursing strategy based on We-Chat platform and Specialist Nursing Outpatient Clinics on a routine basis. Compare the performance and effect of high-quality-low-protein diet between the two groups.

Conclusions: In the observation group, there were 10 men and 12 women with an average age of 42.6 ± 2.3 years; in the control group, there were 12 men and 12 women with an average age of 40.2 ± 2.1 years. There was no significant difference between the two groups in height, weight, education level, and basic diseases (P > 0.05). The observation group’s preparation of CKD high-quality-low-protein diet, three-day diet diary, and daily protein intake were better than the control group (P < 0.05).

Conclusions: The continuous nursing strategy based on We-Chat platform and Specialist Nursing Outpatient Clinics can effectively improve the compliance of CKD3-5 patients with high-quality-low-protein diet.
POI1384

A Kidney Education Program Integrated into Middle School Science Classes Increases Student Kidney Knowledge, Improves Health Behaviors, and Increases Kidney Health Literacy

Background: Chronic kidney disease (CKD) is a serious and growing public health problem. Literature shows primary disease prevention is successful when incorporated early in life. There are few reports about CKD prevention efforts in youth.

Methods: A 3-lesson kidney program was designed by health and wellness staff, school teachers and researchers, and aligned with U.S. school science standards. It was integrated into two middle school science classes, located in high-risk areas of renal failure. The 3-lesson program covered kidney physiology, epidemiology and environmental and genetic risk factors. Students were tested before and after the kidney program. We used linear regression to examine bivariate and multivariate associations between demographics and test responses comparing pre- and post-tests.

Results: Two-hundred and nine 6th and 7th grade students received the 3-lesson kidney program. One-hundred and eighteen (57%) were male, 44 (23%) non-Hispanic Caucasian, 26 (12%) non-Hispanic African American, 26 (12%) other races, and 98 (48%) were Hispanic. Students increased significantly for health literacy (from mean SD 3.1 (0.05) to 3.4 (0.05) p=0.02), kidney general knowledge (2.3 (1.1) to 3.9 (3.6) p<0.01), kidney physiology (3.9 (1.1) to 4.6 (1.0) p<0.01) and student ratings of kidney importance (4.0 (0.9) to 4.3 (0.7) p<0.01). Students also reported increases in daily activity and reduced consumption of fruit juices. In analyses adjusted for school, race, gender, ethnicity and age, health literacy, kidney general knowledge, kidney physiology, kidney importance and behaviors remained significantly improved.

Conclusions: A 3-lesson kidney program seamlessly delivered by teachers during science classes at two middle schools in high-risk areas for renal failure improved student health literacy, knowledge and behaviors. Next steps will be to examine impact in larger cohorts and clinical indices over time.

Funding: Other NIH Support - UL - NIH - NCATS grant

POI1385

Nephrology Exposure and Quality of Education in Residency and Medical School
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Background: Interest in nephrology as a specialty has been declining among residents. Lack of exposure to nephrology has been identified as one of the factors possibly accounting for this loss of interest.

Methods: We used the results of our previously published qualitative analysis on residents’ perception of nephrology to inform and design a survey of 60 questions. The survey was delivered using the secure web application “REDCap to 680 residents across eight medicine residency programs in different regions nationally.

Results: 184 residents (27%) responded to the survey. 56% (103) were male and 77% (142) were American graduates. During medical school, 82% of respondents were taught nephrology as a unique discipline, while 33.5% rotated on a nephrology service. During residency, 75% of respondents rotated in nephrology and the rotation took place during PGY1 for 68% of the respondents. On a scale of 1 (poorest) to 100 (best), the quality of nephrology education was rated favorably during residency and during the pre-clinical years of medical school, and less favorably during the clinical year of years of medical school (Fig. 1). Out of 134 residents (73%) who expressed interest in pursuing fellowship training, only 5.8% selected nephrology. Only 6.3% of residents identified a mentor in nephrology vs. 29.7% in general medicine and 26.6% in cardiology (Table 1).

Conclusions: We observed a “dip” in the quantity and quality of nephrology exposure during the clinical years of medical school. More work is needed to characterize the significance of this dip and to understand whether or not this may represent an opportunity to improve the visibility and impact of nephrology on trainees.

Funding: Private Foundation Support

POI1386

Internal Medicine Residents’ Perceptions of Nephrology as a Career: A Focus Group Study
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Background: The interest in nephrology as a career has declined dramatically over the past several years. Only 62% of nephrology fellowship positions are filled for the upcoming 2020 appointment year. The purpose of this study was to identify perceptions, attitudes, motivators and barriers to a career in nephrology among internal medicine residents.

Methods: Focus groups of internal medicine residents (N=25) from the University of Colorado were performed. Questions were aimed at exploring perceptions, attitudes, and barriers to a career in nephrology and ways to increase interest in nephrology. All focus groups were conducted on the University of Colorado Denver Anschutz Medical Campus. Focus groups were recorded and transcribed. Thematic analysis was used to identify key concepts and themes.

Results: Residents’ described many barriers to a career in nephrology including lack of exposure, lack of advances in the field, low monetary compensation, too complex, lack of role models/mentors and low prestige/non-competitive. Most residents had no exposure to outpatient nephrology. Lack of new therapeutics was a significant deterrent to nephrology. Nephrology teaching in medical school was described as not clinically relevant and too complicated. Several residents felt they were not smart enough for nephrology. Only 3 residents had a role model within nephrology. Residents used the word “stigmatized” to describe nephrology and discussed how low prestige decreases their interest in a field. Participants expressed suggestions to increase interest in nephrology through earlier and more outpatient nephrology exposure, enhanced interactions with nephrologists and research and advancements in the field.

Conclusions: Residents’ identified several modifiable barriers to a career in nephrology. Changing how nephrology is taught in medical school, enhancing interactions with nephrologists through increased exposure and highlighting research and advancements in nephrology may change the perception of nephrology and increase the number of residents entering the field.

Funding: Other NIH Support - NHLBI R01 HL.132868

POI1387

Changes in the Demographics and Research Focus of Renal Physic-ian-Scientists in the United States
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Background: The enormous strides in biomedical research made over the past 50 years are in large part due to the contributions of physician-scientists. However, while the renal physician-scientist workforce has been thought to be falling, these changes have not been quantified. The purpose of this study was to compare changes in the demographics and the research focus of established physician and non-physician principal investigators
Methods: We mined NIH RePORTER for NIDDK-funded, kidney-focused RO1s and K series grants to determine the PI demographics, the terminal degree(s) of the PIs (physician versus non-physician) and to determine the relative number of clinical and basic science proposals. As an age-surrogate, we compared the year at which the respective RO1 PI received either their M.D. (physicians) or their Ph.D. (non-physicians) degrees. Taking these values, along with published data as to the median age at which students received their M.D. or Ph.D. in the U.S. in both 2005 and 2020, we estimated the ages of the NIDDK RO1-funded physician and non-physician workforce doing kidney research in the U.S.

Results: Amongst grants focused on kidney, the apparent median age of non-physician, RO1-funded PIs was similar in 2005 and in 2020. However, the apparent median age of physician, RO1-funded PIs is approximately 6 years older in now in 2020 than that in 2005. While the number of basic science grants was similar for physician PIs in 2005 and 2020, the number of clinically-focused RO1s increased. The number of NIDDK K series-funded physicians peaked in 2010 and then declined. However, the percent of physician-scientist RO1s held by women has risen from 15% in 2005 to 25% in 2020, while physician-scientist K series awards held by women has risen from 35% to 48% over that time period.

Conclusions: The representation of women in the physician-scientist workforce doing kidney research has increased. However, this physician-scientist workforce is older and relatively fewer are engaged in basic science research.

Funding: NIDDK Support

Background: Medical simulation develops clinical skills by implementing scenario in a true-to-life environment, but without exposing patient to any risk. There has been no information on use of high-fidelity simulation in undergraduate nephrology teaching. Scenarios are provided in Fig. 1. Aim of this study was to analyze students’ opinions and reactions to the simulation module in nephrology.

Methods: The survey consisting of the Satisfaction with Simulation Experience scale (SSES) and open-ended question concerning the overall impression of classes was conducted among 103 5-year medical students, who took part in the simulation training in nephrology. SSES consisted of three parts (debriefing, reasoning, education). Statements from the open-ended question were interpreted by means of the Atlas.ti software for qualitative data analysis.

Results: The overall score for simulation classes was 4.39±0.69 points. Students rated debriefing, reasoning and education at 4.43±0.78, 4.32±0.7 and 4.39±0.73 points, respectively. 87.4% and 84.5% of participants agreed that simulation developed their clinical reasoning and decision-making skills in nephrology, respectively. 87.4% and 84.5% of participants agreed that simulation developed their clinical reasoning and decision-making skills in nephrology, respectively. 87.4% and 84.5% of participants agreed that simulation developed their clinical reasoning and decision-making skills in nephrology, respectively. 87.4% and 84.5% of participants agreed that simulation developed their clinical reasoning and decision-making skills in nephrology, respectively. 0.7±0.73 points, 0.78, 4.32 ±0.69 points. Students

Conclusions: Medical simulation is a valuable constituent of the nephrology course. Putting greater emphasis on practical aspects from the beginning of training may enable students to benefit more from simulation modules.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

**Figure 1. Medical simulation scenarios conducted as a part of undergraduate nephrology course.**
larger percentage of readers found the tweetorial more useful compared to the case report. About 80% confirmed their educational experience was affected during the pandemic, and 90.4% found the SKG an effective educational experience during this time period. **Conclusions:** Innovative teaching methods provided by the SKG was found to be beneficial in teaching complicated electrolyte concepts. Our data reinforces the ability of FOAMed to cater to different learning styles and to complement traditional medical education specifically during periods of social distancing such as COVID-19 pandemic.

**POI1391**

**Glomerular Disease Education Across Nephrology Fellowship Programs**

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**Background:** Glomerular disease (GN) education is an important, albeit a challenging component of nephrology fellowship training. We hypothesized that trainee experience varies widely across programs, leading to differences in self-reported competency levels in the diagnosis and managing of GN.

**Methods:** The Glomerular Disease Study & Trial Consortium (GlomCon) conducted an anonymous online survey to evaluate the educational experience of nephrology trainees. We used multiple-choice questions to obtain data about: a) curriculum-based education, b) dedicated specialty clinic, and c) exposure to pathology. We leveraged a visual analogue scale of 1-100 (higher number indicating a higher comfort level) to assess self-reported levels of clinical competency. The survey was disseminated via email, the GlomCon website, and Twitter.

**Results:** There were 107 responses across all years of fellowship training – first-year (25%), second-year (34%), third-year (22%), and fourth-year (19%). A total of 44% reported no GN clinic at their institutions. The presence of an onsite nephropathologist was reported by 63% of responders and 37% reported no onsite nephropathologist or limited exposure. In a visual analogue, the mean competency for GN diagnosis and treatment were 59±26 and 52±25, respectively. Trainees with no onsite nephropathologist and those with limited exposure scored significantly lower in diagnosing GN compared to those with an onsite nephropathologist (51±25 vs. 64±26, p=0.05). Trainees with more exposure to GN specialty clinic had a higher comfort level in treating GN (Fig). Figure demonstrates frequency of trainees in each group with a comfort level above the overall median score (51).

**Conclusions:** Trainees report a wide variation in GN education across fellowship programs. A lack of exposure to onsite nephropathologist and a dedicated GN curriculum were associated with lower scores in self-reported clinical competency in caring for patients with glomerular disease.

**POI1392**

**Frequency and Severity of Moral Distress in Nephrology Fellows: A National Survey**

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**Background:** Moral distress is a negative affective response to a situation that conflicts with an individual’s values. Health care practitioners who care for chronically ill patients frequently experience moral distress. Little is known about the frequency and severity of moral distress in nephrology fellows.

**Methods:** We used the modified Moral Distress Scale-Revised to assess the frequency and severity of moral distress in nephrology fellows. Using a 5-point (0-4) scale, fellows rated both the frequency (never to very frequently) and severity (not at all disturbing to very disturbing) of scenarios commonly encountered in training. Responses of a 3 were used to define “frequent” and “moderate-to-severe” moral distress. We identified scenarios most commonly associated with moderate-to-severe moral distress. The survey was sent to 148 program directors with a request to forward to their fellows.

**Results:** The survey was forwarded by 64 fellowship directors to 386 fellows, 142 of whom (40%) responded. Their mean age was 33 ± 3.6 years; 43% were female; and 55% were international medical graduates. The most common scenarios causing moderate to severe moral distress include: Other providers giving overly optimistic descriptions of the benefits of acute (54% seeing frequently, 66% rating the distress as moderate to severe) or chronic dialysis (43%; 64%), initiating dialysis in patients when they deemed it futile (50%; 77%), continuing dialysis in a hopelessly ill patient (45%; 81%) and carrying a high patient census (43%; 75%). Approximately 27% considered quitting fellowship during training, including 9% at the time of survey completion.

**Conclusions:** Moral distress is frequently encountered by nephrology trainees and is often moderate to severe in intensity. To address this issue, organizational changes (e.g., reduced workload, ethics guidelines), curricular changes (emphasizing primary palliative care, communication, and ethical decision-making skills) as well as opportunities for reflection and self-care (e.g., Balint groups, Schwartz rounds) may be helpful.

**Funding:** NIDDK Support, Private Foundation Support

**POI1393**

**The Sustainable Pediatric Nephrology Workforce Project (SUPER-POWER): A Pilot Study of Burnout and Resilience**

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**Background:** Physician well-being is an important contributor to both job satisfaction and patient outcomes. Rates of burnout among physicians vary by specialty, ranging from 35-70%. Among pediatric residents, longitudinal data demonstrates consistent rates of burnout around 50-60%, although little is known about burnout among pediatric subspecialty fellows. The degree of burnout among pediatric nephrology subspecialty fellows specifically remains unknown. We sought to evaluate prevalence and predictors of burnout among U.S. pediatric nephrology fellows and faculty, and their interactions.

**Methods:** A multi-center pilot survey of United States pediatric nephrology training programs was conducted. September 2019 – April 2020. Burnout was assessed through the Maslach Burnout Inventory and predictors included demographic, job-related and career satisfaction questions. Other validated assessments included: quality of life, perceived stress, resilience and sleep.

**Results:** A total of 30/34 available fellows and 86/102 faculty from 11 institutions (of 42 programs nationally) completed the survey. The prevalence of burnout was 13% among fellows and 16% among faculty. Demographic (age, gender, year of training, faculty rank, marital status) and program factors (fellowship size, faculty size, current block rotation, vacation or weekend off timing) were not significantly associated with burnout. Faculty and fellows with burnout reported significantly lower quality of life (5.3 vs 7.9), higher perceived stress (2.4 vs. 1.4) and lower satisfaction with career choice (66% vs. 22%) and work life balance (28% vs. 0%), compared to those without burnout (p<0.05 for all). Other important factors associated with burnout included lower institutional support for wellness programs and lower satisfaction with both colleague and faculty support.

**Conclusions:** Larger studies are needed to explore if burnout is truly less prevalent among pediatric nephrology fellows andfaculty than pediatric residents and graduate physicians. Future studies should explore how to promote well-being through addressing key factors such as overall learning/working environment, stress reduction, and building resilience.

**POI1394**

**Protein Kinase A Catalytic-α and Catalytic-β Proteins Have Non-Redundant Functions**


**Background:** Vasopressin regulates osmotic water transport in the renal collecting duct by PKA-mediated control of the water channel aquaporin-2 (AQP2). Collecting duct principal cells express two seemingly redundant PKA catalytic subunits, PKA catalytic α and β. Understanding the distinct functions of these two PKA catalytic subunits may reveal new targets for disease and therapeutic intervention.

**Results:** Using a combination of acute and chronic models of diabetes insipidus, we evaluated the functional contributions of PKA catalytic α and β. In acute diabetes insipidus, we observed significantly enhanced water reabsorption in PKA catalytic α-null mice compared to wild-type mice (p<0.05). In chronic diabetes insipidus, we observed significantly reduced water reabsorption in PKA catalytic α-null mice compared to wild-type mice (p<0.05). These findings suggest that PKA catalytic α plays a critical role in regulating water reabsorption in the collecting duct.

**Conclusions:** These findings suggest that PKA catalytic α plays a critical role in regulating water reabsorption in the collecting duct.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
addition, scRNA-seq identified three distinct CTAL (Slc12a1, Pcna reductions in dietary K+ diet revealed NDI was dependent on the development of free-water reabsorption, polyuria and polydipsia was observed within four days, eliminated from the diet, coincidence with the development of hypokalemia. Loss tissues were harvested for western blotting and immunocytochemistry at the end of the Iroquois homeobox transcription factors, with Cldn10 expressed in one and Cldn10+ cluster of the CTAL and DCT. The new data have allowed the creation of a publicly accessible web Lihe Chen, Chung-Lin Chou, Mark A. Knepper. National Heart Lung and Blood Institute, Bethesda, MD.

Background: Several distinct epithelial cell types have been proposed to form the transition region from the cortical thick ascending limb of Henle (CTAL) to the distal convoluted tubule (DCT) to the connecting tubule (CNT). However, a complete understanding of the cellular composition and transcriptional profiles of the cells in this region is lacking.

Methods: We developed a FACS protocol to enrich cells from the mouse CTAL-DCT-CNT region and carried out single-cell RNA-seq analysis (scRNA-seq) of 9099 such cells. We also used small-sample RNA-Seq to determine transcriptional profiles of microdissected renal tubule segments.

Results: Unbiased clustering and UMAP visualization revealed a single cluster of cells showing Slc12a1 expression without Prah1, which we identified as DCT2 cells. These cells express ENaC subunits but little or no H1ll12 or Agn2 mRNA. These DCT2 cells also express Calb1, Slc12a1, Slc22a5, Pigs, and Trp5. In contrast, there were 6 tightly arranged clusters of cells expressing both Slc12a3 and Prah1, which we identify as DCT1 cells. DCT1 heterogeneity appears to be associated with variable expression of Slc9a1, Calb1, and Ckb among other mRNAs. An additional DCT1 (Slc12a3+Prah1+) cluster showed marked enrichment of cell cycle and cell proliferation associated mRNAs (e.g. Pena, Mik67, Cadl1, and Top2a), which fits with the normal plasticity of DCT cells. In addition, scRNA-seq identified three distinct CTAL (Slc12a1+) cell subtypes. One of these expressed Nosi, Avpr1a, and Pappa2, consistent with macula densa cells. The other two CTAL clusters were distinguished by Cldn10 and P repreh5, one and Cldn10 and P repreh3 in the other. These two CTAL types were also distinguished by alternative expression of Iroquois homeobox transcription factors, with Irx1 and Irx2 in the Cldn10+ CTAL cells and Irx3 in the Cldn10- CTAL cells.

Conclusions: This work identifies unexpected diversity among cell types populating the CTAL and CNT. The new data have allowed the creation of a publicly accessible web resource for the support of future studies.

Funding: Other NIH Support - Intramural Grant

POI1395

Single-Cell RNA Sequencing Reveals Transcriptomes of DCT1, DCT2, Macula Densa, and Two Subtypes of Cortical Thick Ascending Limb Cells

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The Phosphorylated States of Human Aquaporin 2 Revealed by Liquid Chromatography Coupled to Tandem Mass Spectrometry Phosphoproteomic Analysis of Urinary Exosomes

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Background: Aquaporin-2 (AQP2) is a key water channel to enhance water permeability of collecting ducts. Multiple phosphorylation sites at the C-terminal of AQP2 have been identified including S256 (serine at the 256 residue), S261, S264 and S269. It is not clear how the phosphorylation state of AQP2 is regulated. Our group has reported that AQP2 is located in exosomes. Exosomal AQP2 excretion in human urine.

Methods: We examined the phosphorylation profile of AQP2 using liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) analysis, in parallel with immunoblots by commercially available phosphorylation-site specific anti-human AQP2 antibodies.

Results: The most dominant phosphorylated AQP2 peptide was phosphorylated at S256 (pS256), followed by pS261, less pS264 and much less pT269. The results were confirmed by the western blot analysis using antibodies specific to each phosphorylated AQP2. To document the time-course of urinary exosomal AQP2 phosphorylation by VP, a VP analogue was administered to a patient with central diabetes insipidus. It induced total urinary AQP2 excretion plateauing at 68 mg per minute within a transient increase (peaking at 30-60 min) of pS261 and a progressive increase of pS256. All four corresponding phosphorylation sites of human AQP2 including T269 were phosphorylated and the phosphorylation sites at S256 and S261 were tightly linked to total exosomal AQP2 excretion.

Conclusions: We conclude that human AQP2 is predominantly phosphorylated at S256 and moderately at S261 in urinary exosomes. T269-phosphorylation may not be needed for exosomal AQP2 excretion in human urine.

Funding: Government Support - Non-U.S.
Bayesian Identification of Transcription Factors That Regulate Aqp2 Transcription
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Background: Renal collecting duct and connecting tubule cells selectively express the water channel aquaporin-2 (AQP2) and Aqp2 gene expression is strongly regulated by vasopressin. However, the transcription factors (TFs) responsible for regulation of expression of AQP2 remain largely unknown. Here, we used Bayesian data integration techniques to identify these TFs.

Methods: The general strategy is to use Bayes’ Rule to integrate several -omic datasets to stratify a curated list of 1334 TFs present in the mouse genome with regard to probability of regulating Aqp2 gene transcription. First, existing proteomic and transcriptomic data were used to select the TFs most strongly expressed in mpkCCD cells. Then, we used our existing ATAC-Seq, histone H3K27-acetylation Chip-Seq, and RNA-polymersase II ChIP-Seq data to identify enhancer regions in the CTFC loop surrounding the Aqp2 gene. The sequences within these enhancers were analyzed to identify recognized TF binding motifs within them; and these motifs were matched to TFs on the Bayesian list to identify the TFs most likely to bind Aqp2 regulatory regions.

Results: The analysis showed that the TFs most likely involved in regulation of Aqp2 gene expression are associated with six enhancer regions in the CTCF loop surrounding the Aqp2 gene. Of the six enhancers, of particular interest is a 517 bp region identified 5.0 kb upstream from the Aqp2 gene transcription start site (TSS) that is predicted to bind Tcf7l2 (Wnt signaling), response to oxidative stress (Nrf2 signaling), and Glis (Hedgehog signaling). Also within this enhancer region are high probability binding sites for TFs previously identified to regulate Aqp2 gene transcription, viz. Nfκb1/Nfκb2, Nkx1-1/Rela, and Ghrh2. Another enhancer is 5.8 kb downstream from the Aqp2 TSS and contains binding sites for three TFs already implied in Aqp2 transcriptional regulation, namely Celtah, Ap1-1 (Fos), and E12/E47, as well as sites for several TFs that are far from studied with respect to Aqp2 regulation.

Conclusions: The Bayesian analysis has defined the enhancer regions within the CTCF loop surrounding the Aqp2 gene and identified the TFs most likely to bind to these regions, providing a roadmap for future studies to understand regulation of Aqp2 gene expression.

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Kidney Osmoregulation Is Regulated by RNA Polymerase Pausing
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Background: Osmoregulation is a complex but critical component of renal physiology that relies on the regulation of gene expression. While many genes and some transcription factors that are involved in osmoregulation have been identified, the initiating regulatory step that triggers the gene expression response to changes in osmolarity remains unknown. To address this knowledge gap, we identified the pausing of RNA Pol II as a key regulatory step.

Methods: We used the Precision nuclear Run-On and Sequencing assay (PRO-seq), to identify locations of nascent RNA bound to actively transcribing RNA polymerases in inner medulla collecting duct cells (IMCD).

Results: We began by studying Akr1b3, the gene that encodes aldose reductase which is the enzyme that reduces glucose to sorbitol and is essential for osmoregulation in the kidney. We exposed IMCD cells to increasing concentrations of sodium chloride and determined that in hypertonic conditions Akr1b3 gene expression increased by approximately 1.7 fold greater, respectively, and high FSS, L-WNK1 abundance was 5.4 ± 0.3 and 10.6 ± 1.7 fold greater, respectively, to that measured in the absence of flow (p < 0.001). In static MDCK cells, BKct did not colocalize with L-WNK1 at the apical membrane; however, colocalization of the two proteins was detected in cells subject to low or high FSS.

Conclusions: In conclusion, (i) apical expression of L-WNK1 is in micropunctured CCDS is rapidly stimulated by increases in luminal flow rate, and (ii) FSS favors apical colocalization of L-WNK1 with BKct, responses that may facilitate BK channel-mediated FIKS in the CCD.

Funding: NIDDK Support

Flow Regulation of WNK1 in the Cortical Collecting Duct (CCD)
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Background: A high K diet (HKD) x 10 d increases (i) luminal flow rate in the distal nephron and (ii) expression of apical immunodetectable L-WNK1 in CCD intercalated cells (IC), which we propose enhances apical BK channel activity measured as flow-induced K+ secretion (FIKS) (Webb et al, 2015). We previously demonstrated that fluid shear stress (FSS) x 30 min induces expression of ERK and p-38, both BK channel modulators, in a CCD principal cell (PC) model (Carrizoza-Gaytan et al, 2014). The objective of this study was to test the hypothesis that an increase in tubular fluid flow rate rapidly induces apical localisation of L-WNK1 in the CCD.

Methods: CCDS isolated from NZW rabbits fed a HKD x 10 d were micropunctured at slow (t=4) or fast (t=4) luminal flow rates x 1 hr, fixed on the rig, immunoprocessed with antibodies (Abs) directed against L-WNK1 (1:450, fluorescein 2x Abs) and rhodamine-conjugated peanut lectin (PNA) or Dolichus biflorus lectin (DBA), which bind to apical surfaces of IC and PC, respectively, and examined by confocal microscopy. MDCK cells were subject to no (static), low or high FSS x 1 hr (n=3 each condition) and fixed for immunodetection of L-WNK1 and BKct in situ or harvested for semi quantitative immunoblotting of isolated plasma membranes.

Results: Expression of IC apical L-WNK1 relative to that in the total cell was 40.0±1.1 % greater in CCDS perfused at fast flow compared to those perfused at slow flow (t=4) (p<0.01). In plasma membrane preparations of MDCK cells subject to high and high FSS, L-WNK1 abundance was 5.4±0.3 and 10.6±1.7 fold greater, respectively, to that measured in the absence of flow (p<0.001). In static MDCK cells, BKct did not colocalize with L-WNK1 at the apical membrane; however, colocalization of the two proteins was detected in cells subject to low or high FSS.

Conclusions: In conclusion, (i) apical expression of L-WNK1 in ICs is micropunctured CCDS is rapidly stimulated by increases in luminal flow rate, and (ii) FSS favors apical colocalization of L-WNK1 with BKct, responses that may facilitate BK channel-mediated FIKS in the CCD.

Funding: NIDDK Support

Inhibition of Actin-Related Protein 2/3 Complex Blocks Vasopressin-Induced AQP2 Membrane Accumulation
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Background: Aquaporin 2 (AQP2) is a water channel protein located primarily on principal cells of the kidney collecting ducts and is crucial for regulating body water homeostasis. Regulation of AQP2 trafficking is subject to hormonal control, mainly via the canonical vasopressin (VP) signaling pathway which stimulates AQP2 membrane accumulation. Active actin cytoskeleton remodeling has been known to also play an important role in AQP2 trafficking, however, the mechanism is incompletely understood.

Methods: We applied CK-666, a pharmacological inhibitor of actin nucleator actin-related protein (Arp) 2/3 complex on our AQP2-transfected cells and animal (rat) models. Results were observed by using immunohistochemistry and confocal microscopy. VP signaling pathway and phosphorylation of AQP2 on various serine residues were studied with Western blotting.

Results: Using CK-666, an Arp2/3 complex inhibitor, we found that VP induced AQP2 membrane accumulation was inhibited both in rat kidneys and LLC-AQP2 cells in vitro. Instead of distributing throughout the cytoplasm, AQP2 in cells treated with CK-666 was concentrated in vesicles forming a perinuclear patch, which was also positive for Rab11 (a recycling endosome marker) and clathrin (a trans-Golgi Network (TGN) marker). Similar perinuclear AQP2 patches appear in cells incubated at 20°C (cold block), which allows endocytosis to continue, but prevents protein exit from the TGN. By rewarming the cells to 37°C, these perinuclear patches dissipate, and AQP2 quickly redistributes throughout the cytoplasm (cold block release). However, we found that in cells exposed to a 20°C cold block and treated with CK-666, AQP2 patches failed to dissipate upon rewarming, suggesting that CK-666 blocked the release of AQP2 from the TGN in the exocytotic pathway. This effect of CK-666 was independent of VP signaling and did not alter the VP-induced phosphorylation state of AQP2 at residues serine-256, serine-261, and serine-267.

Conclusions: Inhibition of the Arp2/3 complex blocks VP-induced AQP2 plasma membrane accumulation by blocking AQP2 exocytosis at the level of the TGN and the recycling endosome but did not affect VP signaling pathway. This result suggests that actin filament nucleation and growth via Arp2/3 activity is essential for AQP2 recycling and trafficking.
STCH Regulates NKCC2 Biogenesis by Both the Endoplasmic Reticulum-Associated Degradation and the Endoplasmic Reticulum-Lysosome-Associated Degradation Pathways

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Background: Mutations in the apically located Na-K-2Cl co-transporter NKCC2 lead to type I Bartter syndrome, a life-threatening kidney disease. We previously showed that export from the ER constitutes the limiting step in the maturation and cell surface expression of NKCC2. Yet very little is known about the molecular components of NKCC2 ER quality control. Using the yeast two hybrid system and co-immunoprecipitation assays, we identified chaperone stress 70 protein (STCH), as a binding partner of the immature form of NKCC2. STCH is supposed to function as an ER chaperone but the precise molecular role of STCH remains obscure.

Methods: Protein expression was monitored in transiently transfected HEK cells, using immunoblot and confocal imaging. Protein maturation and stability were assessed by Endo-H digestion and cycloheximide chase (CHX) assay. Western Blotting was used to identify the principal (PC) and intercalated (IC) cells of the medullary CD, respectively.

Results: Co-immunolocalization experiments revealed that NKCC2 interacts with STCH mainly at the ER. However, CHX assay together with Endo-H digestion revealed that STCH is initially synthesized in the ER as a core-glycosylated protein before being gradually converted to a hybrid N-glycosylated form. These data are in an agreement with a previous study showing that STCH contains a mannose-6-phosphorylation site, suggesting therefore that STCH expression is not restricted to the ER. STCH knock-down increased NKCC2 protein abundance in a dose-depend manner, whereas STCH knock-down over-expression had the opposite effect. CHX assay showed that in cells over-expressing STCH, NKCC2 stability and maturation are heavily impaired. STCH induced reduction in NKCC2 expression were offset partially by the proteasome inhibitor MG132. Interestingly, leupeptin and chloroquine, two potent inhibitors of the lysosome, mimicked MG132 effect on NKCC2 regulation. Accordingly, the simultaneous presence of proteasome and lysosome inhibitors, completely abolished STCH-induced down-regulation of NKCC2.

Conclusions: Our data demonstrate the presence of an STCH mediated ER quality control of NKCC2 in renal cells. They suggest a model whereby, in addition to the proteasome-dependent ERAD, the ER quality control of NKCC2 mediated by STCH, involves also the ER-to-lysosome-associated degradation pathway, revealing therefore a new regulatory mechanism governing the co-transporter biogenesis.

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Underline represents presenting author.

PO1404

Resolving the Kidney's Reaction to Acute Dehydration on the Single-Cell Level

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Background: Dehydration is a common clinical finding and frequent among the elderly or patients with chronic diarrhea. Acute kidney injury frequently develops as a result of a fluid deficit. There is growing evidence that recurrent dehydration can cause chronic kidney disease. The kidney's response to fluid deprivation is incompletely understood. Having a gene expression atlas of the kidney's reaction to fluid deprivation at single cell resolution might help to understand biological mechanisms but also to identify biomarkers and therapeutic targets.

Methods: We performed single-cell RNA sequencing of dissociated mouse kidneys after 24 hours of water restriction (n=2) and control kidney (n=2). We assigned cell type information based on known marker genes, and systematically analyzed gene expression differences between baseline and water-restricted animals within different cell types. We furthermore applied a computational approach to spatially sort cells based on gene expression similarities to investigate corticomedullary gene expression profiles.

Results: Our data show cell type-specific differential gene expression in all kidney tubules with the most prominent response in collecting duct principal cells (CD-PC). Pathways dysregulated in CD-PC included sodium and water reabsorption, immune system modulation and endoplasmic reticulum (ER) stress. Pathway activation displayed regional cortico-medullary differences.

Conclusions: Fluid deprivation induces regional and cell type-specific responses in kidney cells. Genes and pathways identified by single cell transcriptomics comprise biomarkers and therapeutic targets for dehydration-associated pathologies.
were evaluated in Wistar rats to monitor COX-2 and RAS, as well as kidney morphology, morphology, and bone histometry. Cultured macula densa (MD) cells were treated with Ca2+/angiotensin II (Ang II), p38 MAPK inhibitor or NF-kB inhibitor in various combinations to reveal molecular pathways mediating effects of RAS on COX-2.

**Results:** Inhibition of calcineurin in cultured MD cells using CaS or siRNA increased COX-2 expression. p38 MAPK inhibition of the 3 key UPR targets, NACCC2 and NACCC4, translocation of ABCG7 variant B, and completely normalized by simultaneous administration of a RAS inhibitor candesartan for 3 days or 3 weeks. In contrast, administration of a selective COX-2 inhibitor, celecoxib, largely recapitulated effects of CaS and significantly reduced the beneficial effects of celecoxib on the immunostaining pattern. Therefore, COX-2 suppression is a major factor contributing to CNI nephrotoxicity.

**Conclusions:** In summary, the present study established calcineurin as an endogenous COX-2 inhibitor, acting via suppression of p38 MAPK and NF-kB activity in MD cells. CNI-induced RAS activation critically reduces COX-2 activity, thus dispersing local stimulatory effects of calcineurin inhibition. Our data support the use of RAS inhibitors for alleviation of CNI nephrotoxicity.

**Funding:** Government Support - Non-U.S.

**PO1407**

A Novel Mouse Model for Familial Hypomagnesemia with Hypercalcuria and Nephrocalcinosis (FHNC) Bearing the Most Frequent Human CLDN16 Mutation

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**Background:** Mutations of claudin (CLDN) 16 and CLDN 19 cause FHNC, characterized by an urinary loss of calcium (Ca) and magnesium (Mg), hypomagnesemia, nephrocalcinosis and renal failure. Cldn16 and Cldn 19 are co-expressed at the tight junction (TJ) of the thick ascending limb (TAL) of Henle’s loop and play a key role in paracellular reabsorption of Ca and Mg. Here, 25% of filtered Ca and 70% of filtered Mg are reabsorbed. Cldn16 knock-out mouse failed to faithfully recapitulate the human disease, as it was complicated by neither nephrocalcinosis nor renal failure. Cldn 16 knock-down mice have a renal loss of NaCl and hyperaldosteronism. We hypothesized that a Cldn 16 knock-down line is the most frequent (p.L151F) would be helpful to delineate the abnormalities caused by mutated Cldn16.

**Methods:** Cldn 16+/16+ and Cldn 16+/L151F/L151F mice were generated by CRISPR Cas9-based mutagenesis. Cldn16 16 and Cldn 16+/L151F/L151F female mice were housed in metabolic cages at 3 months of age. Daily food and water intake, body weight were recorded. Blood and urine composition were analyzed. Nephrocalcinosis and Cldn expression in TAL were studied on kidney sections by alizarin red coloration and immunofluorescence.

**Results:** At 3 months, weight, food and water intake, blood parameters (Na, Cl, Ca, Mg, Pi, creatinine) did not differ between Cldn 16+/+ and Cldn 16+/L151F/L151F mice. Cldn 16+/L151F/L151F mice had significantly higher urinary excretions of Ca, Mg and Pi and a lower urinary pH; urine volume, osmolality, Na, K and aldosterone were unaltered. At 6 months calciuric was significantly increased in Cldn 16+/L151F/L151F mice. No nephrocalcinosis was seen at 12 months of age. Almost never seen at TJ and Cldn 16+/L151F/L151F seems to be expressed at TJ in Cldn16+/L151F/L151F mice suggesting that Cldn16+/L151F/L151F has a negative effect on Cldn19 expression.

**Conclusions:** Cldn16+/L151F/L151F mice have a urinary loss of Ca and Mg, as typically observed in human FHNC. No evidence of NaCl wasting was found. Further studies are ongoing on male mice, renal function and PTH, bone and dentall phenotypes. This model will help to better understand the link between an altered CLDN 16 and the observed in patients with FHHNC. No evidence of NaCl wasting was found. Further understanding this mechanism should lead to improved understanding of UA homeostasis and new insights into UA treatment.

**Funding:** NIDDK Support

**PO1409**

SPAK Signaling Stimulates the Activity and Protein Expression of Large Conductance Ca2+-Activated Potassium (BK) Channels

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**Background:** 20-20 loop proline alanine rich kinase (SPAK) plays important roles in regulating the function of numerous ion channels and transporters. With no-lysine (WNK) kinase phosphatases SPK kinase to active the SPK signaling pathway. Our previous studies have shown that WNK kinases induce the activity of the large-conductance Ca2+-activated K+ (BK) channel and its protein expression via the ERK1/2 signaling pathway. It remains largely unknown whether SPK kinase directly modulates the BK activity and protein expression in kidney.

**Methods:** Electrophysiology, cell culture, western blot, siRNA knockdown, and SPAK knock-out (KO) mice were used in the study.

**Results:** We first determined the effects of SPK gene deletion using SPAK KO mice on BK channel activity in the isolated, split-open renal collecting ducts (CD) from WT and SPAK KO mice. We found that there is no BK channel activity in principal cells (PCs) of cortical CD (CCD) in SPAK KO mice, whereas there is BK channel activity in PCs from WT mice. We further investigated the effects of overexpression and siRNA knockdown of SPK expression on BK in HEK293 cells. Overexpression of SPAK downregulated BK protein expression with a significant increase in phosphorylation of ERK1/2 phosphorylation, whereas knockdown of SPAK expression using siRNA significantly reduced BK protein expression associated with increased ERK1/2 phosphorylation, both in a dose-dependent manner. Knockdown of ERK1/2 prevented SPAK siRNA-mediated inhibition of BK protein expression. Similarly, pretreatment of HEK293 cells with either the lysosomal inhibitor bafilomycin A1 or proteasomal inhibitor MG132 reversed the inhibitory effects of SPAK knockdown on BK protein expression. In addition, we found that BK protein abundance in the renal cortex of SPAK KO mice was significantly decreased and ERK1/2 phosphorylation was significantly enhanced. BK protein abundance and SPAK phosphorylation levels in WT mice, while reducing ERK1/2 phosphorylation levels.

**Conclusions:** These findings suggest that SPAK stimulates BK channel activity and protein expression by reducing ERK1/2 signaling-mediated lysosomal and proteasomal degradations of the BK channel.

**Funding:** NIDDK Support, Veterans Affairs Support

**PO1410**

High Dietary K+ Attenuates Salt-Induced NCC and mTORC1 Activity in Dahl Salt-Sensitive Rats

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**Background:** Na+ reabsorption by renal Na+-Cl cotransporter (NCC) plays a key role in blood pressure (BP) regulation. Dahl Salt-Sensitive (DSS) rats exhibit aberrant NCC activity and salt-sensitive hypertension (HTN) when fed a high-salt diet. The renal mammalian target of rapamycin complex 1 (mTORC1) is also implicated in the pathogenesis of DSS HTN. Studies in normotensive mice suggested an inverse relationship between blood [K+] and NCC activity; however, the effect of dietary K+ on NCC activity in DSS rats is in still controversial. Moreover, the impact of dietary K+ on mTORC1 activity is unknown. Hypothesis: Dietary K+ supplement downregulates salt-induced NCC and mTORC1 activity in DSS rats.

**Methods:** 3 month old male DSS rats were randomly placed on high salt (4% NaCl, HS) or low salt (5% KCl, LS) for 3 months. High Salt (HS), n=3) or HS + high K+ (5% K(+), HS+HK, n=4) diet for 28 days. Another group of DSS rats, maintained on HS diet for 14 days, were placed on HS+HK for another 14 days (HS→HS+HK, n=4). NCC activity was assessed by Hydrochlorothiazide (HCTZ, NCC antagonist) injection (20 mg/kg, intraperitoneal) induced natriuretic response. Protein abundance was determined by western blotting. The ratio of phosphorylated ribosomal protein S6 to total S6, was used as mTORC1 activity marker.

**Results:** In response to HCTZ, urinary Na+ excretion was trending lower in HS+HK compared to HS+HK, n=4). NCC activity was assessed by Hydrochlorothiazide (HCTZ, NCC antagonist) injection (20 mg/kg, intraperitoneal) induced natriuretic response. Protein abundance was determined by western blotting. The ratio of phosphorylated ribosomal protein S6 to total S6, was used as mTORC1 activity marker.

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were trending lower in HS→HS+HK compared with HS group. Interestingly, mTORC1 activity was significantly reduced in HS→HS+HK.

Conclusions: Trending lower response in HS+HK and HS→HS+HK to HCTZ suggests that dietary K+ may counteract and reduce salt-induced NCC activation. Downregulation of mTORC1 reveals that dietary K+ can reverse salt-induced mTORC1 activation. Critical, our data suggest that compared with the initial phase, K+ is more effective in reducing salt-induced NCC and mTORC1 activity when added later to the diet, which may attenuate established HTN in DSS rats.

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POI1411

Four Weeks of Dietary Potassium Restriction Causes Distal Convoluted Tubule Remodeling

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Background: Previous studies have described a 'renal potassium switch' within the distal nephron that turns on the thiazide-sensitive NaCl cotransporter (NCC) in the distal convoluted tubule (DCT), in response to low potassium intake and offset response to high potassium intake. Studies using genetically modified mice indicate that decreased NCC activity is associated with decreased DCT length and mass; increased NCC activity is associated with increased, DCT length and mass. The aim of our study was to test whether dietary potassium intake causes the DCT remodeling physiologically.

Methods: Male C57Bl/6 mice were provided either control potassium diet or low potassium diet for four weeks and blood and kidneys were harvested. To determine the length of the DCT in three dimensions, we used Ethyl-cinnamate-based optical clearing, combined with whole-mount immunolabeling, confocal microscopy and three-dimensional morphometric analysis.

Results: Mice on low potassium diet for four weeks were severely hypokalemic (plasma potassium <2 mEq/L) compared with mice on control diet (4.2 mEq/L). Western blot analysis of the whole kidney confirmed that total and phosphorylated NCC were higher in mice on low potassium diet, compared to mice on control diet. By immunolabeling with pThr53-NCC antibody, we visualized the DCTs in optically cleared kidney slices. Three-dimensional morphometric analysis suggested that four-weeks of low potassium diet (44.8±4.6 mEq/L) increased DCT length by 13% compared to NK diet (412.9±46 mm, n=6).

Conclusions: Our results indicate that the DCT remodels physiologically to maintain potassium homeostasis. Additional animals are currently being studied.

Funding: NIDDK Support

POI1412

Pendrin Null Mice Develop Hypokalemia During Dietary Na+ Restriction Through an Epithelial Sodium Channel-Dependent Mechanism

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Background: Pendrin is an electroneutral Cl-HCO3 exchanger expressed in the apical regions of intercalated cells. It is thought to modulate NaCl absorption, while mitigating urinary K+ loss. However, the effect of pendrin gene ablation on K+ homeostasis has not been examined directly. The purpose of this study was to determine if pendrin gene ablation reduces serum K+ concentration, the conditions under which this occurs and the mechanism(s) responsible.

Methods: Pendrin null and wild type mice were given a diet deficient in Na+, K+, and Cl+ or diet supplemented with Na+, K+, Cl+ and/or water. We measured urine and serum electrolytes as well as K+ channel and Cl+ transporter abundance by immunoblot and immunohistochemistry.

Results: Serum K+ was ~1 mEq lower in pendrin null than in wild type mice after 7 days of the Na+, K+, Cl+ diet-deficient diet. This difference was attenuated, but not eliminated, with moderate dietary K+ supplementation. Differences were eliminated with either dietary K+ supplementation or with ENaC blockade, while differences were enhanced when ENaC was constitutively upregulated. Further studies determined whether the lower serum K+ observed in the pendrin null mice occurs from greater urinary K+ excretion. Over the first 3 days of the Na+, K+ diet-deficient diet, pendrin null mice develop a lower serum K+ and a higher arterial pH and HCO3- concentration, likely from greater intravascular volume contraction from their enhanced urinary Na+ excretion, although urinary K+ excretion was similar in both groups over this time period. However, starting at day 4 of the diet, the pendrin null mice excrete more K+ than the wild type mice. At day 8 of the ion-deficient diet, pendrin null mice have marked hypokalemia, likely due to both the metabolic alkalosis as well as greater urinary K+ excretion, in part, from inappropriately high Maxi-K+ channel abundance.

Conclusions: Pendrin null mice develop marked hypokalemia during dietary Na+ restriction in part due to a contraction alkalosis as well as increased urinary K+ excretion that occurs in part from relatively high Maxi-K channel abundance.

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POI1413

Architecture of the Distal Neprhon Mineralocorticoid Receptor-Dependent Transcriptome Defined

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Background: The mineralocorticoid receptor (MR, Nr3c2) is responsible for aldosterone-regulation of Na+ and K+ balance and blood pressure. Although a handful of aldosterone/MR-dependent genes have been identified, their regulation cannot fully explain how aldosterone activates electronic Na+-K+ exchange in the aldosterone sensitive distal nephron (ASDN). Here, we apply RNA-Seq and bioinformatic approaches in isolated tubule segments of MR KO vs. Control mice to define a more complete inventory of MR-regulated genes.

Methods: MRKO/Pax8−/−LCLC mice were used as a doxycyline (DOX)-inducible Nr3c2 gene KO model. After DOX treatment, four groups were prepared to distinguish between MR effects on mice on normal K+ diet (CT-NK) or high K+ diet (CT-HK) and MR knockout mice on normal K+ diet (KO-NK) or 4) low K+ diet (KO-LK). RNA-seq analysis was carried out in the micro-dissected connecting tubule and cortical collecting duct tube segments (5-6 mice per group and ~10 fresh ASDN tubules per mouse). Differential expression (DE) genes were identified (FDR <0.05) and used for further bioinformatic analyses.

Results: 927 and 2010 DE genes were identified from comparisons of MR-KO NK vs. CT-NK and MR KO-LK vs. CT-HK, respectively. Diet effects were not detected. Absence of transcripts on the third exon of Nr3c2 gene confirmed complete disruption of Nr3c2 gene in the MR KO. All known aldosterone-response genes, including Sgk1, Scnn1a, Ndk2, Per3, Tsc2d3, Zbtb16, Mphk and Apol1 were significantly decreased in MR KO-LK compared to CT-HK. In addition, 5 DE genes (Sgk1, Scln1a, Ndk2, Fxyd4 and Fxnl) were selected as the most promising "Aldosterone-regulated sodium reabsorption" profile. However, genome-wide identification of GR and MR binding sites revealed that 526 of the significantly down-regulated genes in MR KO mice are potential MR-regulated genes. Pathway enrichment analysis of 2010 DE genes showed that DE genes were highly enriched in mitochondria-associated metabolic processes.

Conclusions: The inventory of MR-regulated genes in the ASDN is much larger than previously imagined. In addition to pathways that directly up-regulate epithelial sodium channel (ENaC) and the Na+–K+ ATPase, the data suggest that aldosterone-MR may directly influence metabolism to make energy-consuming transport highly efficient.

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POI1414

Effect of Patiromer and Sodium Zirconium Cyclosilicate on Blood Pressure in a Rat CKD Model Induced by 5/6th Nephrectomy

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Background: Patiomer (PAT) is a sodium-free, non-absorbed polymer drug approved for treatment of hyperkalemia (HK) in adults. In clinical studies of patients with CKD and HK, decreases in BP were observed during PAT treatment. The objective of this study was to evaluate effect of PAT and another K+ binder, sodium zirconium cyclosilicate (SZC), on BP in a CKD rat model.

Methods: 36 Sprague Dawley (SD) rats underwent 5/6th nephrectomy (Nx) and each had a telemetry device implanted. Animals were randomized into 3 groups of 12, PAT (4 g/kg), SZC (4 g/kg), or vehicle was administered daily via oral gavage for 8 wks. Blood pressure (BP) was measured by telemetry once weekly with a wireless telemetry (BL) line. Blood and urine samples were collected weekly. All values are mean ± SD.

Results: Systolic BP from BL to WK 8 increased in vehicle-treated rats (136 ± 4.0 mmHg to 154 ± 4.8 mmHg), PAT-treated rats (132 ± 3.7 mmHg to 140 ± 3.6 mmHg), and SZC-treated rats (133 ± 4.1 mmHg to 158 ± 5.3 mmHg). PAT-treated rats had significantly lower systolic BP at WK 8 compared to rats in vehicle and SZC-treated groups (P<0.001) (Figure). Mean BP change from BL in PAT-treated rats (8 ± 3.2 mmHg) was significantly lower vs vehicle group (16 ± 2.9 mmHg, P=0.001) and vs SZC-treated group (23 ± 4.2 mmHg, P<0.001). PAT, while mean BP change from BL in SZC-treated rats was significantly higher vs vehicle group (P<0.005). Serum K+ levels were in range of normokalemia (4.0-6.2 mEq/L in normal SD rats) from BL to WK 8 in all groups (5.6 ± 0.26 mEq/L to 5.5 ± 0.22 mEq/L in vehicle-treated rats, 5.6 ± 0.43 mEq/L to 5.3 ± 0.25 mEq/L in PAT-treated rats, and 5.3 ± 0.24 mEq/L to 4.9 ± 0.35 mEq/L in SZC-treated rats). There was no difference in serum creatinine levels among the 3 groups during the study.

Conclusions: With 8 wks of PAT treatment, SD rats with 5/6 Nx exhibited significantly lower BP compared to vehicle-treated and SZC-treated rats. Additional analyses are warranted to determine mechanisms of PAT’s effect on BP in this model of CKD.

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transiently transfected these cDNA constructs in NHERF1-deficient opossum kidney cells, associated membrane expression by confocal microscopy; and Npt2a function by ([32P]phosphate uptake.

Results: Npt2a (T635), Npt2a (E635), or Npt2a (A635) alone showed dose-dependent expression and negligible ([32P]uptake. Npt2a (T635) with NHERF1 colocalized at the plasma membrane and increased ([32P]uptake seven-fold. Npt2a (E635) and Npt2a (A635) appeared at the plasma membrane, but neither co-localized with NHERF1 nor showed ([32P]uptake. Each Npt2a plus14-3-3 cDNA construct exhibited apparent membrane localization, but none co-localized with 14-3-3 epsilon or exhibited significant ([32P]uptake. 


discussion: We conclude that 14-3-3 is not an inhibitor of the Class I PDZ binding motif of Npt2a. 14-3-3 promotes Npt2a membrane localization but not function in NHERF1 deficient states and may not be dependent on the phosphorylation status of the -2 Thr.

Funding: Veterans Affairs Support

POI147

Metabolic Acidosis Exacerbates Pyelonephritis in Mice Prone to Vesicoureteral Reflux

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Background: Acute pyelonephritis is a serious bacterial infection in children. The prevalence of acute pyelonephritis is due in large part to uropathogenic E. coli (UPEC). Although an association between pyelonephritis and abnormalities in acid-base balance is common in young children, the impact of metabolic acidosis (MA) on progression of acute pyelonephritis is not fully understood. In the current study the effect of metabolic acidosis was investigated in a piglet model of pyelonephritis.

Methods: MA was induced in fetal mice by feeding mice NaCl (2% w/w) supplementation of food. Acid-base status was assessed by blood gas analysis using an iStat® G4 and urine pH. U-TEST, Urinary Tract Infection of mice (6-8 wks) with Uropathogenic E. coli (UPEC strain CT70) 0.5 X10^7 cfu/50 μl was performed via the transurethral injection. Kidney injury was assessed in bladders and kidneys was determined by culture of tissue homogenates. Collecting duct (CD) fragments and neutrophils were enriched from collagenase-digested kidney by magnetic-sorting utilizing DBA-lectin and monoclonal antibody Ly6G (1A8). Cytochrome (IL-1β, TNFα, IL-6) and chemokine (CXC1L, CXC2L, CXC51) in CD cells was quantitated by qRT-PCR. Ly6G cells were enumerated by imaging utilizing a Cellometer K2 Image Cytometer. Statistics: T-test or two-tailed Mann-Whitney U-Test p<0.05 or P = 0.02 for Bonferroni correction.

Results: NH4Cl fed-mice were acidic ([HCO3-]; 17±0.6*, Ur pH: 5.8±0.02*) compared to normal ([HCO3-]; 22±0.6; Ur pH: 6.0±0.1, N4±0.0*). MA concurrent with UPEC-UTI markedly increased kidney UPEC burden in innate immune competent HeN mice (HeN = 4E2±2E6 versus MA HeN= 1E6±1E6; p<0.02 MW U-TEST), but not Tle4-deficient HeJ mice (HeJ= 2E6±1E6 versus MA HeJ= 5E5±1E5). MA markedly increased CD4+ Th1 and Th2 cytokines in infected HeN mice characterized by a 18-24 fold increase in chemokine/cytokine mRNA abundance and a 4.5±0.6 fold increase in Ly6G+ neutrophil infiltrates over normal-infected mice, N3= 3; p<0.01 versus normal, TTEST.

Conclusions: Concurrent metabolic acidosis exacerbates pyelonephritis in innate immune competent mice that is characterized by an elevated cytokine and chemokine expression and kidney neutrophil infiltrates.

POI148

Oxidized Alkyl Phospholipids Stimulate Proximal Tubule Sodium Transport via PPARY/ERK Pathway

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Background: We previously reported thiolaalkinediones stimulated proximal tubule (PT) sodium transport via non-genomic PPARY/ERK pathway. However, the contribution of endogenous PPARY ligands to PT transport has been unknown. In this study, we investigated effects of 1-O-hexadecyl-2-azelaoyl-phosphatidylcholine (azPC), an endogenous lipid oxidation product (LOP) acting as a potent PPARY agonist, on PT sodium transport.

Methods: We measured basolateral Na+/HCO3- cotransporter 1 (NBCe1) activity in lumen-collapsed PTs and luminal Na+/H+ exchanger (NHE) activity in freshly-isolated rat and human PTs obtained during surgery for renal cell carcinoma by using a pH-sensitive dye BCECF. NBCe1 activity in lumen-collapsed PTs was measured by the rate of pH decrease in response to HCO3- reduction. Luminal NHE activity in lumen-opened PTs was measured by the rate of pH decrease caused by Na+ removal in the presence of VATPase inhibitor, E0555. To examine the signaling pathway of azPC, we used a PPARY antagonist (GW9662) and a MEK inhibitor (PD98059) and siRNA against PPARY. The expression of PPARY mRNA was determined by quantitative PCR. ERK phosphorylation was analyzed by western blotting.

Results: In freshly-isolated human and rat PTs, 0.3 μM azPC stimulated NBCe1 activity and NHE activity. The stimulating effects were completely suppressed by GW9662 or PD98059 without affecting the basal activities. siRNA against PPARY completely suppressed the stimulation of both NBCe1 and NHE activities by azPC in rat PTs. We
found that azPC enhanced ERK phosphorylation in human and rat renal cortex tissue. This observation was also completely suppressed by GW9662 or PD98059.

**Conclusions:** These results indicated azPC stimulated both NBCe1 and NHE activities through PPARγ/ERK pathway in PTs. The stimulatory effect of azPC, one of the LOPS on PT sodium reabsorption, could be a novel mechanism of volume expansion and hypertension induced by atherosclerosis.

**POI419**

**A Novel Distal Convoluted Tubule-Specific Tamoxifen-Inducible Cre-Recombinase Driven by the NaCl Cotransporter Gene**

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**Background:** The use of knockout and transgenic mouse models coupled with Cre-lox technologies has revolutionized research in kidney transport physiology by allowing site-specific genetic recombination in individual nephron segments. Although several groups have tried to generate a distal convoluted tubule (DCT)-specific mouse, Cre-recombinase driven by the thiazide-sensitive NaCl cotransporter (NCC) promoter, this goal has remained elusive. The only previously recognized mouse model available allowed targeted gene modification in the DCT is the DCT-specific mouse with Cre-recombinase under control of the PASH gene encoding parvalbumin. The model, however, has limitations including activity in neurons that prevent comprehensive characterization of transport pathways in the DCT.

**Methods:** CRISPR/Cas9 was used to introduce Cre-ERT2 into the 3′ UTR near the stop codon of the Slc12a3 gene encoding NCC (Slc12a3-Cre-ERT2 mice). Here, we crossed Slc12a3-Cre-ERT2 mice with VFP floxed mice to test whether the Cre expression would mimic that of NCC, and to determine whether the construct is ‘leaky’.

**Results:** Without tamoxifen, approximately 6% of NCC positive cells expressed VFP, indicating minimal leakage. After five days of tamoxifen injection, mice showed 85% VFP expression in almost all NCC positive cells and there was complete overlap of VFP expression in NCC positive cells. Crossing to TdTomato mice revealed higher leakage (64.5%), suggesting differential sensitivity of the floxed site. Western blotting revealed no differences in abundances of total or the active-phosphorylated form of NCC in Slc12a3-Cre-ERT2 mice of either sex compared to controls. Furthermore, functional analysis of NCC showed no effects on NCC activity in Slc12a3-Cre-ERT2 mice. Plasma K⁺ and Mg²⁺ concentrations, and thiazide-sensitive Na⁺ and K⁺ excretion did not differ in Slc12a3-Cre-ERT2 mice compared to controls.

**Conclusions:** Thus, the Slc12a3-Cre-ERT2 mice have high recombination efficiency and complete fidelity in cell-specificity. Our data show that Cre expression is entirely localized to the DCT and the genetic modification has no effect on NCC expression and renal function. The Slc12a3-Cre-ERT2 mice are the first mice generated with Cre recombinase activity along the entire DCT, and will be a powerful tool to study DCT function.

**Funding:** NIDDK Support, Veterans Affairs Support, Private Foundation Support

**POI428**

**A Case of Central Diabetes Insipidus due to Pituitary Adenoma Complicated by Amphotericin-Induced Nephrogenic Diabetes Insipidus**

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**Introduction:** Amphotericin B (Amph B) is an anti-fungal agent that exhibits its action by binding to ergosterol, the main component of the fungal cell membrane. Its main site of action is the principal cell where it causes an increase in membrane permeability by insertion of pores into the membrane, causing leakage of potassium into tubular lumen leading to hypokalemia. It also causes nephrogenic diabetes insipidus (NDI) by preventing insertion of vasopressin-induced aquaporin 2 (AQP-2). Reports in the literature have suggested that liposomal formulations might be less nephrotoxic than conventional ones.

**Case Description:** A 37-year-old male with history of pituitary adenoma s/p trans-sphenoidal resection of pituitary tumor with subsequent central diabetes insipidus (CDI) on maintenance desmopressin DDAVP (1mcg BID) presented to hospital for suspected meningitis. He was started on liposomal Amph B Smg/kg (550mg) for empiric fungal coverage. Lumbar drain cultures returned positive for Candida albicans on Hospital Day (HD) 1 and Amph B was continued. Renal was consulted for evaluation of worsening polyuria. Increased dose of DDAVP was recommended. He continued to be polyuric despite dosing dose adjustment. Amph B induced NDI was suspected secondary to refractory polyuria and hypokalemia. Amph B was discontinued on HD 7, after which his polyuria improved gradually. He was switched to fluconazole to complete the remainder of the treatment duration.

**Discussion:** Our patient with h/o CDI developed worsening polyuria on Amph B treatment, unresponsive to escalating DDAVP. Improvement with cessation of Amph B supports causality of concurrent drug-induced NDI. Amph B renal toxicity frequently presents with AKI with potassium wasting. NDI induced by Amph B is rare. A high index of suspicion is required for diagnosis of NDI occurring on top of CDI. Early discontinuation of Amph B usually leads to resolution of symptoms.

**POI429**

**Water Load Test in the Diagnosis of Syndrome of Inappropriate Antidiuresis (SIAD): Results from the Waterline Study**

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**Background:** SIAD is caused by an inadequate kidney reabsorption of water, mainly under the action of antidiuretic hormone. The latest international recommendations stated the diagnosis of SIAD relies on hypotonic hyponatraemia with inadequate urine osmolality. Blood volume has to be normal, with adrenal, thyroid, and renal insufficiency excluded. These guidelines ruled out the usefulness of abnormal response to water load test (WLT) due to the lack of published evidence.

**Methods:** In the Waterline study (NC704256499), we retrospectively analyzed data from patients who underwent a WLT (oral administration of 20 mL/kg of water) in our department.

**Results:** From 02/2001 to 10/2019, 173 adults were included. Out of them, 80 (46%) had a SIAD and 21 (12%) were considered ‘normal’, 72 (42%) had hyponatraemia of other origin. Among the SIAD patients, 33 (41%) had a fasting plasma sodium (PNa) Æ±15 mEq/l (‘nephronic SIAD’), 47 (59%) had ‘hyponatric SIAD’: We found no differences in demographic data or medical history between these two groups. During WLT, ‘nephronatic SIAD’ patients behaved specifically by exerting hyponatraemia (while normal individuals did not), resembling ‘hyponatric SIAD’ patients (Figure 1). While their fasting urine osmolality (U-Osm) was initially higher, ‘nephronatic SIAD’ and ‘hyponatric SIAD’ patients reached the same minimum U-Osm (389±257 vs. 350±202mOsm/kgH₂O, p=0.76). Additionally, they reached a higher minimum value of PNa than ‘hyponatric SIAD’ patients (132±2 vs. 127±3mM, p=0.0001). These results were confirmed in an independent cohort of 38 WLT where 24 (63%) were ‘nephronatic SIAD’.

**Conclusions:** We conclude that, without WLT, a diagnosis of SIAD could be missed in 40 to 65% of SIAD patients.
Methods: We performed a post-hoc analysis of original data from the Edelman study. In a linear regression model, the effects of important clinical characteristics on the relation between (Na+ - K+)/TBW and serum [Na+] were examined: sex, body weight and presence of edema. Using piecewise regression, we analyzed differences in slope and y-intercept for increasing values of (Na+ - K+)/TBW. Serum [Na+] was calculated by multiplying serum water [Na+] by 0.93.

Results: Data was available for 85 measurements in 82 patients; 57 males, 25 females, with a mean age of 57±15 years. Serum [Na+] ranged from 103 to 150 mmol/L. The association between serum [Na+] and (Na+ - K+)/TBW was different for high and low weight subgroups. Sex and presence of edema do not alter the association. In piecewise regression, a significant change in slope was found in 149 mmol/L (Na+ - K+)/TBW (figure, 1.12 vs 0.56, p = 0.01).

Conclusions: The coefficients of the Edelman equation are significantly affected by weight, sex and body water content. The less steep-sloped line for the higher (Na+ - K+)/TBW and high weight groups may reflect an increase in osmotically inactive Na+ storage. This may explain the inaccuracy of Edelman based formulas in daily clinical practice.

PO1431

Hyponatremia: It’s in the Eye of the Beholder
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Introduction: An 85 year old Asian American female presented with 2 days history of worsening right eye pain, headache, scalp tenderness, and hypotensive urgency. Medical history was notable for keratoconjunctivitis sicca, osteoarthritis, and central retinal occlusion of the left eye. Initial labs showed erythrocyte sedimentation rate of 75 mm/hr, and C reactive protein of 3 mg/dL. A presumptive diagnosis of Giant Cell Arteritis (GCA) was made. She was started on high dose oral prednisone. Hypertension was treated with labetalol, amiodipine, and pain with opioids. Over the course of the next 36 hours she began to have somnolence. Initial sodium (Na) on admission was 131 mmol/L, with prior normonatremia. She was given a normal saline bolus followed by infusion due to concern for hypovolemia and reduced oral intake. This resulted in a consistent drop in her serum sodium acutely to 116 mmol/L and a nephrology consultation was sought.

Case Description: Our evaluation showed euvolemia with confusion and obtundation. Labs showed serum osmolality of 252 mOsm/kg, urine osmolality of 626 mOsm/kg and Urine Na consistently around 90-129 mEq/L. A diagnosis of SIADH with desalination was made. She was treated with free water restriction, 3% saline, salt tablets, and furosemide. Na improved to 120 mmol/L however it dropped again next day to 117 mmol/L requiring repeated doses of 3% Saline. Daily urine osmolality continued to decrease to 500s osm/kg and later to 360 mOsm/kg as did urinary sodium 48 hours after these interventions. Peri-ocular swelling and a herpes zoster rash appeared on her eye 48 hours later. PCR for herpes was positive.

Discussion: Acyclovir was started and corticosteroids stopped. Over 8 days the hyponatremia resolved with Herpes Zoster Ophthalmicus (HZO) treatment. HZO is a rare cause of SIADH thought to be due to dysregulation of stimulating signals from nucleus tractus solitarius to the supraoptic and paraventricular nuclei in the brainstem. In our case pain and opioids may have also been factors. Desalination needs to be considered cause of SIADH thought to be due to dysregulation of stimulating signals from nucleus.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1434

Should Sodium Monitoring Be Included in Routine Prenatal Care?
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Introduction: The American College of Obstetricians and Gynecologists does not recommend serum chemistries as part of routine prenatal care. Our case demonstrates the clinical utility in diagnosing hyponatremia prior to symptom development in mother or newborn.

Case Description: A 39-year-old pregnant female with no known prenatal issues underwent a spontaneous vaginal delivery; the infant was initially apneic and had a witnessed seizure. Her initial serum sodium was 120 mEq/L, and he was treated with phenobarbital and hypertonic saline. Serum sodium corrected by 4 mEq/L, during the first 7 hours, and increased from 120 to 133 mEq/L over the first 24 hours. Brain MRI performed on day 4 demonstrated no abnormal findings. The mother’s baseline sodium level was unavailable. She received 1 L of D5LR and 1 L of LR during labor. She had urinary retention following delivery and a Foley catheter was immediately drained 2 L of urine. Her initial postpartum serum sodium level was 123 mEq/L, without associated symptoms. Urine osmolality was 64 mOsm/kg on admission. History revealed typical daily fluid consumption of 6 L. Two days prior to admission, she abruptly increased fluid intake to 13 L per day in response to contractions. Twelve hours into admission, serum sodium corrected from 123 to 134 mEq/L in the setting of a relative reduction in fluid intake to 5 L.

Due to concern for a chronic component of hyponatremia, free water and DDAVP were given to slow the rate of correction. With the effect of DDAVP, urine concentrated to 695 mOsm/kg, illustrating the regeneration of an osmotic gradient within 30 hours. The patient was admitted and placed on a 1.5 L fluid restriction. By the next morning, she was back to baseline levels and remained normonatremic for the remainder of her admission. Blood pressure and urine output remained well within normal limits. The patient was discharged home on sodium 132 mEq/L.

PO1435

Hyponatremia: A Real Headache
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Introduction: Pituitary apoplexy is a condition characterized by pituitary gland injury via either infection or hemorrhage. This can result in endocrinological dyscrasias. We describe a case of SIADH secondary to pituitary apoplexy.

Case Description: A 64-year-old woman with a past medical history of atrial fibrillation on rivaroxaban presented to the hospital with nausea, vomiting, and new onset headache for 1 week. She received 1 L of saline in the emergency room and her nausea resolved. Basic chemistry was significant for a serum sodium of 124 mEq/L. A physical exam including neurological assessment was unremarkable as was a CT scan of the head. The patient was admitted and placed on a 1.5 L fluid restriction. By the next morning, she had a serum sodium of 112 mEq/L, serum osmolality as 238 mOsm/kg, urine osmolality at 434 mOsm/kg, urine sodium at 143 mmol/L, and urine potassium at 45 mmol/L. The patient was immediately transferred to the ICU and nephrology was consulted for severe hyponatremia due to SIADH. Given the acute drop from 124 mEq/L to 112 mEq/L over a 24-hour period, the patient was aggressively treated with hypertonic saline boluses as well as continuous infusion. Fluid restriction was tightened to 500 ml daily. SIADH was initially thought to be due to hypovolemia and vomiting, however, the differential was revisited when the severe hyponatremia persisted despite resolution of her nausea and hypovolemia. Given the new onset headache in an older adult, a MRI of the brain was obtained which revealed a convexity in the sella that was identified as a 1 cm pituitary hemorrhage. Rivaroxaban was discontinued. Further evaluation of pituitary hormones were all within normal limits. The hyponatremia corrected over 3 days and the patient was discharged home with a sodium of 132 mEq/L.

Discussion: SIADH is a rare finding in pituitary apoplexy that can be seen transiently 3-11 days after a pituitary surgery or injury. The mechanism is not known but is suspected to be due to the release of intracellular ADH stores from injured posterior pituitary cells.

PO1436

Dysnatremias and Mortality in CKD: Analysis of the Chronic Renal Insufficiency Cohort (CRIC) Study
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Background: Dysnatremias have been associated with increased mortality in patients with chronic kidney disease (CKD). We studied the association of dysnatremias with mortality and end-stage kidney disease (ESKD) in patients with CKD.

Methods: We included 5,444 patients from the Chronic Renal Insufficiency Cohort (CRIC) over a median time of 8.8 years. We analyzed baseline and time-dependent hyponatremia (<136 mEq/L) and hypernatremia (>145 mEq/L) with all-cause mortality and risk of ESKD using Cox proportional hazard models and competing risks models.

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PO1437

The Prognostic Importance of Serum Sodium Levels at Hospital Discharge and 1-Year Mortality Among Hospitalized Patients
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Background: The optimal range of serum sodium at hospital discharge is unclear. Our objective was to assess the one-year mortality based on discharge serum sodium in hospitalized patients.

Methods: We analyzed a cohort of hospitalized adult patients between 2011 and 2013 who survived hospital admission at a tertiary referral hospital. We categorized discharge serum sodium into five groups: ≤132, 133-137, 138-142, 143-147, and ≥148 mEq/L. We assessed one-year mortality risk after hospital discharge based on discharge serum sodium, using discharge sodium of 138-142 mEq/L as the reference group.

Results: Of 55,901 eligible patients, 4.9%, 29.8%, 56.1%, 8.9%, 0.3% had serum sodium of ≤132, 133-137, 138-142, 143-147, and ≥148 mEq/L, respectively. We observed a U-shaped association between discharge serum sodium and one-year mortality, with nadir mortality in discharge serum sodium of 138-142 mEq/L. When adjusting for potential confounders, including admission serum sodium, one-year mortality was significantly higher in both discharge serum sodium ≤137 and ≥143 mEq/L, compared...
POI1438
Peripheral Administration of 3% Sodium Chloride Is Not Associated with Local Infusion Reactions
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Background: Three-percent sodium chloride (3% NaCl) is a hyperosmolar agent indicated for the treatment of hypotonic encephalopathy or to raise the serum osmolality in other cases of increased intracranial pressure. A barrier to the use of 3% NaCl is the perceived risk of a local infusion reactions when administered through a peripheral vein (Front Med. 2019 Mar 15;6:47), even though it has not been reported in large case series of 3% NaCl (AJKD. 2015 Mar;65(3):435-42). We sought to evaluate reports of local infusion reactions associated with 3% NaCl over a 10-year-period throughout a large healthcare system.

Methods: A query was conducted through Risk Master database to determine if there were any local infusion reactions associated with peripheral 3% NaCl administration throughout the entire UPMC health system over a 10-year time period from May 14, 2010 to May 14, 2020. Search terms included infiltrations, extravasations, phlebitis, IV site issues and IV solutions.

Results: In over 1.1 million events (figure), there were 23,714 intravenous events which were non-chemotherapeutic or non-contrast of which 4,648 (19.7%) were in children. 617 (2.59%) of these events were deemed serious by a patient safety officer. There were no reported local infusion reactions with 3% NaCl.

Conclusions: There were no reported local infusion reactions associated with 3% NaCl in a large healthcare system despite widespread use of 3% NaCl and numerous intravenous events reported. This suggests that 3% NaCl can be safely administered through a peripheral IV.

POI1439
Hyponatremia: Mind the (Osmolar) Gap
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Introduction: Hyponatremia, one of the most commonly encountered electrolyte abnormalities, is associated with considerable mortality and morbidity. It is important to rule out pseudohyponatremia by determining serum tonicity.

Case Description: 65-year-old female with history of hypertension presented with worsening painless jaundice. Initial investigation was notable for an obstructive liver injury; total bilirubin of 28.4 mg/dL (direct 19.5 mg/dL and indirect 8.9 mg/dL), ALP 1225 U/L, AST 237 U/L, ALT 384 U/L and GGT 2274 U/L. She was also found to have a sodium of 126 mmol/L and potassium of 2.5 mmol/L. With fluids and potassium repletion, her sodium plateaued at 131 mmol/L. Further investigation revealed a measured serum osmolality of 301 mOsm/kg with an osmolar gap of 33 mOsm/kg, and a urine osmolality of 589 mOsm/kg. Sodium analysis using ion-selective electrode (ISE) showed a correction in the sodium from 131 mmol/L to 139 mmol/L on the same specimen, confirming the diagnosis of pseudohyponatremia. Lipid panel showed severe hypercholesterolemia (total cholesterol 1016 mg/dL, LDL 868 mg/dL, HDL 31 mg/dL and triglycerides at 604 mg/dL). Patient underwent endoscopic retrograde cholangiopancreatography and biliary sphincterotomy with biopsy consistent with adenocarcinoma of the pancreas. Following sphincterotomy, lipid panel and serum sodium normalized without further intervention.

Discussion: Serum sodium is elevated in cholestasis because its metabolic degradation and excretion are impaired. Much of the cholesterol is in the form of lipoprotein-X, an abnormal lipoprotein observed only in patients with cholestasis. Standard methods of sodium analysis, indirect ISE, calculates electrolyte concentration on the assumption that the non-aqueous portion of serum, predominantly proteins and lipids, comprises approximately 7% of a patient’s plasma volume. In our patient with significant hyperlipidemia, this led to falsely low indirect ISE values. Direct potentiometric measurements use undiluted samples and are not subjected to this artifact, a method also used in blood gas analysis. This case demonstrates a rare presentation of pseudohyponatremia and highlights the importance of its consideration in cases where the serum osmolality is normal or when an osmolar gap is present suggesting reduced plasma water content or the presence of ineffective osmoles.

POI1440
Development of Hyponatremia and Overcorrection in a Patient with COVID-19 and Vasopressin Exposure
Meghana Essawarang, Niralee Patel, Samira S. Farouk, Icahn School of Medicine at Mount Sinai, New York, NY.

Introduction: Hyponatremia in the setting of elevated antidiuretic hormone (ADH) is a common phenomenon. However, exogenous ADH from vasopressin administration for hemodynamic support does not cause clinically relevant hyponatremia, despite its widespread use. Further, discontinuing vasopressin may lead to rapid rises in sodium that may be missed. Here, we present a case of a critically ill patient who developed hyponatremia in the setting of vasopressin use, with subsequent rapid overcorrection that required re-lowering of serum sodium after discontinuing vasopressin.

Case Description: A 40-year-old male with no known history was admitted to the ICU for respiratory failure due to COVID-19 pneumonia. Initial labs showed normal renal function and electrolytes. He received azithromycin, hydroxychloroquine, and glucocorticoids and required extracorporeal membrane oxygenation. During the first 45 days of hospitalization, he had persistent hypernatremia (sodium as high as 154 mEq/L) despite free water flushes (FWF) and intermittent IV 5% dextrose in water (D5W). On day 45, vasopressin and norepinephrine were initiated for hypotension. Over the next 72 hours, serum sodium decreased from 148 to 128 mEq/L (Figure 1). Urine osmolality (UOsm) and sodium were 684 mOsm/Kg and 145 mEq/L, respectively. During this 72-hour period, the patient received about 1L/day FWF. On day 35, vasopressin was discontinued for 11 hours, during which time the sodium rose from 126 to 138 mEq/L and UOsm decreased from 205 to 82 mOsm/kg. He received D5W to re-lower the sodium. Vasopressin was also restarted, and the sodium stabilized near 132mEq/L.

Discussion: Although pneumonia may have contributed to high ADH release in this patient, the timing of vasopressin administration prior to the development of hyponatremia and the acute rise in sodium after vasopressin discontinuation suggests an important role for exogenous ADH. Clinicians should pay close attention to fluctuations in sodium levels in patients receiving IV vasopressin, particularly when therapy is discontinued, given the risk of rapid overcorrection and development of osmotic demyelination syndrome.
Continuous Renal Replacement Therapy (CRRT) for Overcorrection of Hyponatremia After Left Ventricular Assistance Device (LVAD) Placement
Abdulhadi T. Gelalidou, Pooja D. Amaraparukar, Jonathan J. Suarez. Emory University School of Medicine, Atlanta, GA.

Introduction: Rapid correction of severe hyponatremia can result in osmotic demyelination syndrome, central pontine myelinolysis and locked-in syndrome. Rapid correction is believed to occur as an increase in serum sodium (Na) by 10-12 mEq/L in the first 24 hours and 18 mEq/L in the first 48 hours. Rapid lowering serum Na in a short period after rapid correction of hyponatremia could prevent these complications. Conventional strategies use hypertonic intravenous fluids and desmopressin to lower overcorrected hyponatremia. However, CRRT can correct serum sodium in a very predictable and controlled manner.

Case Description: A 35-years old woman with a history of non-ischemic cardiomyopathy with an ejection fraction of 5-10% was admitted with an acute CHF exacerbation. Her hospitalization was complicated by AKI and hyponatremia. She underwent LVAD placement and her sodium increased from 111 to 137 mEq/L within 18 hours of surgery. She was started on CRRT using continuous venovenous hemodiafiltration (CVVHDF) with post-filter 5% dextrose in water to lower her sodium level to close to 120 mEq/L. The patient tolerated the treatment well with no immediate central nervous system complications or even delayed neurological complications at the two month follow up.

Discussion: To our knowledge, this is the first case report describing the use of CRRT for overcorrection of hyponatremia after LVAD placement. The overcorrection of hyponatremia after LVAD placement was likely due to the kidney’s restored ability to excrete diluted urine from improved renal perfusion. Given the total fluid volume of hypertonic intravenous fluids and unpredictability of desmopressin we recommend considering early initiation of CRRT to treat overcorrection of hyponatremia after LVAD placement. Another consideration should be made for Initiation of CRRT prior to LVAD placement in patients with severe hyponatremia to prevent the rapid correction from occurring in the intraoperative setting.

Neuroprotective Hyponatremia in Acute Liver Failure Using CRRT: A Challenging Scenario
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Introduction: Acute liver failure is associated with severe complications, including encephalopathy. Cerebral edema may occur, leading to increased intracranial pressure. Urgent medical management sometimes includes neuroprotective hydronephrosis and ammonia control using convective techniques. We describe a patient where high-volume CVVHDF was used to increase ammonia clearance while maintaining therapeutic hyponatremia.

Case Description: A 64-year-old female with severe bipolar disorder presented into the ED ~24hours after voluntary ingestion of ~150 tablets (75g) of acetaminophen. She was initially confused with normal blood pressure. Laboratory work showed severe metabolic acidosis with the following values: lactate 9.1 mmol/L, pH 6.99, ammonia 409 mmol/L, ALAT 6398 U/L, creatinine 250 g/L. NAC and IV bicarbonate were quickly initiated, and a short plasmapheresis treatment was started 12hours later, inducing moderate hypercalcemia, hypernatremia (153 mmol/L) and normalising INR temporarily. Encephalopathy, oliguria and hemodynamic instability progressed. High-volume CVVHDF (90 mL/kg/h) was started at day 3 to optimise ammonia clearance and electrolytes. Hypernorm NaCl 2.3% (50 mmol) was added to a low calcium 5L dialysate preparation (PrismOcal22) to obtain [Na] of 150 mEq/L. Over the next 3 days, additional hypertonic NaCl was required (until 80 mmol) (dialysate [Na] 155 mmol/L) to reach the ~150 mmol/L sodium targeted. However, after numerous medical complications, the patient was declared inelible to liver transplantation and palliative care was initiated. She died 3 weeks after initial admission.

Discussion: Usage of high-volume CRRT in severe hepatic encephalopathy increases despite the paucity of evidence. Commercial standard solutions of dialysate used for CRRT usually have fixed sodium concentration (140 mmol/L). Adding sterile hypertonic sodium-free potassium-binder exchanges calcium for potassium thus avoiding extra sodium load that is undesirable in patients with hypertension; moreover, Kayexalate also binds calcium thus decreasing calcium intake. Hyperkalemia is one of the common metabolic abnormalities seen in patients with renal failure. Management includes combination of low-potassium diet with additional potassium-binding medications if necessary. However, these measures are impractical in infants whose dietary intake is predominantly milk based and both breast as well as the renal milk formula, Similac PM 60:40, have high potassium content. Low-potassium milk formulas such as Renastart® and Renacal® are not readily available. Pretreatment of milk with Kayexalate has been utilised as an effective means of reducing the milk potassium content. As Kayexalate exchanges sodium for potassium, it results in extra sodium load that is undesirable in patients with hypertension; moreover, Kayexalate also binds calcium thus decreasing calcium intake. Patiromer (Veltassa®), a recently introduced sodium-free potassium-binder exchanges calcium for potassium thus avoiding both hypernatremia and hyperkalemia.

Methods: Potassium binding effectiveness of Patiromer was compared with Kayexalate by pretreating Similac® PM 60:40 milk formula. Three different concentrations of Kayexalate (3.4, 6.8, and 13.6 g/L) and Patiromer (8.4, 16.8, and 33.6 g/L) were used. Supematant samples were collected at 30, 60, and 120 minutes respectively. Samples were analyzed for sodium, potassium, calcium, and magnesium. The experiment was conducted in duplicate.

Results: Results are shown in Table.

Conclusions: Both Kayexalate and Patiromer were effective in lowering the potassium concentration. While Kayexalate increased the sodium content of the formula by almost 100 to 300%, and reduced the calcium concentration by 40%, Patiromer did not. Both Kayexalate and Patiromer decreased the magnesium concentration with the decrease being more pronounced with Kayexalate. Knowledge of these electrolyte changes is crucially important in the care of infants with renal disease as they are vulnerable to negative consequences of electrolyte imbalance.

Funding: Commercial Support - Relypsa, Inc

Effect of the Sodium Chloride Load on the Plasma Sodium Level in Infant Milk Formula Similac PM 60:40

Background: Hyperkalemia is one of the common metabolic abnormalities seen in patients with renal failure. Management includes combination of low-potassium diet with additional potassium-binding medications if necessary. However, these measures are impractical in infants whose dietary intake is predominantly milk based and both breast as well as the renal milk formula, Similac PM 60:40, have high potassium content. Low-potassium milk formulas such as Renastart® and Renacal® are not readily available. Pretreatment of milk with Kayexalate has been utilised as an effective means of reducing the milk potassium content. As Kayexalate exchanges sodium for potassium, it results in extra sodium load that is undesirable in patients with hypertension; moreover, Kayexalate also binds calcium thus decreasing calcium intake. Patiromer (Veltassa®), a recently introduced sodium-free potassium-binder exchanges calcium for potassium thus avoiding both hypernatremia and hyperkalemia.

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Funding: Commercial Support - Relypsa, Inc
Post-Discharge Outcomes Among Hyperkalemic Patients Treated with and Without Sodium Polystyrene Sulfonate in the Inpatient Setting

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Background: Sodium polystyrene sulfonate (SPS) is a common treatment option for hyperkalemia (HK) in the inpatient (IP) setting. However, the post-discharge outcomes of patients with HK treated with and without SPS in the IP setting are not well characterized.

Methods: Adult patients with ≥1 IP stay with HK (≥5.0 mEq/L) between January 2013 – June 2018 were included using electronic medical record data from the Research Action for Health Network (2012-2018). Patients treated with SPS during the IP stay were matched 1:1 to patients not treated with SPS on discharge status (dead/alive) and HK severity (most severe K lab during IP stay). Patient characteristics, K levels, HK treatments, length of stay (LOS), and deaths during IP stay were described. All-cause and HK-related IP readmission, and HK recurrence (in any setting) within 30, 60 and 90 days post-discharge were described and compared using conditional logistic regressions.

Results: A total of 4,847 SPS users were matched to non-SPS users (23.2% K=5.0-5.5, 36.8% K=5.5-6.0, 40.0% ≥6.0 mEq/L). During the stay, the 11.7% of patients died in both cohorts. Mean age was 65.7 and 62.1 years for the SPS and non-SPS users. SPS users had a higher burden of comorbidities than non-SPS users, including CKD (79.1% vs 57.2%) and heart failure (49.8% vs 37.7%, both p<0.001). The LOS was similar for SPS and non-SPS users (9.0 v 9.1 days) and most patients had their last K level normalized (≤5.0 mEq/L) during the stay (83.0% vs 86.2%, p<0.001). Use of temporizing agents was common for SPS and non-SPS users (58.2% vs 43.5%, p<0.001); however, very few SPS users received SPS at discharge (0.4%). The 30-day all-cause and HK-related IP readmission rates were 27.0% and 13.6% for SPS users and 19.3% and 5.4% for non-SPS users, respectively. HK recurred within 30 days in 23.0% of SPS patients and 7.1% of non-SPS users. The differences remained after adjusting for baseline and IP stay characteristics (odds ratio [95% CI]: all-cause readmission=1.4 [1.2, 1.6]; HK readmission=2.4 [2.0, 2.9]; HK recurrence=3.1 [2.7, 3.6]). The adjusted results were similar for 60 and 90 days post-discharge.

Conclusions: Despite treatment with SPS in the IP setting there was a high burden of readmission and HK recurrence among patients with HK.

Funding: Commercial Support - AstraZeneca

POI1446

Serum Potassium Levels at Hospital Discharge and 1-Year Mortality Among Hospitalized Patients

Michael A. Maq,1 Charat Thongprayoon,2 Wisit Cheungsapitorn,2 Sorlko Thirunavukkaras,1 Api Cheewcharat,2 Stephen B. Ericsson,1 Mayo Clinic's Campus in Florida, Jacksonville, FL; 1Mayo Clinic Minnesota, Rochester, MN.

Background: The aim was to assess the relationship between discharge serum potassium levels and one-year mortality in hospitalized patients.

Methods: All adult hospital survivors between years 2011 and 2013 at a tertiary referral hospital who had available admission and discharge serum potassium levels were enrolled. End-stage kidney disease patients were excluded. Discharge potassium was defined as the last potassium measured within 48 hours prior to hospital discharge and categorized into ≤2.9, 3.0-3.3, 3.5-3.9, 4.0-4.4, 4.5-4.9, 5.0-5.4 and ≥5.5 mEq/L. Cox proportional hazard analysis was performed to assess the independent association between discharge potassium and one-year mortality after hospital discharge, using discharge potassium of 4.0-4.4 mEq/L as the reference group.

Results: Of 57,874 eligible patients, with a mean discharge serum potassium of 4.1±0.4 mEq/L, the estimated one-year mortality rate after discharge was 13.2%. A U-shaped association was observed between discharge potassium and one-year mortality, with nadir mortality in the discharge potassium of 4.0-4.4 mEq/L. After adjustment for clinical characteristics, including admission potassium, both discharge potassium of ≥3.9 mEq/L and ≥4.5 mEq/L were significantly associated with increased one-year mortality, compared with the discharge potassium of 4.0-4.4 mEq/L. Stratified analysis based on admission serum potassium showed similar results except that there was no increased risk of one-year mortality if discharge potassium group was ≥3.9 mEq/L in patients with an admission potassium of ≥3.0 mEq/L.

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PO1449

Hyperkalaemia Secondary to Carabepenem Use
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Introduction: Hyperkalaemia can be a life-threatening complication and can often occur in the hospital setting as the result of the use of certain medications. In particular, hyperkalaemia has already been described as a rare complication of etapenem use.

Case Description: A 24-year-old gentleman with no past medical or surgical history presented with a week history of abdominal pain and nausea. He underwent a CT scan that showed a perforated appendix with small abscesses. Upon admission, his creatinine level was 1.28 mg/dL and his potassium level was 4.24 mEq/L. He was initiated on intravenous fluids and etarpenem 1g IV once daily. His renal function improved and his creatinine level decreased to 0.83 mg/dL however he developed hyperkalaemia with a potassium level that peaked at 5.9 mEq/L. He was switched to meropenem, however the hyperkalaemia persisted and resolved only when he was switched to ciprofloxacin.

Discussion: Carabepenem use is associated with severe hyperkalaemia and this complication seems to stem from a class-effect rather than the effect of a specific drug.

PO1450

Relationships Between CKD Duration, Serum Potassium Level, and Adverse Outcomes
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Background: Patients with chronic kidney disease (CKD) are at increased risk of hyperkalaemia as the kidneys are important in maintaining potassium homeostasis. This study examined the relationship between CKD duration, serum potassium level (K+) and adverse clinical outcomes.

Methods: This retrospective cohort study used linked primary and secondary care data from that UK Clinical Practice Research Datalink (CPRD) GOLD and Hospital Episode Statistics (HES), respectively. Eligible patients were aged ≥18 years with new or existing CKD stage 3+ (READ code or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² without prior dialysis) between January 2008 and June 2018, or during lookback (2003 to 2007). Index date was 01 January 2008 ( prevalent cases) or CKD diagnosis date (incident cases); whichever occurred later. Adverse outcomes were all-cause mortality (ACM) and major adverse cardiovascular events (MACE), a composite of arrhythmia, heart failure, myocardial infarction, and stroke. Crude incidence rates of ACM, MACE, and hospitalization were calculated. Results: A total of 1,039,245 patients with at least one S-K record each were analysed. Of these, 297,702 CKD patients, 58.6% were female and mean age was 74.7 years (standard deviation, SD 11.3) at index, with mean follow up of 5.6 years (SD 3.20).

Conclusions: In patients with CKD, comorbidities – specifically HF, diabetes, and RHTN – increase the risk of HK. This risk increases as renal function declines. As such, CKD patients, particularly those with comorbidities, may benefit from additional monitoring for HK.

Funding: Commercial Support - AstraZeneca

PO1451

Can Potassium Be a Predictor of Cardiovascular Mortality?
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Background: Epidemiologic data demonstrates association between hyperkalaemia and mortality. Patients with ST-segment elevation myocardial infarction (STEMI) often have hyperkalaemia that is associated with hyperkalaemia, such as Chronic Kidney Disease (CKD) and Diabetes Mellitus (DM). The aim of our study was to analyse hyperkalaemia as a prognostic factor in patients with STEMI.

Methods: Retrospective single-center analysis of all patients admitted for STEMI and undergoing primary percutaneous coronary intervention in a two-year period (January 2009 to December 2010). Demographic aspects, comorbidities, potassium level at admission and outcomes were evaluated. Hyperkalaemia was defined as potassium level superior to 5 mmol/L.

Results: Overall, 276 patients were included (mean age 62 ± 14 years, 75% males), 55% had hypertension, 20% diabetes mellitus and 14% previous myocardial infarction. Only 14% were pretreated with renin-angiotensin-aldosterone system inhibitors (RAASI). The median potassium at admission was 4 mmol/L (IQR 3.7 - 4.4mmol/L), and the median creatinine level at admission was 0.88 mg/dL (IQR 0.74 - 1.1mg/dL). 5-year all-cause mortality was 23%. Univariable analysis revealed that age (p < 0.001), previous myocardial infarction (p = 0.038) and hyperkalaemia at admission (p = 0.039) were associated with 5-year all-cause mortality. After adjustment for therapy with RAASI, higher potassium level at admission was associated with 5-year all-cause mortality (adjusted HR 1.55, 95%CI 1.01-2.38; p = 0.045).

Conclusions: In our study, potassium at admission was a predictor of 5-year all-cause mortality. Potassium measurement is an easy tool to help in risk stratification in this population. Further studies are needed to access if pharmacological control of potassium levels will change prognosis.

PO1452

Epidemiology of Hyperkalaemia Among Patients Presenting at the Emergency Department in China
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Background: In China, the clinical burden of hyperkalaemia (HK) among patients presenting emergency department (ED) is not well described.

Methods: Data containing hospital information system (HIS) records of 157 hospitals, covering 30 provinces in China were extracted from Beijing Data Center for National Use of ED Drugs. Patients presenting ED (aged ≥18 years) with record(s) of serum potassium (S-K) from 2015.1.1 to 2017.12.31 were included. Hyperkalaemia were defined as S-K > 5.0 mmol/L. The proportion of patients experience at least one hyperkalaemia and the severity of hyperkalaemia were calculated among overall outpatient and patients with chronic kidney disease (CKD), heart failure (HF), hypertension (HTN), and diabetes mellitus (DM). The geographic and season distribution of the proportion among overall patients were calculated.

Results: A total of 1,039,245 patients with at least one S-K record each were analysed. Of these, 56.2% were female and mean age was 47.7 years (standard deviation, SD 12.9). Mean S-K at index was 4.67 ± 0.9mEq/L. 52.6% of patients had S-K levels >5.0 mmol/L at their index visit.

Conclusions: The proportion of HK in ED patients with CKD, HF, HTN or DM were higher than that in overall ED patients, and the severity of HK increased in patients with CKD, HF, DM and HTN.

The composition of patients at different S-K intervals in hyperkalaemia patients with/ without CKD, HF, HTN, or DM in ED

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
POI1453

Machine Learning Models for Risk Prediction of Adverse Events in Hyperkalemic Patients
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Background: Hyperkalemia is a common electrolyte abnormality in heart failure (HF) and chronic kidney disease (CKD) patients. Although increased risks of adverse events in hyperkalemic patients have been well reported, there is limited information on causality of adverse events. Considering multifactorial conditions of hyperkalemic patients, we aimed to develop predictive models using novel machine learning algorithms.

Methods: We utilized a Japanese hospital claims registry, Medical Data Vision. We extracted hyperkalemic patients with either CKD and/or HF aged ≥18 years, defined as patients with ≥2 serum potassium values ≥5.1 mmol/L from April 2008 to September 2018. Extracted dataset was split into 80:20 for training and validation. The risk of adverse clinical events including all-cause death, hospitalization for cardiac events, hospitalization for HF, and renal replacement therapy (RRT) introduction over 3 years after hyperkalemic episodes was modeled using gradient boosted tree (XG), neural network (NN), and logistic regression (LR) based on 81 clinical variables collected in 12 months before hyperkalemic episodes.

Results: Of 74,974 hyperkalemic patients, 8,480 patients were included. Mean age was 75.6 years and 53.7% were male. The ROC curve and calibration analyses showed excellent performance for death (AUC=0.841 [XG], 0.815 [NN], 0.838 [LR]), hospitalization for cardiac events (AUC=0.782 [XG], 0.718 [NN], 0.743 [LR]), HF (AUC=0.775 [XG], 0.850 [NN], 0.855 [LR]), and RRT (AUC=0.958 [XG], 0.917 [NN], 0.946 [LR]). Clinical variables with high importance were identified (Figure).

Conclusions: The machine learning model successfully predicted high-risk hyperkalemic patients for adverse events. Despite the need for model validation, these results support the use of predictive models to select high-risk-hyperkalemic patients.

Funding: Commercial Support - AstraZeneca K.K.

POI1454

Extracellular Volume and Plasma Potassium Determine Urinary Prostaglandin E2 Excretion in Kidney Disease
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Background: Prostaglandin E2 (PGE2) is the most abundantly produced prostaglandin in the kidney where it plays a key role in renin secretion and electrolyte handling. It is unknown whether urinary PGE2 excretion is a reflection of these functions in patients with kidney disease. Here, our aims were to (1) analyze the changes in urinary PGE2 excretion during interventions modulating extracellular volume (ECV) or electrolyte homeostasis and (2) identify the determinants of urinary PGE2 excretion.

Methods: Urinary PGE2 and PGE2 metabolite (PGEM) excretions were measured in two studies in chronic kidney disease patients: 1) a randomized cross-over trial comparing a low sodium (Na+) diet (60 mmol/day) with amiloride/hydrochlorothiazide (n=26, each intervention 2 weeks), 2) a 2-week intervention with potassium chloride supplementation (40 mmol/day, n=28), and in patients with diabetic kidney disease from a 12-week randomized trial comparing dapagliflozin (n=23) with placebo (n=23) with glimepiride (n=19). The baseline data of these studies were combined (n=96) to identify determinants of urinary PGE2 excretion using multivariable linear regression with correction for age, sex, eGFR, and study.

Results: A low Na+ diet, amiloride/hydrochlorothiazide, and dapagliflozin reduced ECV and increased plasma renin. Amiloride/hydrochlorothiazide and dapagliflozin increased total urinary PGE2 excretion by 5.3% (95% CI 1.9-8.7%) and 5.8% (95% CI 0.9-10.8%), respectively, while a low Na+ diet increased PGE2 excretion by 5.9% (95% CI 1.2-10.6%). Potassium supplementation had no effect on ECV, plasma renin, or urinary PGE2 excretion. Total linear regression showed that total urinary PGE2 excretion was associated with plasma renin (β 0.3, 95% CI 0.2-0.4), urinary Na+ excretion (β 0.003, 95% CI 0.0007-0.006), and plasma potassium (β 0.7, 95% CI 0.3-1.0).

Conclusions: Interventions that decrease extracellular volume increase urinary PGE2 excretion. In addition, plasma renin, urinary Na+ excretion, and plasma potassium are independently associated with urinary PGE2 excretion. Our data suggest that in patients with kidney disease urinary PGE2 excretion not only reflects the kidney’s response to changes in extracellular volume but also plasma potassium.

Funding: Private Foundation Support, Government Support - Non-U.S.

POI1455

Patient and Clinician Preferences for Hyperkalemia Treatment: A Qualitative Study
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Background: Treatment options for chronic hyperkalemia include the potassium binders Kayexalate®, Veltassa®, and since 2018, Lokelma®. In a qualitative research study, we explored which treatment characteristics are important to patients with hyperkalemia and treating clinicians.

Methods: Adult patients in the US who had received treatment for chronic hyperkalemia in the past 12 months and US clinicians who had treated ≥10 patients with chronic hyperkalemia with potassium binders in the last 3 months participated in focus group discussions consisting of concept elicitation and a ranking exercise, guided by a semi-structured discussion guide, with potential attributes identified through review of product labels.

Results: Twenty-five patients (52.4 ± 14.8 years; 56% male; 32% on dialysis; 20% kidney transplant recipients) and eight clinicians (n=4 nephrologists, n=2 cardiologists, n=1 hospitalist) participated. For patients, the most commonly reported medication side effect was diarrhea (64%), followed by abdominal pain and cramping (56%), nausea and/or vomiting, bloating/flattulence, and cramping in hands and legs (all 36%). The most disliked treatment characteristic was the medication’s taste/texture; 58% of patients scored it among the most important treatment characteristics. Although most patients reported gastrointestinal-related side effects, 54% did not report diarrhea and 46% did not report abdominal cramping in the top three characteristics. For clinicians, the most commonly encountered medication side effect was diarrhea (50%), followed by abdominal cramping (25%) and constipation (25%), and the most commonly considered treatment characteristic when prescribing a binder was taste/texture (50%), followed by time before/after taking medications (38%), time to onset (38%) and adherence (38%). Sustained efficacy followed by time to onset were ranked by 88% of clinicians in the two most important characteristics. Medication preparation, medication storage, and compliance were ranked low by both patients and clinicians.

Conclusions: Different potassium binder characteristics are most important to patients (taste/texture and abdominal cramping) and clinicians (sustained efficacy and time to onset). Clinicians should therefore take patient preference into consideration when prescribing a potassium binder.

Funding: Commercial Support - AstraZeneca

POI1456

Patient Palatability and Preference Study of Three Potassium Binders in Patients with CKD and Hyperkalemia: Rationale and Design of the APPETIZE Study
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Background: Patients with CKD are at risk of hyperkalemia (HK) which has been associated with a higher risk of cardiovascular events and mortality. Recently accepted K+ binders provide new treatment options to fulfill the unmet need for HK treatment beyond traditional K+ binders, which are poorly tolerated by patients and are associated with GI side effects.

Methods: APPETIZE is a cross-sectional, randomised cross-over study with the aim to evaluate the palatability of and patient preference for 3 currently available K+ binders: Sodium Polystyrene Sulphonate (SPS) or Calcium Polystyrene Sulphonate (CPS), Sodium Zirconium Cyclosilicate (Lokelma®) and Calcium Patiromer Sorbitex (Veltassa®). A single (patient) blind side-by-side, sip and spit taste-test approach will be utilised where patients will be presented with a single full, per label dose of each product to represent the real-world patient experience. Patient ratings, assessed on a 0-10 scale and emotional response using the AdSAM tool® to evaluate feelings (Appeal, Engagement and Empowerment) will be used to assess patient centric attributes: taste (primary outcome), texture, smell, mouthfeel and likelihood of adherence (secondary outcomes) of each product. Preferential ranking will be performed after all 3 products have been tested. Sixty CKD patients (both dialysis and non-dialysis) with HK per country (480 overall) from US, Canada, Spain, Italy, Germany, France, Sweden and Norway will be included, with equal proportions of patients ever-treated and never-treated with K+ binders.

Conclusions: Interventions that decrease extracellular volume increase urinary PGE2 excretion. In addition, plasma renin, urinary Na+ excretion, and plasma potassium are independently associated with urinary PGE2 excretion. Our data suggest that in patients with kidney disease urinary PGE2 excretion not only reflects the kidney’s response to changes in extracellular volume but also plasma potassium.

Funding: Private Foundation Support, Government Support - Non-U.S.
Results: APPETIZE will describe, compare and rank palatability and preference of 3 currently available K+ binders by country. Initial results are anticipated towards end of 2020.

Conclusions: Utilizing innovative methodology, APPETIZE will generate evidence intended for patients and physicians (including nephrologists and cardiologists) regarding patient palatability, patient preference and predicted likelihood of adherence for currently available K+ binders.

PO1457

Fixing the Kidneys to Fix the Heart: BRASH Syndrome, a Case Report

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Introduction: BRASH (bradycardia, renal failure, AV-nodal blockade, shock, and hyperkalemia) is a multi-system syndrome. Immediate potassium removal is necessary and will result in resolution of cardiac arrhythmia.

Case Description: A 69 y/o male presented with generalized weakness, oliguric for 2 weeks and subsequence anuric. Lab was significant for hyperkalemia (6.2). EKG showed sinus bradycardia (HR 30), but without pathognomonic features of hyperkalemia. (Fig 1) Medical history significant for nephrectomy from an MVA injury, and IgA nephropathy s/p right renal transplant, hepatitis C, diabetes on insulin, and heart failure on Carvedilol 25mg BID. The patient was admitted to ICU and treated with calcium gluconate and insulin. Cardiology team was consulted for temporary pacers with eventual pacemaker insertion planned. However, upon discussion with the nephrology team, suspicion of BRASH syndrome was raised. Urgent CRRT was started. Rapid correction of potassium resulted in normalization of heart rate immediately. The patient received CRRT for 24 hours, and discharged on scheduled hemodialysis.

Discussion: BRASH syndrome is an uncommon presentation of a vicious cycle in the setting of hyperkalemia from acute kidney leading to the accumulation of AV node blockade medications. This synergizes bradycardia and hyperperfusion. Hypoperfusion, in turn, worsens renal failure leading to a cycle that continues until the patient deteriorates into lethargy, shock, and potentially death. Nowadays, despite commonplace to see turn, worsens renal failure leading to a cycle that continues until the patient deteriorates into lethargy, shock, and potentially death. Nowadays, despite commonplace to see.

Conflict of Interest: No

PO1459

Effect of Lactated Ringer Solution Use on Serum Potassium in Advanced Kidney Disease

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Background: Lactated Ringer’s (LR) solution is a balanced crystalloid containing 4 mEq/L of potassium (K). Its use is restricted in hyperkalemia and in those with advanced kidney disease given potential concerns of exacerbating hyperkalemia. We assessed the effect of LR on serum K levels in patients with advanced kidney disease.

Methods: Retrospective evaluation of 191 patient encounters with advanced kidney disease [defined by estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73m2] given potential concerns of exacerbating hyperkalemia. We assessed the effect of LR on serum K levels in patients with advanced kidney disease.

Results: Average age of patients was 59 years. 19 patients had AKI, 60 patients had CKD, and 61 had ESKD (including 11 who had renal transplantation). Average LR use was 1.9L per patient. Hyperkalemia [defined by serum K ≥ 5.2 mEq/L] was seen in 27 patient encounters (14.1% of the study population). However, 16 of these patients had average K of 5.8 mEq/L prior to LR use. 11 among them were managed with medications alone and 4 patients needed dialysis. Average and highest K levels among all patients within 24 hours post LR use were 4.2 mEq/L and 4.4 mEq/L respectively. 131 patient encounters had sepsis. There was 1 death attributable to hyperkalemia.

Conclusions: 27 out of 191 patient encounters (14.1%) with advanced kidney disease on LR within 24 hours post-LR administration, and 16 had known hyperkalemia prior to LR use. Our study demonstrates that LR use is not independently associated with hyperkalemia in advanced kidney disease, a population subset who frequently cannot renally execute K adequately. Further large scale clinical studies are warranted to confirm our findings.

PO1460

Association Between Dyskalemias and Short-Term Hospital/Emergency Department Visits in Patients with Advanced CKD Transitioning to Dialysis

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Background: Intestinal potassium excretion is increased in patients with advanced CKD. This compensatory mechanism may be enhanced by laxative use; however, little is known about the association of laxative use with longitudinal potassium (K) balance in advanced CKD.

Methods: In 34,697 US veterans who transitioned to ESRD from 2007-2015 and with ≥2 K measurements during the last 1-year period before ESRD transition, we examined the association of time-varying laxative use with change in K (slope) over the 1-year pre-ESRD period, using multivariable linear mixed-effects models. The difference in K-slope by laxative use status was tested by the interaction of laxative use with time varying K.

Results: Overall, the mean age was 68 years; 98% were male; 32% were African American, and 76% were diabetic. In the crude model, there was a significant difference in K-slope between laxative use and non-use, with declining K-slope observed only for laxative use (median, -0.010 vs. 0.008 mEq/L/year, P=0.02; Table). Although the magnitude of K-slopes was clinically negligible, the between-group difference remained significant even after multivariable adjustment, with laxative use being associated with decline in K (median, -0.013 vs. 0.003 mEq/L/year, P=0.02; Table).

Conclusions: Laxative use was modestly and independently associated with decline in K over the last 1-year pre-ESRD period, suggesting increased intestinal potassium excretion by laxatives. Further studies are warranted to test whether active interventions with laxatives can improve potassium management in advanced CKD beyond their traditional indication.

Funding: NIDDK Support

Changes in plasma potassium concentration associated with time-varying laxative use status during the last 1-year pre-ESRD period (n=34,697)

Table 1: Initial EKG on presentation.
Three % of patients experienced a hospital/ED visit. Both hyper- and hypokalemia were significantly associated with higher risk of a hospital/ED visit in the crude (OR [95% CI] 2.73 [2.22-3.37] and 2.28 [1.68-3.09], respectively) and multivariable-adjusted models (2.47 [1.98-3.09] and 1.88 [1.37-2.58], respectively) (Figure).

**Conclusions:** Hyper- and hypokalemia are associated with higher short-term risk of hospital/ED visits in patients with advanced CKD. Preventing dyskalemias may help in reducing the incidence of short-term hospital/ED visit.

**Funding:** NIDDK Support

**Characteristics of CKD Patients with Hyperkalemia: A Report from the DISCOVER CKD Retrospective Cohort**

**Methods:** The DISCOVER CKD retrospective cohort was extracted using the US TrifinRX hospital-EMR and Japan Medical Data Vision (JMDV) databases. The study included patients aged >18 years (>20 JMDV) with a diagnostic CKD code (stage 3A to Stage 5 including renal replacement therapy [RRT]) or 2 estimated glomerular filtration rate (eGFR) measurements between 2007-16. RAASi included ACE inhibitors, ARBs, MR antagonists, and ENaC inhibitors. Patients were included if they had one of the following interventions performed within 30 days of the hyperkalemia measurement: a) RAASi discontinuation, b) RAASi dose decrease, c) new K+ wasting diuretic prescription, d) K+ wasting diuretic dose increase, or e) sodium polystyrene sulfonate [SPS] prescription. The primary outcome was recurrence of hyperkalemia within 1 year. Secondary outcomes included major adverse cardiovascular events (MACE) and all-cause mortality within 1 year. Multivariable Fine and Gray sub-distribution models accounting for the competing risk of death were used for recurrent hyperkalemia and MACE outcomes. Multivariable Cox proportional hazards models were used for the all-cause mortality outcome.

**Results:** A total of 21,723 patients were included: RAASi discontinuation (N=13,539), RAASi decrease (N=5,075), new diuretic (N=1,010), diuretic increase (N=1,245), and e) sodium polystyrene sulfonate [SPS] prescription. RAASi discontinuation was associated with a lower 1-year risk for recurrent hyperkalemia and MACE compared with other common hyperkalemia interventions (see Figure). However, there was no clear difference in 1-year all-cause mortality among these interventions.

**Conclusions:** RAASi discontinuation is associated with a lower 1-year risk for recurrent hyperkalemia and MACE compared with other common ambulatory interventions for hyperkalemia.

**PO1462**

**Ambulatory Treatments for RAAS Inhibitor-Related Hyperkalemia and the 1-Year Risk of Recurrence**

**Background:** Hyperkalemia commonly occurs with RAAS inhibitor (RAASi) use. The effectiveness of common outpatient interventions in preventing recurrent hyperkalemia has never been directly compared.

**Methods:** Population-based, retrospective cohort study of Ontario (Canada) residents aged ≥66 years old on RAASi therapy with ≥1 outpatient hyperkalemia (≥5.3 mmol/L) measurements between 2007-16. RAASi included ACE inhibitors, ARBs, MR antagonists, and ENaC inhibitors. Patients were included if they had one of the following interventions performed within 30 days of the hyperkalemia measurement: a) RAASi discontinuation, b) RAASi dose decrease, c) new K+ wasting diuretic prescription, d) K+ wasting diuretic dose increase, or e) sodium polystyrene sulfonate [SPS] prescription.

**Results:** A total of 21,723 patients were included: RAASi discontinuation (N=13,539), RAASi decrease (N=5,075), new diuretic (N=1,010), diuretic increase (N=1,245), and SPS (N=854). RAASi discontinuation was associated with a lower risk for recurrent hyperkalemia and MACE over 1 year compared with other common hyperkalemia interventions (see Figure). However, there was no clear difference in 1-year all-cause mortality among these interventions.

**Conclusions:** RAASi discontinuation is associated with a lower 1-year risk for recurrent hyperkalemia and MACE compared with other common ambulatory interventions for hyperkalemia.
Lethal Refractory Hyperkalemia and Metabolic Acidosis in a Patient with Secondary Hemophagocytic Lymphohistiocytosis (HLH)

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Introduction: Renal replacement therapy (RRT) is used as an adjuvant therapy to treat severe electrolyte and acid-base abnormalities. We describe a case of severe metabolic acidosis (lactic acidosis) and hyperkalemia which was refractory to treatment with simultaneous continuous renal replacement therapy (CRRT) and hemodialysis (HD) in a patient with HLH.

Case Description: A 63-year-old female with a history of diabetes mellitus, warm antibody autoimmune hemolytic anemia was admitted to the hospital with hypotension and hyperglycemia diagnosed on outpatient labs. Her hospital course was complicated with fevers, severe lactic acidosis, worsening thrombocytopenia and anemia. Infectious and rheumatologic workup was negative. Presumed diagnosis of secondary HLH was made with elevated serum ferritin (100,000 ng/mL), elevated triglyceride levels (346 mg/dl), low fibrinogen levels (70 mg/dl), fevers, bicytopenia and elevated soluble IL-2 receptor levels (34177 units/ml). She was treated with etoposide and dexamethasone for secondary HLH. Nephropathy was consulted for hyperkalemia, metabolic acidosis and elevated lactate in our patient with normal renal function. Hyperkalemia was thought to be due to ongoing hemolysis. Despite medical management with intravenous bicarbonate, albuterol and insulin, the hyperkalemia persisted so RRT was initiated. Her potassium levels did not improve despite her serum pH increasing to 7.33. Serum lactate remained persistently elevated to 21 mmol/L. Neither high diastolic flow rates (DFR) up to 7.5 liters per hour with a 2 meq/dl potassium bath nor hemodialysis which followed, using a zero potassium dialysate bath, lowered the potassium level. The patient continued to have a wide complex ORS interval on her ECG and episodes of ventricular tachycardia and suffered from a cardiac arrest when her potassium was 6.9 meq/dl. Suspected malignancy associated secondary HLH was thought to be the possible etiology of her refractory lethal metabolic problems.

Discussion: HLH has been associated with severe type B lactic acidosis from excessive cytokine overproduction. Often, CRRT with higher DFR than recommended have been used in the past to achieve solute clearance. Our case was unique as the patient continued to have refractory hyperkalemia and elevated lactate despite receiving CRRT and HD and had poor outcomes.
CT Images: A: Coronal view shows a left psoas abscess (yellow arrow), & bowel wall thickening (blue arrows). B: Axial view shows abscesses in the liver & spleen. C: Axial view with bone window shows osteolytic lesions with soft tissue components in the right aspect of the T10 vertebra.

Blood & urine chemistry results. HD Hospital Day

**POI467**

**A Case of the Cons: How Contraception Confused Congenital Adrenal Hyperplasia for Conn**


**Introduction:** Drospirenone is a synthetic progestin oral contraception (OCP) with anti-androgen and anti-mineralocorticoid properties. We present a case of hypokalemic alkalosis and hypertension masked by drospirenone use.

**Case Description:** A 21-year-old female with presumed polycystic ovarian syndrome (PCOS) was referred for hematuria, facial rash, and positive ANA concerning for lupus nephritis. Her only medication was drospirenone-ethinyl estradiol for oligomenorrhea, acne and hirsutism. Blood pressure (BP) was 98/67 mmHg and heart rate 88 bpm with orthostasis. She had male pattern hair loss and dense comedones on her cheeks. Labs were significant for normal renin function, 2+ hematuria with ischemic RBCCs, negative BHCG and ANA titer 1:64. Glomerulonephritis and rhabdomyolysis work-ups were negative. Hematuria was attributed to breakthrough uterine bleeding. Gynecology held her OCP to allow for withdrawal bleeding. At 6-week follow-up, she reported muscle cramps and increased facial hair. BP was 176/98 mmHg. Hypertension was confirmed with ambulatory BP monitoring. Labs were significant for potassium 2.8 meq/L, bicarbonate 37 meq/L, urine sodium 14 meq/L, potassium 54 meq/L, chloride 38 meq/L. Mineralocorticoid excess due to primary hyperaldosteronism (Conn’s syndrome) was suspected but plasma renin activity was <1 and aldosterone was <1. Syndrome of apparent mineralocorticoid excess was considered but the presence of hypertension prompted investigation of congenital adrenal hyperplasia (CAH). Work-up found elevated levels of ACTH (146 pg/mL), DHEA-S (694 mcg/dL), 11-deoxycorticosterone (452 ng/dL), and testosterone (92 ng/dL), but normal 17-OH progesterone, LH and FSH. Ultrasound showed bilateral adrenal enlargement, normal right and left ovaries with two dominant follicles. She declined genetic testing for 11-beta hydroxylase deficiency (11BHD). Clinical and lab findings were consistent with non-classical CAH due to 11BHD. She started hydrocortisone with suppression of ACTH, decrease in 11-deoxycorticosterone, and normalization of BP and electrolyte abnormalities.

**Discussion:** 11BHD is rare form of CAH, which can be confused with PCOS and other syndromes of mineralocorticoid excess. In this case, drospirenone use controlled symptoms but potentially delayed diagnosis of 11BHD. Clinical trials should assess drospirenone in treatment of endocrinopathies.

**POI468**

**Posaconazole-Induced Hypokalemia in a Hemodialysis Patient**

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**Introduction:** Posaconazole is a commonly used antifungal agent that is used for prophylaxis in many transplant recipients. Its side effect profile can vary from cardiovascular effects to metabolic derangements, such as hypokalemia. A prior case report of apparent mineralocorticoid excess (AME) secondary to Posaconazole therapy has been reported in 2017; however, this has not previously been reported in the ESRD patient population.

**Case Description:** A 68-year-old male with past medical history of idiopathic pulmonary fibrosis who underwent left lung transplant in December 2019 was consulted for acute kidney injury (AKI). Etiology of AKI was attributed to Tacrolimus induced thrombotic microangiopathy that ultimately required initiation of hemodialysis. Posaconazole 200mg PO daily was used for anti-fungal prophylaxis. Throughout the hospitalization, persistent hypokalemia was observed despite dialyzing the patient against a 4K bath. Further hypokalemia evaluation revealed plasma renin level at lower limit of normal (0.5 ng/mL/hr) and low plasma aldosterone level at <3.0 ng/dl. 24 hr urinal cortisol-to-cortisone ratio was non-diagnostic likely due to an inadequate collection (creatinine 160 mg/24 hr).

**Discussion:** We identified a case that mimics apparent mineralocorticoid excess syndrome, where patients receiving Posaconazole behave as if they have increased serum aldosterone levels; however, when serum levels are measured, aldosterone levels are in fact low. Patients are unable to metabolize cortisol to cortisone due to a defect in 11β-hydroxysteroid dehydrogenase. This leads to an accumulation of cortisol, allowing it to bind to the aldosterone receptor and increase sodium entry intracellularly via the epithelial sodium channel (ENaC). Stimulation of the ENaC then leads to potassium secretion and subsequent hypokalemia. 

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
An Interesting Case of Hypokalemia

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Introduction: Hypokalemia (serum potassium <3.5 meq/L) is one of the most common abnormalities encountered in nephrology practice. With careful history and laboratory investigations, the cause can usually be found.

Case Description: A 68-year-old caucasian male with Hypertension was referred for persistent hypokalemia. Medications were KCL 360 mEq/day, amlodipine, carvedilol, doxazosin, hydralazine and lisinopril. Labs showed hypokalemia (2.4 mmol/L) and metabolic alkalosis (HCO₃, 31 mmol/L). Urinary potassium losses were significant. After aldosterone level returned low, focus shifted towards hypercortisolism as a cause of MC activity. Studies confirmed raised cortisol and high ACTH. Pituitary gland workup was negative. Investigation for ectopic ACTH production revealed bilateral adrenal hyperplasia and discrete left adrenal mass. Adrenal hormone workup detected raised catecholamines. Adrenal vein sampling for ACTH showed laterization to the left. After alpha and beta-blockade, laparoscopic left adrenalectomy was done. Intraoperative biochemistry and pathology confirmed ACTH-secreting pheochromocytoma. After resection of ectopic ACTH source, patient became normokalemic and was discharged with steroid replacement.

Discussion: In the distal nephron, cortisol is inactivated to cortisone by 11-beta-dehydroxysteroid dehydrogenase 2 (11βHSD2). Hypercortisolism causes relative deficiency of 11βHSD2 due to enzyme saturation. Cortisone then stimulates non-selective MC receptor. Systematic workup led to diagnosis of ACTH-secreting pheochromocytoma. After resection of ectopic ACTH source, patient became normokalemic and was discharged with steroid replacement.

Acknowledgments: The authors would like to thank the medical staff at Columbia University Irving Medical Center for their assistance and support.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

472
CYP24A1-Hypercalcemia in Pregnancy

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Introduction: Hypercalcemia due to primary hyperparathyroidism and malignancy is common. However, rare genetic mutations in VitD metabolism (CYP24A1 & SLC34A1) are often culprits.

Case Description: 33-year-old woman with chronic hypercalcemia, nephrocalcinosis, CKD 3, HTN was admitted at 34-weeks of gestation for symptomatic hypercalcemia (13.2 mg/dL). Labs showed ↓PTH (9 pg/mL), ↓/↔25-VitD (35 ng/mL) & ↑/≈1,25-VitD (65 pg/mL). Defect in VitD pathway was suspected. 25-VitD:24,25-VitD ratio returned (178). Genetic testing confirmed compound heterozygous CYP24A1 mutation.

Discussion: CYP24A1 gene encodes 24-hydroxylase which inactivates 25-VitD and 1,25-VitD to 24,25-VitD and 1,24,25-VitD. Biochemical profile includes ↑ serum & urinary calcium, ↓PTH, ↓25-VitD:24,25-VitD ratio +/- 1,25-VitD & 25-VitD. 25-VitD:24,25-VitD > 80 warrants genetic analysis. Azoles inhibit 1-hydroxylase & urinary calcium, ↓PTH, ↓1,25-VitD, and can be utilized. Steroids ↓1,25-VitD production by activated macrophages, inhibit intestinal calcium absorption and induce CYP24A1, but this cohort is often resistant. Pregnancy upregulates 1-hydroxylase, rendering patients with CYP24A1 mutations sensitive to hypercalcemia. Antiparathyroid therapy options are limited. To limit adverse impact on maternal and fetal health, delivery may be required.

Maternal hypercalcemia with CYP24A1 mutations

POI473

A Case of Medication-Induced Hypercalcemia: But It Is Not What You Think

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Introduction: Hypercalcemia is a life-threatening complication of CKD. Patients with diabetes mellitus, congestive heart failure, and those receiving renin angiotensin aldosterone inhibitors are at particularly high risk of developing hypercalcemia. We present a case of hypercalcemia, possibly related to patiromer.

Case Description: A 71-year-old man with past medical history of hypertension, right nephrectomy for renal cell cancer and chronic kidney disease stage GIIIb-IV A3. Serum Cr levels range was 3.5-3.9 mg/dL. Patient was placed on losartan 100 mg to slow the progression of his CKD, and as a result he developed mild to moderate hypercalcemia (5.6-2.6 mM/dL). His hypercalcemia persisted despite dietary modification. Patiromer was begun at a dose of 8.4 g/day. Dose was uptitrated to 25.2 g/day to maintain potassium levels < 5.5 mEq/dL. A few months later he developed mild hypercalcemia with serum calcium levels ranging between 10.4-11.5 mg/dL. The patient was not receiving any oral calcium or vitamin D supplements. His work up included 25 hydroxy Vit D and 1-25 dihydroxy vitamin D levels which were normal at 28 ng/mL and 40 pg/mL respectively. Magnesium levels were normal 1.8-2.0 mg/dL. His PTH level was suppressed for his level of kidney function at 13pg/mL. TSH level was normal at 4 mIU/L. PTH-rp was 13 (normal: 14-27). Urine and serum protein electrophoresis did not reveal paraproteinemia. Given the absence of a clear explanation for his non-PTH mediated hypercalcemia, patiromer was considered as a possible cause. Patiromer was stopped and zirconium cyclosilicate was started. Serum Ca levels began to decline and returned to normal at 9.8 mg/dl two months after the discontinuation of patiromer.

Discussion: Patiromer is a cation exchange resin approved by the FDA in 2015 for the treatment of hyperkalemia. It binds potassium in exchange for calcium predominantly in distal colon, facilitating increased fecal potassium excretion. Clinical trials that led to the approval of patiromer did not find any increase in serum calcium levels. However, hyperparathyroidism was noted. This prompted the recommendation for the need to monitor magnesium levels while receiving the drug. There are only two other reports in the literature of hypercalcemia attributed to patiromer. Our findings call for further investigation and the need for monitoring serum calcium following the initiation of this treatment.

POI474

An Unusual Source of Hypercalcemia

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Introduction: Hypercalcemia is a common electrolyte abnormality seen in daily practice. This case describes elevated serum calcium from a common cause, but an unexpected source.

Case Description: A 62-year-old female presented with complaints of fatigue, weight loss, and weakness. She was found to have a calcium level of 14mg/dl, acute kidney injury with a creatinine of 2.9 mg/dl from a baseline of 1.6mg/dl, and severe weight loss of 60lbs in the past 6 months. She had been evaluated for malignancy with no concerning findings. Initial workup included: parathyroid hormone (PTH) 8pg/mL, 25, vitamin D 22ng/mL, and creatinine phosphokinase 75u/L. There was concern for occult malignancy so further workup included a serum and urine protein electrophoresis that was negative, parathyroid hormone-related protein (PTHrp), 1,25 dihydroxy vitamin D, and Histoplasma antigen. She had a full-body computed tomography (CT) scan without contrast to look for occult malignancy which was negative for any granulomas, masses, adenopathy, or bony lesions. 1.25 vitamin D was elevated at 238 pg/mL. PTHrp was
elevated at 5.4 pmol/L. It was thought that Positron Emission Testing (PET) was needed and showed extensive skeletal muscle uptake that was nonspecific. With this result, she underwent a biopsy of the quadriceps muscle. She then had electromyography consistent with myositis with a nonspecific pattern. The muscle biopsy showed non-necrotizing intramuscular granulomas consistent with sarcoid-like myositis. She was started on prednisone 60mg daily. Within three days, her serum calcium had decreased to normal.

**Discussion:** Sarcoidosis is a multisystem disorder of unknown etiology, which is characterized by the accumulation of nonnecrosing granulomas involving tissues. The pathogenesis is unclear, but the histopathologic findings of sarcoidosis in the muscles appear to be granulomatous inflammation in muscle that leads to muscle fibrosis and tissue injury. The most common is a chronic myopathy with insidious onset of proximal muscle weakness. In our case, the elevated serum calcium and creatinal guided the diagnosis. Hypercalcemia in granulomatous disease has been described to be secondary to high levels of calcium that increase intracellular reabsorption of calcium. Sarcoidosis, though a common entity, can declare itself through extrapleural sources and must remain in the differential for all hypercalcemia cases.

**PO1475**

**Amiloride Effects on Urine Calcium in the Setting of Urolithiasis**

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**Background:** Medical management of urolithiasis often targets the biochemical properties of urine to prevent further development of stone burden. Thiazide diuretics are commonly used for recurrent stone formation in patients with hypercalcemia. However, data related to the use of thiazide-sparing diuretic amiloride is relatively scarce and the aim of this study is to investigate amiloride’s effects on urinary calcium and other properties of urine in prevention of urolithiasis.

**Methods:** All nephrolithiasis patients who were prescribed amiloride for treatment of hypercalcemia between the years 2011 and 2019 at a single tertiary care center were retrospectively reviewed. Patients met criteria if they had a pre and post treatment 24 hour urine collections. Pre and post urinary calcium levels were compared. Other comparative measures include levels of other stone risk factors measured on urine collections, stone events on treatment and adverse reaction to medications.

**Results:** A total of 31 patients were started on amiloride. Of those, 15 patients tolerated the medication and completed follow-up urine testing. Amiloride was given due to intolerance of thiazide (11, 73%), persistent hypercalcuria on thiazide (3, 20%), or as combination with thiazide (1, 7%). Maximum treatment dose ranged from 2.5 mg daily to 5 mg BID. Mean duration on treatment was 57.2 months (SD 32.5-96). Three (20%) patients stopped due to delayed intolerance and 2 (13%) due to elevated urinary calcium. In the overall cohort, there was no significant difference in urine parameters (Table 1) including urinary calcium (286.3 mg/g creatinine vs 310.0 mg/g creatinine, p=0.552). Three (20%) had a stone event at a mean of 23.3 months on treatment with 1 surgery, and 2 passage of stones. Six (40%) patients showed metabolic activity with new or growing stones.

**Conclusions:** In patients that have failed thiazides for treatment of hypercalcuria, switching to or adding amiloride did not result in lower urinary calcium levels. 24 Hour Urine Parameters before and after amiloride treatment

**PO1476**

**Hospital-Acquired Phosphate Derangements and Associated In-Hospital Mortality**

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**Background:** We aimed to report the incidence of hospital-acquired hypophosphatemia and hyperphosphatemia along with their associated in-hospital mortality.

**Methods:** We included 15,869 adult patients hospitalized at a tertiary medical referral center from January 2009 to December 2013 that had normal serum phosphate levels at admission and at least two serum phosphate measurements during their hospitalization. The normal range of serum phosphate was defined as 2.5-4.2 mg/dL. In-hospital admission and at least two serum phosphate measurements during their hospitalization. Admissions that had hypophosphatemia and hyperphosphatemia were defined as hospital-acquired if both hospital-acquired hypophosphatemia and hyperphosphatemia were 35% and 27%, respectively. Hospital-acquired hypophosphatemia and hyperphosphatemia were associated with odds of 1.56 and 2.60 for in-hospital mortality, respectively (P-value=0.001 for both). Compared with patients with persistently normal in-hospital phosphate levels, patients with hospital-acquired hypophosphatemia only (OR 1.64), hospital-acquired hyperphosphatemia only (OR 2.74), and both hospital-acquired hypophosphatemia and hyperphosphatemia (i.e., phosphate fluctuations; OR 4.00) were significantly associated with increased in-hospital mortality (all p<0.001).

**Discussion:** Hospital-acquired serum phosphate derangements affect approximately half of hospitalized patients and are associated with increased in-hospital mortality rate.

Association between hospital-acquired serum phosphate derangements and in-hospital mortality

**PO1477**

**Pseudohyperphosphatemia Caused by Severe Leukocytosis in a Patient with Chronic Lymphocytic Leukemia (CLL) and Tumor Lysis Syndrome (TLS)**


**Introduction:** TLS is an oncologic emergency, which can cause life-threatening electrolyte derangements. Classical laboratory abnormalities in TLS include hypercalcemia, hyperkalemia, hypocalcemia, and hyperuricemia. In cases of severe hyperleukocytosis, false laboratory abnormalities can occur, and can lead to apply inaccurate, potentially harmful treatments.

**Case Description:** A 71-year-old man with a history of CLL was admitted for dyspnea and volume overload. He had recently started venetoclax one week prior to presentation. Labs revealed a WBC of 79,300/mm3 (33% blasts), creatinine 1.49 mg/dL (baseline 0.80 mg/dL), serum potassium 7.2 mmol/L, CO2 8 mmol/L, calcium <5.0 mg/dL, and uric acid 9.2 mg/dL. He was diagnosed with TLS associated with venetoclax. Despite aggressive phosphorus repletion, the patient remained severely hypophosphatemic, though he was never symptomatic. Given the incongruence between lab values and clinical status, we suspected a lab error. We ordered STAT labs, sent on ice, which revealed normal serum phosphorus (4.5 mg/dL) on the same day that labs processed by standard protocol revealed a low level (0.9 mg/dL). Other discordant results noted were hyperkalemia (>9.5 mmol/L but 3.7 on a point-of-care arterial blood sample), hypoxia (pO2 ~48 mmHg on ABG but 98% on pulse oximetry room air), and hypoglycemia (serum blood glucose 9 mg/dL but 86 on point-of-care finger testing).

**Discussion:** This abstract reports the first case of reported pseudohyperphosphatemia in a patient with CLL. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be due to increased metabolic demands by blasts, which decrease oxygen tension and glucose levels in vitro. Increased leukocyte fragility in CLL patients. The pathophysiology of pseudohyperphosphatemia is thought to involve a sodium-phosphate co-transporter, though the exact underlying pathophysiology is unknown. Pseudohyperphosphatemia and pseudohypocalcemia, also described in hematologic disorders, are thought to be...
Discussion: Hypermagnesemia is a rare event and occurs in the context of high Mg intake (i.e., esophageal stricture treatment) or Mg administration in acute or chronic kidney disease. Mg acts as a calcium channel blocker, causing hypotension, bradycardia, muscle paralysis, somnolence, hypocalcemia, respiratory failure, and eventually cardiac arrest. The severity of manifestations is concentration dependent. Management includes IV fluid administration to dilute Mg and calcium (if the patient is making urine). Hemodialysis is often required for those with severe AKI or ESRD. This case illustrates the challenges of care coordination and duplicate medication prescribing among multiple physicians/practices. OIC was preventable with a bowel regimen. She received 3 different NSAIDs which decreased her expected renal function. Magnesium citrate was rapidly absorbed systemically in the context of ileus and Mg toxicity developed in the setting of low GFR. Nephrology consultation was delayed, resulting in prolonged severe hypotension, late hemodialysis initiation and ultimately death. These complications were entirely avoidable with a more thoughtful approach to medication prescribing.

POI1479
Constipation to Neuromuscular Deficits: A Case of Hypermagnesemia
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Introduction: Magnesium is a relatively safe over-the-counter cathartic and antacid, but may have dangerous side effects. Hypermagnesemia can be precipitated by renal insufficiency, active gastrointestinal illness, or excessive intake of magnesium-rich food. Symptoms, which include neuromuscular and cardiovascular effects, can start when levels exceed 4.8mg/dL.

Case Description: A 60-year-old female with a medical history of bipolar affective disorder, seizures, migraines, type 2 diabetes, and past subarachnoid hemorrhage was discharged with a magnesium level of 2.3mg/dL. Her electrolytes and kidney function continued to correct with hydration, diuretics. Her electrolytes and kidney function continued to correct with hydration, diuretics.

Discussion: Case demonstrates the importance of physician awareness regarding the effects of hypermagnesemia. Although hypermagnesemia is multiple symptoms, “few clinicians associate these symptoms with high levels of serum magnesium, due to an overall unfamiliarity with this condition.” An article reported that more than 86% of patients with hypermagnesemia are clinically unrecognized, and in most hospitals, the measurement of magnesium is based on the physician’s judgement. Treatment consists of magnesium removal (IV fluids, loop diuretics, or dialysis), stopping magnesium use, and gastrointestinal decontamination. Calcium can also be used as an antagonist by competitively inhibiting magnesium. Prompt recognition is necessary because when magnesium levels are greater than 7.2mg/dL, patients can develop hemodynamic changes (bradycardia, hypotension) and once levels exceed 12mg/dL, symptoms can become fatal (respiratory failure, heart block, cardiac arrest, and flaccid quadriplegia).

POI1480
Clinicopathological Characteristics and Long-Term Prognosis of Monoclonal Immunoglobulin Light-Chain-Associated Fancconi Syndrome
Jiaying Li, Xiaoxiao Shi, Peng Xia, Limeng Chen. Peking Union Medical College Hospital, Dongcheng-qu, China.

Background: Monoclonal immunoglobulin light chain-associated Fancconi syndrome (LC-FS) is a rare disease which involved the proximal tubules. As most of the cases came from western countries, we aimed to analyze the clinicopathological characteristics of Asian LC-FS and its long-term prognosis. Methods: From January 1998 to February 2019, 26 patients who were diagnosed with both FS and monoclonal gamopathy in Peking Union Medical College Hospital were retrospectively reviewed. Results: At diagnosis, the mean age of the 26 Asian LC-FS patients was 54.7±14.7 years, with females accounting for 57.7%. The underlying malignancies included monoclonal gammopathy of renal significance (MGRS), n=14 (53.8%), multiple myeloma (MM, n=10, 38.5%), Waldenstrom macroglobulinemia (WM, n=1) and primary plasma cell leukemia (PPCL, n=1). The most common symptoms were fatigue (95.7%), asthenia (88.5%) and nocturia (61.1%). Their mean eGFR was 68.0 (6.0 to 26.4) mL/min/1.73m², with different degrees of proximal tubular dysfunctions, including normoglycemic glomerulonephritis (88.0%), hyperphosphaturia (84.2%), aminoaciduria (84.0%), hypouricemia (80.8%), hyperphosphatemia (80.8%), RTA (73.1%), and hypokalemia (42.3%). For kidney function, different degrees of proximal tubular dysfunctions, including normoglycemic glycosuria was discharged with a magnesium level of 2.3mg/dL. Her electrolytes and kidney function continued to correct with hydration, diuretics.

Discussion: Case demonstrates the importance of physician awareness regarding the effects of hypermagnesemia. Although hypermagnesemia is multiple symptoms, “few clinicians associate these symptoms with high levels of serum magnesium, due to an overall unfamiliarity with this condition.” An article reported that more than 86% of patients with hypermagnesemia are clinically unrecognized, and in most hospitals, the measurement of magnesium is based on the physician’s judgement. Treatment consists of magnesium removal (IV fluids, loop diuretics, or dialysis), stopping magnesium use, and gastrointestinal decontamination. Calcium can also be used as an antagonist by competitively inhibiting magnesium. Prompt recognition is necessary because when magnesium levels are greater than 7.2mg/dL, patients can develop hemodynamic changes (bradycardia, hypotension) and once levels exceed 12mg/dL, symptoms can become fatal (respiratory failure, heart block, cardiac arrest, and flaccid quadriplegia).

POI1482
Metformin-Associated Lactic Acidosis and Blindness
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Introduction: Metformin, a first line medicine in the treatment of diabetes mellitus, can rarely cause lactic acidosis, usually in patients with acute or chronic kidney disease stage III onwards. We report a case of blindness associated with severe lactic acidosis in a patient with diabetes on metformin and show that the ophthalmologic symptoms may not be a direct result of the severe lactic acidemia. Case Description: A 77 year old female with CKD stage III and type 2 diabetes on metformin twice daily developed confusion, hypoglycemia and sudden visual loss. Over the prior 3 days, she had nausea, vomiting and diarrhea as well as a reduced urine output. On admission to the hospital, her vitals were stable. She had no other focal neurological deficits. Her creatinine was 4.4 mg/dL (with a baseline of 1.4), potassium 5.9 meq/L, bicarbonate 3 meq/L and blood lactate 23.8 mmol/L. Her arterial blood pH was 6.7. She underwent emergent hemodialysis and mid-way through her 4 hour session, she had complete resolution of her visual loss. By the end of her dialysis, her bicarbonate rose to 18. Ultimately, in a few months, she recovered her renal function back to a serum creatinine of 1.8-1.9, a little higher than her baseline. Discussion: Some publications suggest vision loss (due to effect on retinal horizontal cell function) and optic nerve ischemia are associated with metformin induced lactic acidosis (MALA) at pH <7.09. It improves after correction of acidosis. But, in our case, the vision improved even before the acidaemia corrected. We suggest that, since acute reversible blindness has been described with MALA, but not in patients with hypotension- or sepsis-induced lactic acidosis, this neurologic symptom may be a direct result of abnormal retinal horizontal cell function induced by metformin at a low pH, or the metabolic effects of metformin, rather than due to the acidaemia alone. Hemodialysis helps correct electrolyte abnormalities and lactic acidosis. Also, metformin has a large volume of distribution. Its removal by dialysis is uncertain. But there are some case reports suggesting its clearance by HD. Further studies are thus warranted.
PO1483

Metabolic Acidosis Is a Predictive Factor for All-Cause Mortality in Patients with CKD

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Background: The consequences of metabolic acidosis are wide-ranging, consistent with the fact that many critical cell functions require physiologic pH (Salamah Al, Am J Physiol Regul Integr Comp Physiol 2014). The extent to which metabolic acidosis contributes to mortality in patients with chronic kidney disease (CKD) is unknown.

Methods: Optum®-de-identified Electronic Health Records dataset 2007 to 2017 was queried to identify patients with non-dialysis CKD Stages 3–5 with bicarbonate tests 28–365 days apart, at least two consistent serum bicarbonate tests in 2 years, at least one year of follow-up and at least 2 years of post-index data or who died during that period. Cohorts with metabolic acidosis and normal serum bicarbonate were established based on the baseline serum bicarbonate (12 to < 22 mEq/L or 22 - 29 mEq/L). All-cause mortality was measured at 2 years in patients with metabolic acidosis vs. normal serum bicarbonate at baseline. The impact of baseline serum bicarbonate on 2-year mortality, adjusted for age, sex, race, diabetes, hypertension, heart failure, Charlson Comorbidity Score (index of comorbidity burden), and baseline eGFR and log albumin-to-creatinine ratio (ACR) was evaluated using logistic regression models.

Results: 51,558 patients qualified for analysis; 17,350 with metabolic acidosis, and 34,208 with normal serum bicarbonate at baseline. Unadjusted rates of mortality within 2 years were higher among patients with metabolic acidosis vs. normal serum bicarbonate (30.9% vs. 10.2%, respectively, P < 0.0001) and within all CKD stages (P < 0.001). Each 1 mEq/L lower serum bicarbonate value was independently associated with a 15% higher risk of all-cause mortality, OR: 0.853, 95% CI: 0.846-0.861. These findings were consistent in subgroup and sensitivity analyses.

Conclusions: The presence of metabolic acidosis was associated with a high 2-year risk of all-cause death in patients with CKD. This finding was independent of age, sex, race, pre-existing comorbidities, and baseline eGFR and ACR.

Funding: Commercial Support - Tricida, Inc.

PO1485

Lactate Gap as Initial Indicator for Ethylene Glycol Toxicity

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Introduction: Ethylene glycol poisoning is a medical emergency which on initial presentation can be missed if the clinician does not have a high index of suspicion. Treatment of ethylene glycol toxicity is time dependent in preventing morbidity and mortality; thus early recognition and intervention is of critical value. In this case report we aim to focus on the lactate gap as the first indicator of ingestion.

Case Description: 50-year-old female was brought in by EMS after being found unresponsive and covered in vomitus. Vital signs were stable. The patient was thought to have had a seizure causing the lactate acidosis and was post ictal. Labs are shown below. Ethylene glycol toxicity was made the presumptive diagnosis. The patient was transferred to the medical ICU and given a loading dose of fomepizole while hemodialysis was being arranged. The patient then had one session of hemodialysis in the medical ICU and repeat blood gas is displayed below.

Discussion: The diagnosis of ethylene glycol poisoning remains challenging due to non-specific signs and symptoms on presentation. Presentation and lab values may differ depending on the time and amount since ingestion. Access to real-time ethylene glycol concentration is uncommon in many health facilities, so the diagnosis relies upon a high index of suspicion. Laboratory studies, specifically the “lactate gap”, can be used in aiding the diagnosis. The “lactate gap” is a lab artefact due to a chemical cross reaction. Most POC whole blood analyzers use the enzyme lactate oxidase which cross reacts with the breakdown products of ethylene glycol, specifically glycolate. The lab instrument cannot differentiate between lactate and glycolate because of their structural similarity.

Laboratory serum analyzers which are used for routine venous blood samples have less cross-reactivity and thus show a minimal elevation of lactate in comparison. In addition to securing the diagnosis, the lactate gap can be used to monitor clearance of the metabolites.

PO1486

Anion Gap (AG) and Negative Osmotic Gap (OG) due to Remdesivir’s (R) Excipect

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The FDA advises against using R in adults with eGFR ≤ 30 ml/min unless the potential benefit outweighs the potential risks because SBECD accumulates. We report 2 cases of AG with the FDA protocol.

Case Description: Case A: 77 obese © with bilateral AKA, and initial serum creatinine (Scr) of 1 mg/dL, currently decreasing (0.6 mg/dL). On day 5 R was initiated while a mild ketosis resolved (β OH-butyrate 0.6–0.3→0.1 mmol/L). An AG as high as 16 mmol/L (Alb→2 g/dL) ensued, wherein the AG of the 1st blood sample after each R infusion correlated inversely with the time elapsed after the infusion. Like ketones, lactate was low throughout R therapy. By the time R started, Scr had risen and plateaued at 1.8 mg/dL and the AG mirrored the subsequent increase and decrease in Scr, and vanished by day 9, when her Scr was 1.7, after peaking at 2.6 mg/dL, in spite of continuing R, consistent with SBECD cleared by GFR, like cr. Her initial normal Scr already meant AKI in this elderly sedentary, bilateral AKA patient. Her OG, only 7 on day 2 of R, further decreased by 11, to a negative OG of –4 mOsm/Kg H2O the next day, suggesting polyanion accumulation. The calculated osmolarity of a Na SBECD solution is (n – 1)×Na[Na] = 1.5×[Na], not 2×[Na] since n = 6.5, which explains the negative OG. Case B: 42 ©, with morbid obesity and initial Scr of 1 mg/dL. R started on day 2, as Scr rose fast but her AG was 10 mmol/L. Again, the AG rapidly rose to 16 mmol/L (Alb→2→2 g/dL), and paralleled the rise and drop in Scr. CRRT was started when Scr was 6 mg/dL. Here again, prior to CRRT the AGs of the 1st samples following each R infusion were inversely related with the time from R infusion. While R was continued, CRRT caused parallel decreases in AG and Scr, since it clears cr and SBECD equally. The R loading dose contains 6 g and the 9 subsequent daily doses 3 g SBECD. Since the mass of SBECD is 2163.83 mg, the initial anion gap ≤ 18 mmol/L, following initial daily R.

Discussion: Depending on plasma volume, rate of escape from plasma, GFR, and timing after the infusion, SBECD can cause an AG, and negative OG, when the GFR is low.
POI1487
Anion Gap and Cardiovascular Mortality
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Background: Anion gap has been shown to be independently associated with hypertension, but the association of anion gap and cardiovascular mortality has been unexplored.
Methods: We conducted a prospective cohort study using the National Health and Nutrition Examination Survey (NHANES), a nationally representative cross-sectional survey of the US non-institutionalized population. Anion gap (mEq/L) was calculated as serum sodium (mmol/L) – (serum chloride (mmol/L) + serum bicarbonate (mmol/L)). We used weighted Cox proportional hazards models to assess the associations between anion gap with cardiovascular specific mortality, as recorded by the National Death Index. Multivariable models were adjusted for demographics data, BMI, smoking status, diabetes, systolic blood pressure, cardiovascular disease history, ACEi/ARB, diuretics, serum albumin, total cholesterol, total protein, total calorie intake, hemoglobin, cancer diagnosis, eGFR and urine albumin and creatinine ratio.
Results: This study was performed on 39,189 participants [mean (SD) age, 46.86 (19.25) years; 20,194 (51.5%) female]. During 875 (4436210 weighted) person-years of follow-up, 936 participants (3169889 weighted participants) died of cardiovascular disease. A history of cardiovascular disease at the time of enrollment was reported in 3875 of follow-up, 936 participants (3169889 weighted participants) died of cardiovascular disease. In analyses restricted to those with a history of cardiovascular disease at baseline and excluding those with a history of cardiovascular disease at baseline, the risk of mortality in adults.
Conclusions: Higher anion gap may be a risk factor for cardiovascular-related mortality in adults.

POI1488
Profound Lactic Acidosis due to Dextrose Infusion and the Role of Thiamine
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Introduction: Severe metabolic acidosis due to dextrose infusion is a rare but life-threatening complication for which treatment options are poorly described. Normally dextrose is metabolized to pyruvate during glycolysis. Pyruvate is converted to acetyl-CoA via pyruvate dehydrogenase (PDH); this requires abundant oxygen. Thiamine is an essential cofactor of PDH. During anaerobic conditions, pyruvate is converted to lactate during a process known as anaerobic glycolysis, producing a type A lactate. Pyruvate may also be converted to lactate when oxygen levels are normal via aerobic glycolysis. Aerobic glycolysis produces type B lactate and occurs due to a number of conditions, including thiamine deficiency.
Case Description: A 54-year-old woman with malignant insulinoma was admitted for severe hypoglycemia. The patient was given continuous 20% dextrose infusion; she developed severe lactic acidosis on day seven. Serum bicarbonate was undetectable on blood gas at the time of renal consult; serum lactate was >20. The patient became unstable due to the acidosis, became obtunded, was intubated, and was placed on continuous renal replacement therapy (CRRT). The acidosis failed to improve for 36 hours. Thiamine deficiency was suspected and thiamine level was confirmed in this patient, thiamine deficiency was suspected and thiamine level was confirmed to be low at 59 mmol/L (normal 78-185). Supplementation was initiated with rapid normalization of lactic acidosis.
Discussion: Thiamine is essential for normal aerobic metabolism, and its deficiency may lead to accumulation of pyruvate and conversion to lactate. Because thiamine is water soluble, its stores are limited. Thiamine deficiency can occur readily if intake is suboptimal in people who have risk factors, such as long-term heavy alcohol ingestion in this patient. Thiamine deficiency is a potential cause of lactic acidosis that is reversible with supplementation. A high index of suspicion is necessary for diagnosis in patients with risk factors but no other apparent cause of lactic acidosis.

POI1489
Persistent Lactic Acidosis due to Thiamine Deficiency
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Introduction: Lactic acidosis is one of the most common causes of metabolic acidosis in hospitalized patients. Clinically it is usually associated with obviously impaired tissue oxygenation, but also occurs in situations where systemic impairment in oxygenation does not exist or is not readily apparent. Here we present a case of persistent lactic acidosis found to be due to thiamine deficiency and resolved rapidly after thiamine supplementation.
Case Description: A 38 year-old woman presented with 4 day-history of abdominal pain, vomiting, diarrhea, and not able to eat. She has a history of alcoholism in remission, vitamin B12 deficiency, PTSD and bipolar disorder. Her medications included cyproheptadine, disulfiram, lithium, trazodone, and ziprasidone. Vital signs were normal except for mild sinus tachycardia, and the rest of her examination was unremarkable. Laboratory results indicated normal CBC, glucose, BUN, Cr, LFT, and urine analysis. Serum Na, K, Mg, Ca, and PO4 were all low. Serum ethanol and salicylate were not detected, and urine drug screen was negative. Serum HCO3 was low at 14 mmol/L with anion gap of 26. Serum ketone was negative, but serum lactic acid was severely elevated at 9 mmol/L. ABG was consistent with compensated metabolic acidosis. Cardiac echo and other imaging studies did not reveal significant abnormalities. The patient received intravenous fluid replacement and supplementation for various electrolyte abnormalities. While her symptoms of gastroenteritis had improved, the serum lactic acid continued to remain high (7-9s). Since most of the apparent causes of lactic acidosis were excluded in this patient, thiamine deficiency was suspected and thiamine level was confirmed to be low at 59 mmol/L (normal 78-185). Supplementation was initiated with rapid normalization of lactic acidosis.
Discussion: Thiamine is essential for normal aerobic metabolism, and its deficiency may lead to accumulation of pyruvate and conversion to lactate. Because thiamine is water soluble, its stores are limited. Thiamine deficiency can occur readily if intake is suboptimal in people who have risk factors, such as long-term heavy alcohol ingestion in this patient. Thiamine deficiency is a potential cause of lactic acidosis that is reversible with supplementation. A high index of suspicion is necessary for diagnosis in patients with risk factors but no other apparent cause of lactic acidosis.

POI1490
Methanol Intoxication Secondary to Adulterated Cane Alcohol “El Chorrito”
Introduction: Methanol intoxication is a rare and lethal form of poisoning that may cause severe anion gap and osmolar metabolic acidosis (MA), visual disturbances, neurological dysfunction and death. We present a group of seven unrelated cases with methanol intoxication from cities in southern Mexico of a total of 106 intoxicated patients and 43 deaths reported.
Case Description: Upon arrival to Hospital Civil of Guadalajara a group of seven patients presented with severe MA, high anion and osmolar gap, neurologic and visual deterioration, respiratory failure requiring mechanical ventilation and hemodynamically unstable requiring vasopressor. Intake of methanol was accidental, since a batch of adulterated alcoholic bottles was identified and distributed by “El Chorrito” store. Methanol concentrations is not available in our hospital. CT Scan revealed hemorrhage in basal ganglia and white matter involvement in all of them. Fomepizole is not available in Mexico so an ethanol infusion with vodka was started. All patients initiated hemodialysis (HD) as soon as possible and all underwent at least two sessions. Acid base balance was restored but five (71%) of the seven patients died. The remaining two patients persist in critical conditions requiring mechanical ventilation, no neurologic response and vasopressor dependent.
Discussion: This case series illustrates the poor clinical outcomes suffered by patients with methanol poisoning and the limitations of our public health system. Unfortunately the time lapse upon arrival was prolonged and organ damage irreversible leading to mortality in the majority of the cases.
**PO1491**

**Starvation Ketoacidosis in a Patient with Muscular Dystrophy**  
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**Introduction:** Patients with muscular dystrophy have low muscle mass; thus, they have lower glycogen stores and are more prone to develop ketoacidosis with minimal stress or decreased oral intake. Here we present a rare presentation of ketoacidosis in a patient with muscular dystrophy with concurrent ketoacidosis and hyperchloremic metabolic acidosis who was treated successfully with lactated Ringer’s (LR) and dextrose (D5W).

**Case Description:** A 48 year old woman with a history of muscular dystrophy and chronic, ventilator dependent respiratory failure was referred to our hospital for evaluation of granulation tissue in her trachea. Body mass index was 18 kg/m². Laboratory data on admission were significant for sodium of 132 meq/L, potassium of 4.5 meq/L chloride 114 mEq/L, bicarbonate 12 mEq/L, creatinine < 0.1 mg/dL, and pH 7.23 (venous blood gas) consistent with non anion gap metabolic acidosis. The following day, laboratory data showed sodium 137 mEq/L, chloride 113 mEq/L, bicarbonate 8 mEq/L, and pH 7.29. The calculated anion gap was 16 mEq/L with albumin 4.2 g/dL. The urine anion gap was 30 mmol/L. Serum β-hydroxybutyrate (BHB) was elevated at 6.6 mmol/L. Because of muscular dystrophy with decreased oral intake, the patient’s anion gap metabolic acidosis was attributed to starvation ketoacidosis. The non anion gap metabolic acidosis was attributed to renal tubular acidosis. LR and D5W solutions were administered to treat non anion gap and anion gap metabolic acidosis (starvation ketoacidosis), respectively. After 1-2 days, BHB decreased and electrolytes normalized.

**Discussion:** Few cases have been reported regarding ketoacidosis in patients with muscular dystrophy, and all of these were treated with dextrose and 0.9% saline. In our case, we used LR and D5W due to concurrent non anion gap and anion gap metabolic acidosis, as 0.9% saline administration was projected to worsen the hyperchloremic acidosis. Anion gap metabolic acidosis in patients with muscular dystrophy and without diabetes should raise suspicion for starvation ketoacidosis requiring D5W. LR should be substituted for 0.9% saline in patients with concurrent hyperchloremic acidosis.

**PO1492**

**Metabolic Acidosis Associated with Linezolid Toxicity**  
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**Introduction:** Linezolid is an oxazolidinone antibiotic that inhibits bacterial protein synthesis. It can impair mitochondrial ribosomal function leading to severe lactic acidosis, liver toxicity and myelosuppression.

**Case Description:** A 65-year-old Caucasian woman with PMH of compensated NASH cirrhosis, osteomyelitis diagnosed 4 weeks prior to presentation and now on linezolid, was admitted with abdominal pain. Her vital signs and cardiopulmonary exam were unremarkable. Her abdomen was distended with mild epigastric tenderness. Figure 1 outlines the initial laboratories. Urinalysis was benign and blood cultures were negative. CT abdomen revealed moderate ascites. The anion gap metabolic acidosis (AGMA) were likely explained by Linezolid toxicity. The respiratory alkalosis is related to liver cirrhosis which is associated with increased level of progesterone leading to hyperventilation. Linezolid was stopped and repeat laboratories at 72 hours demonstrated normalization of bicarbonate and lactate values.

**Discussion:** Our patient has a primary AGMA (Corrected AG = 31) with mild respiratory alkalosis (calculated PaCO2 by Winter’s formula = 23). She had an osmolar gap of 5 (The calculated osmolarity = 282 mOsm/kg). The AGMA is likely secondary to lactic acidosis (figure 2). The patient does not have signs of hypovolemia. Ethylene glycol (EG) can lead to a false elevation in L-lactate. However, the normal OG makes EG and methanol toxicity less likely. Normal beta hydroxybutyrate level excludes ketoacidosis. Major risk factors for linezolid toxicity include prolonged exposure, administration of relatively higher doses, and baseline chronic liver or kidney disease. Lactic acidosis often resolves rapidly following discontinuation of Linezolid.
POI493

The Real Life of Oral Alkalization by Urologists and Nephrologists on Extracellular Volume: The AlcalUN Study

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Background: Oral alkalization with sodium bicarbonate (NaHCO3) or citrate is prescribed to treat conditions ranging from metabolic acidosis to nephrolithiasis. While most nephrologists/urologists use these treatments regularly, extracellular volume (ECV) increase is a main feared adverse event for NaHCO3 use. To date, no clinical trial has specifically addressed this aspect in clinical routine.

Methods: AlcalUN (NCT03035812) is a multi-center, prospective, open-label study aiming to evaluate the impact of a chronic oral alkalization on ECV. Patients receiving oral alkalization without NaHCO3 (citrate) comprised the control group. Increased ECV (primary outcome) was assessed based on body weight (BW), blood pressure (BP), and edema at first follow-up visit.

Results: From 02/2017 to 02/2020, 156 patients were enrolled (129 received NaHCO3, 27 citrate). Out of them, 127 (80%) patients had at least one follow-up visit. Normalizing for demographics, patients in the NaHCO3 group had higher incidence of chronic kidney disease (68 vs. 30%, p<0.002) and hypertension (75 vs. 55%, p=0.001), while patients in the No-NaHCO3 group (citrate) had more nephrolithiasis (95 vs. 62%, p=0.001). At baseline, BW, BP, and presence of edema were similar in both groups. After a median of 90 days of treatment, 91 (72%) patients reached the primary outcome, with a median of 90 days of treatment, 91 (72%) patients reached the primary outcome, with similar distribution in both groups (71 vs. 75%, p=0.79). We found similar results after propensity score matching.

Conclusions: Chronic oral alkalization with NaHCO3 does not increase ECV more than citrate, even though it is used in a higher-risk population. These results confirm secondary outcomes from other trials, potentially highlighting the role of chloride load instead of sodium load.

POI494

Effect of Sodium Bicarbonate on Kidney Injury: A Secondary Analysis of the BASE Pilot Trial

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Background: NaHCO3 is used to treat metabolic acidosis in CKD. In the Bicarbonate Administration to Stabilize eGFR (BASE) Pilot trial, a dose-dependent increase in albuminuria was observed with NaHCO3 over 28 weeks, suggesting that NaHCO3 may promote kidney injury. We investigated the effect of NaHCO3 on kidney tubule injury markers (KIM-1 and NGAL) in BASE participants.

Methods: Urinary KIM-1 and NGAL were measured in 176 BASE participants at baseline, week 12, and week 28. Change in urinary KIM-1/Cr and NGAL/Cr was compared within and between the three treatment groups (Placebo, n=49; Lower-Dose [0.5 meq/kg/d] NaHCO3, n=48; and Higher-Dose [0.8 meq/kg/d] NaHCO3, n=79) using linear mixed models.

Results: Mean±SD baseline values were: age 67±12 years, systolic BP 126±13 mm Hg, eGFR 36±9 ml/min/1.73m2, serum iCO2 24±2 meq/L. Median (IQR) urinary values at baseline were: KIM-1/Cr 185 (24, 767) mg/mg, M1/Cr 0.88 (0.43, 1.36) mg/mg, and NGAL/Cr 14.3 (6.44, 34.0) ng/mg. At week 12, urinary KIM-1/Cr levels were not different from baseline in any group. However, at week 28, KIM-1/Cr levels were significantly lower in all three groups. NGAL/Cr was significantly higher in the Higher-Dose NaHCO3 group at week 12; however, there were no other significant within group differences at week 12 or 28. In the between group comparisons, there were no significant differences in KIM-1/Cr (p=0.16) or NGAL/Cr (p=0.07) at either week 12 or 28.

Conclusions: Among BASE Pilot Trial participants, NaHCO3 had no significant effect on urinary KIM-1/Cr or NGAL/Cr levels over 28 weeks.

Funding: NIDDK Support
PO1496
It’s Not a Bad Trip with This Acid: Sodium Thiosulfate Use in Refractory Metabolic Alkalosis
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Introduction: Metabolic alkalosis is often a complication of loop diuretic use. It may at times become rate limiting. Serum bicarbonate (HCO3) levels upwards of 30 mmol/L can make even the most eager clinician stop dead in their tracks in the quest for optimal volume control.

Case Description: Here we highlight two patients, a 63 year old female and an 81 year old gentleman, who while on diuretic therapy developed severe metabolic alkalosis, with peak serum bicarbonate levels of 39 and 44 mmol/L respectively. Several strategies were attempted to mitigate the alkalosis. Potassium was aggressively repleted to maintain a normal serum level of 4.5 and 3.6 mmol/L respectively, however, this was unsuccessful. Acetazolamide was employed but ineffective due to its limited efficacy in the setting of low effective circulating volume and renal insufficiency. Advanced measures such as hydrochloric acid and ammonium chloride were not readily available nor feasible to administer. Ultimately, given the known side effect of sodium thiosulfate (STS) to cause metabolic acidosis, STS was administered, resulting in a decrease in the serum HCO3 level and an ability to resume diuresis.

Discussion: When continued diuresis is necessary and correction of metabolic alkalosis cannot be facilitated by potassium repletion or carbonic anhydrase inhibitors, a novel option is to utilize STS and its known ability to generate an acid load to treat the alkalosis. While the mechanism is unclear, a metabolite of STS, hydrogen sulfide, is proposed to be the source of acid. This strategy for correcting metabolic alkalosis has never been reported in the literature before.

PO1497
A Case of Extreme Alkalosis: A Perfect Combination of Perpetuators
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Introduction: Metabolic alkalosis results from retention of alkali excess. Normally, a physiological response leads to hyperventilation with a secondary increase of PaCO2. The most common cause is H+ loss, through kidney or gastrointestinal tract, usually with concurrent loss of Cl− and K+.

Case Description: 70 y/o caucasian man was admitted for a scheduled surgery due to a stage II urothelial carcinoma. The immediate postoperative period occurred without complications. The patient presented with abdominal distention and gastric stasis. He remained fasting, with gastric tube draining freely. Surgical team performed an exploratory laparotomy with correction of a small bowel internal hernia. In the postoperative period Nephrology collaboration was requested due to acute kidney injury (AKI), with a creatinine (Cr) of 3.39 mg/dL (baseline 1.5 mg/dL) and urea 89.5 mg/dL. On examination the patient was prostrate, severely dehydrated and bradypneic, with oxygen supply FiO2 28%. He maintained gastric passive drainage for 3 days, around 3 to 3.5 L/day. Blood work showed Cr 4.15 mg/dL, urea 103.9 mg/dL, hypokalemia 147 mEq/L, hypochloremia 78 mEq/L, hypokalemia 3.2 mEq/L, uric acid 16.8 mg/dL, albumin 3.2 g/dL and a total corrected calcium 9.5 mg/dL. Urinalysis revealed a pH of 9.0 and arterial blood gas analysis presented severe metabolic alkalosis (pH 7.63, PaO2 90 mm Hg, PaCO2 99 mm Hg, bicarbonate 104.1 mmol/L), low ionized calcium 0.86 mmol/L and lactate 1.9 mg/dL. The patient was immediately admitted in ICU, starting aggressive IV hydration with NaCl 0.9%, IV potassium supplementation and parenteral nutrition.

Discussion: This is an extreme case of metabolic alkalosis where a myriad of contributors gathered in a perfect storm to achieve a bicarbonate concentration above 100 mmol/L, thought to be incompatible with life and, to our knowledge, never reported in the literature before. However, the pH value was maintained in life-compatible values by an extreme respiratory compensation which may have saved the patient before treatment initiation. An approach correcting the cause and, at the same time, the perpetuators are the key factors to successfully treat a metabolic alkalosis. Due to severe AKI and alkalosis, dialysis with low bicarbonate dialysate may be indicated.
Renal Negative Pressure Treatment as a Novel Therapy for Cardiorenal Syndrome

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Background: Decongestion is the primary therapeutic objective in acute decompensated heart failure (ADHF). However, congestion itself can worsen renal function and limit diuresis. Renal pelvic negative pressure treatment (rNPT) should reduce tubular pressure, allowing improved kidney function and diuresis. We hypothesized that rNPT would improve diuresis, natriuresis & renal function in a congestion predominate heart failure (HF) model.

Methods: Ten ~80 kg pigs underwent thoracotomy with implantation of a pericardial, Swan Ganz, & bilateral ureteral JuxtaFlow™ catheters. High dose furosemide (400mg bolus, then 80mg/hr) was administered since HF clinical use of rNPT will be in conjunction with loop diuretics. Each animal served as its own control with randomization of L vs. R kidney to ~30 mmHg rNPT or no rNPT. HF was induced via cardiac tamponade (~200 ml). Decongestion is the primary therapeutic objective in acute decompensated heart failure (ADHF). However, congestion itself can worsen renal function and limit diuresis. Renal pelvic negative pressure treatment (rNPT) should reduce tubular pressure, allowing improved kidney function and diuresis. We hypothesized that rNPT would improve diuresis, natriuresis & renal function in a congestion predominate heart failure (HF) model.

Results: Prior to HF induction, rNPT increased urine output (UO) & creatinine clearance (CrCl) compared to the control kidney during furosemide diuresis (p<0.001 for all, Figure). HF induction achieved the target hemodynamic profile with stable cardiac output & elevated filling pressures (Figure). UO, sodium excretion, & CrCl decreased during HF (p<0.001 for all, Figure), but were higher consistently in rNPT kidney vs. control (p<0.05 for all, Figure). UO (p=0.38) was the same in rNPT during HF as control prior to HF (Figure).

Conclusions: rNPT increased UO and CrCl, with & without HF. Notably, rNPT rescued the congested cardio-renal phenotype with equivalent diuresis & natriuresis during HF with rNPT compared to the non-HF period without rNPT.

Funding: Commercial Support - Jive Labs

Figure 1. (A) Mean 24-h Na+ excretion during 7-d diet. (B) Comparison of the performance of three consecutive spot UCs (blue), single 24-h UC (green) and three consecutive 24-h UCs (red) for estimating Na+ intake (200 mmol/d). Absolute differences between estimated and measured Na+ intake. Data are mean and SD.

Utility of Doppler Ultrasound-Derived Hepatic and Portal Venous Waveforms in the Management of Heart Failure Exacerbation

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Introduction: Careful evaluation of the fluid volume status and systemic hemodynamics is of paramount importance in patients with heart failure. With growing interest in point of care ultrasonography, non-invasive parameters such as hepatic and portal vein waveforms are assuming importance as markers of systemic venous congestion.

Case Description: 43 year old male was admitted for right lower extremity necrotizing fasciitis requiring below the knee amputation. Postoperatively, he subsequently developed volume overload with pulmonary edema and acute renal injury. Given the patient’s sensitive hemodynamic state, volume depletion was driven by doppler ultrasound, specifically portal vein and hepatic vein doppler. After a few days of therapy, the patient had improvement of his renal function, leading to a cessation of dialysis and return of renal function to near baseline.

Discussion: In patients with acute decompensated heart failure, residual clinical congestion at hospital discharge is associated with worse outcomes. A standard assessment of congestion is the measurement of right atrial pressure (RAP) and pulmonary capillary wedge pressures using pulmonary artery catheterization, though its invasive nature precludes routine use. Estimating systolic RAP using inferior vena cava (IVC) ultrasound is now common, though it is not without numerous pitfalls limiting its utility. For example, the changes in size of RAP depend on variations in intrathoracic pressure and lung compliance. Using portal and hepatic vein waveforms can add another piece of information for volume assessment. As shown in our images, the changes initially seen on doppler ultrasound aids in management for decongestive therapy.
Results: A total of 1,099 Chinese CKD patients were recruited, 308 patients were excluded, and 791 patients were finally enrolled in this study. Among them, 291 patients were normotensive and 500 were hypertensive CKD patients. A 1:1 propensity score matching (PSM) analysis was performed with age and estimated glomerular filtration rate (eGFR) matched between 190 normotensive and hypertensive patients. In the full cohort and PSM cohort, multivariate regression analysis showed that the night/day urinary sodium excretion ratio was an independent risk factor for clinical hypertension, whereas 24-h urinary sodium excretion, diurnal and nocturnal urinary sodium excretion were not. When the night/day urinary sodium excretion ratios were further divided into tertiles (tertile 1 < 0.47, tertile 2, 0.47-0.84 and tertile 3 > 0.84), multivariate analysis showed that tertile 3 was independently associated with hypertension in the full and PSM cohorts. In addition, tertile 3 was also independently associated with eGFR ≤ 60 mL/min/1.73 m² and left ventricular hypertrophy.

Conclusions: These data suggested that an abnormal circadian rhythm of urinary sodium excretion was independently associated with hypertension and target-organ damage. Individualized salt intake and therapeutic strategies should be used to normalize the natriuretic dipping profile in CKD patients.

Funding: Government Support - Non-U.S.

PO1504

Mirabilite External Application for the Treatment of Nephrotic Edema: A Randomized Controlled Study

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Background: Lower limb edema is the main symptom of nephrotic syndrome (NS). In addition to well-established treatment for edema, external mirabilite application (EMA) around swollen areas could potentially benefit patients with NS. Mirabilite is hydrous sodium sulfate mineral that quickly turns into thernadite which is known for its ability to highly absorb water.

Methods: A randomized, single-blinded study included 52 patients with NS who were randomly assigned to the experimental group (EMA+diuretic therapy, n=26) and the control group (diurethic therapy, n=26). The study was approved by IRB of the 1st Affiliated Hospital of Guangzhou University of Chinese Medicine. Mirabilite treatment was applied via special cloth bag placed around swollen area on legs, 6 hours per day for 10 days. The primary outcome was the change in leg circumference (LC) and biochemical characteristics of patients. The secondary outcome included body weight and urine output.

Results: Patients from experimental group had significant decrease in LC compared to controls (P<0.001), yet small changes in urine volume output (P=0.436). However, significant correlation of LC with weight gain of mirabilite was observed (r=0.586, P=0.002). Concentration of electrolytes did not change significantly in the groups. Similar effect was observed regarding liver function markers. However, albumin concentration increased significantly in both experimental and control group. After EMA+diuretic treatment patients had significantly lower body weight (P<0.001). Moreover, weight loss was significantly positively correlated with decrease in LC (r=0.612, P=0.000).

Conclusions: This study suggests that EMA is effective in relieving the symptoms of lower extremity edema in NS patients, but it does not help much in the state of water and sodium storage.

Funding: Clinical Revenue Support, Government Support - Non-U.S.

PO1502

Multiple Spot Urine Sampling Is More Precise and Accurate Than 24-Hour Urine Collection for Estimating Urinary Sodium Excretion

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Background: The estimate of sodium excretion (NaE) is important for the management of hypertension, but 24 hours urinary collection (24-hrs UC), the current standard of care, can be inaccurate, unpractical and poorly representative of the usual Na intake. Multiple spot urine sampling is not affected by any of these errors, so we hypothesized that it can be equally or more precise than 24-hrsUC for estimating NaE.

Methods: 4 subjects 24-hrs UC and the related 439 urine samples (1 voiding), were analyzed for uNa and uCr. uNa (in mEq/kg/day) of each voiding were calculated. Individual uNa excretion from 24-hrs UC were compared with all the means of uNa+uCr derived from 2, 3 and 4 random samples from different days for both precision and accuracy using the mean of all the 24-hrs UC as individual “gold standard”. Precision in estimating the gold standard of the 2 methods was measured by comparing the respective coefficient of variations (CV). Accuracy was measured by comparing the P30 and P20 of the 2 methods after transforming uNa/uCrR into uNaE in (mEq/kg/day) by means of the equations (one for children and one for adults) derived from the study data set.

Results: CV of 24-hrs UCs was 25.7% and that of uNa-to-uCr as derived from the mean of 2, 3 and 4 samples were respectively 37.1, 28.2 and 22.5%. The CVs were significantly higher in children. Accuracy: P30 and P20 of the 24-hrs UC were 62.5% and 78.7%, respectively. The corresponding figures obtained from all the 20,258 possible means of 4 samples randomly taken from different days were 73.1% and 94.8%. The internal validation performed by the same subjects 1 year after and the external validation in 8 subjects confirmed the superiority of multiple spot urine sampling.

Conclusions: In real life, with various sources of error systematically affecting 24-hrs UCs, uNa-to-uCr will have an even higher precision and accuracy and should be preferred for estimating uNaE.

PO1503

Abnormal Circadian Rhythm of Urinary Sodium Excretion Correlates Closely with Hypertension and Target Organ Damage in Chinese Patients with CKD

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Background: Whether the abnormal circadian rhythm of urinary sodium excretion is associated with hypertension in chronic kidney disease (CKD) is poorly understood. In this study, we assessed the relationship between the circadian rhythm of urinary sodium excretion and hypertension.

Methods: Urinary samples were collected during both the day (07:00 to 22:00) and night (22:00 to 07:00) to estimate night/day urinary sodium excretion ratios. Blood pressure (BP) and clinical data were also measured.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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Reappraisal of Urinary Sodium Excretion as a Predictor of Clinical Outcomes in Heart Failure

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Background: Congestion is established as the driver of adverse outcomes in heart failure (HF). Since removal of excess fluid and sodium is often the primary therapeutic objective in this setting, accurate monitoring of the progress of diuretic therapy is of critical importance. While weight change and fluid balance have conventionally been used for this purpose, inconsistent collection, inherent delay in data availability, and lack of distinction between water and sodium balance are among their limitations. We sought to explore the contemporary data on the use of urinary sodium (UNa) as a predictor of outcomes in these patients.

Methods: Articles cited in the PubMed database using keywords “heart failure” and “urine sodium” were searched. Available data from clinical trials published between June 2015 and May 2020 were included. The studies were selected if they prognosticated outcomes in the HF population through use of UNa. Pertinent data on clinical and laboratory parameters (e.g. dose and timing of diuretic therapy, eGFR, serum sodium, and UNa) were extracted and reviewed.

Results: A total of 14 studies with 2,350 participants were included, of which 11 were prospective. The study populations consisted of 12 acute HF cohorts, 1 chronic, and 1 with both. The mean age was 67 years (64% men) with an ejection fraction of 35% and an eGFR of 50 ml/min. Most studies (12 out of 14) used UNa concentration, 2 used fractional excretion and clearance of sodium. Surprisingly, while there was substantial variation across studies in the timing of the applied metric, those exploring clinical endpoints unanimously reported a correlation between low UNa excretion and various adverse outcomes (e.g. worsening renal function, HF readmission, and mortality).

Conclusions: Over the past few years, UNa has been the focus of much investigation as a tool for monitoring of therapy and prognostication in patients with HF. The findings of our study are two folds: 1) Regardless of the applied metric and its timing, contemporary data supports the use of UNa as a potent predictor of clinical outcomes in HF that lacks the limitations of conventional methods. 2) There is no consensus on the optimal cut off and time point for measurement of UNa in this setting. In order for UNa to be applied widely as a consistent and reliable tool, this knowledge gap needs to be addressed in future studies.

PO1506

Defective NAD+ Homeostasis in ADPKD and the Effects of PC1CTT on Redox Modulation and Disease Progression

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Background: Autosomal dominant polycystic kidney disease (ADPKD) is caused by mutations in the genes encoding polycystin-1 or 2 (PC1 or PC2). Defective metabolism is a hallmark of ADPKD. The C-terminal cleavage product of PC1 (PC1CTT) can translocate to mitochondria and its expression in Pkd1 KO cells may rescue defective mitochondrial phenotypes. Altered oxidoreductase activity is detected in an ADPKD in vitro model. Here we assess the degree of redox imbalance between NAD/NADH in Pkd1 KO cells.

Methods: In vitro transfection with these constructs. Finally, we expressed 2HA-PC1CTT in a PKD1 KO (PC1CTT-HA) or no additional tag, and applied the assay to lysates from HEK cells of PC1CTT with either an N-terminal HA-tag (2HA-PC1CTT), a C-terminal HA-tag (PC1CTT-HA) localized to nuclei, to that observed in cystic and pre-cystic animals. Transfection of HEK cells with the PC1CTT constructs revealed distinct patterns: 2HA-PC1CTT localized to nuclei, PC1CTT-HA localized to mitochondria and PC1CTT was found in both. PC1CTT and PC1CTT-HA expressing HEK cells exhibited 40% and 60% higher NAD/NADH ratios in comparison to those observed in cystic and pre-cystic animals. Transfection of HEK cells with the PC1CTT constructs revealed distinct patterns: 2HA-PC1CTT localized to nuclei, PC1CTT-HA localized to mitochondria and PC1CTT was found in both. PC1CTT and PC1CTT-HA expressing HEK cells exhibited 40% and 60% higher NAD/NADH ratios than those measured in 2HA-PC1CTT-expressing cells. ADPKD mice expressing 2HA-PC1CTT exhibited a 3-fold increase in kidney-weight/body-weight in comparison to control ADPKD mice.

Conclusions: ADPKD is characterized by defective NAD+ homeostasis. Mitochondrial localization of PC1CTT can potentially rescue this redox imbalance, while nuclear localization of PC1CTT appears to aggravate this imbalance and exacerbate the cystic phenotype in animal models.

Funding: Other NIH Support - RC2 DK120534, Private Foundation Support

PO1507

Cleavage Fragments of Polycystin 1 Respond to Oxidative Stress and Alter Mitochondrial Dynamics and Function

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Background: The PKD1 gene, which is mutated in ADPKD, encodes for the PC1 transmembrane protein containing a cytoplasmic C-terminal tail that undergoes cleavage at multiple sites. Two of these C-terminal fragments, a ~30 kDa fragment (p30), and a ~15 kDa fragment (p15) corresponding to the entire soluble C-terminal tail and the extreme end respectively, are overexpressed in patient kidneys. Metabolic reprogramming is a hallmark of ADPKD. We demonstrate that the C-terminal fragments of PC1 respond to oxidative stress and contribute to metabolic reprogramming by altering mitochondrial dynamics.

Methods: MDCK and OK cell lines were generated stably expressing myc-tagged p30 or p15 under a doxycycline-inducible promoter Protein levels of p30 were determined by western blot and localization by immunocytochemistry. Mitochondrial morphology was classified performing immunocytochemistry combined with image analysis. Fatty acid oxidation was assessed performing OilRedO staining and quantified by measuring the number of lipid droplets.

Results: p30 normally undergoes rapid degradation and is stabilized in response to oxidative stress. Following glutamine starvation, p30 targets mitochondria and results in fragmentation. p15 does not undergo degradation and constitutively targets to the mitochondria where it induces mitochondrial fragmentation. Further, expressing p15 results in accumulation of lipid droplets indicative of impaired mitochondrial β-oxidation.

Conclusions: Our data unmarks p30 as a sensor of metabolic stress. We speculate that p30 stabilization and subsequent p15 cleavage are involved in metabolic reprogramming in ADPKD by altering mitochondrial morphology and function. Elucidating the exact underlying mechanisms is of major importance to understanding disease progression in ADPKD.

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Poster
Results: VV hearts displayed metabolome and lipidome signatures associated with lower levels of glucose and amino acids (aa) and higher levels of lipid species than wild-type (WT) hearts. This VV profile also included decreased Cplt (-28±12%, p<0.05), Ppa(-26±12%, p<0.05), PGC1α (-22±8.4%, p<0.05), phospho-AMPK (-46±12%, p<0.01) and phospho-ACC (-35±15%, p<0.05) expression, indicating downregulation of the fatty acid oxidation and glucose metabolic pathways in VV hearts (49.5±1.8% vs 41.3±3.0%, p<0.01) and a trend of increased basal respiration (p=0.09). These data suggest that glucose and aa may be preferably used as energy substrate in VV hearts. Cardiac expression of fetal genes Npya and Idf1 were increased (33.5±5.4 vs 1.1±0.54 AU, p<0.01) and 2.2±0.94 vs 1.0±0.38 AU, p<0.01, respectively), revealing inappropriate transcriptional transition to the mature state. Unlike Pdd1-deficient kidneys, phospho-RPS6 is downregulated in VV hearts (-58±15%, p<0.01) and glucose is not targeted for aerobic glycolysis, since lactate levels were reduced. These metabolic changes correlated with increased cardiac apoptosis and inflammation but not with hypertrophic remodeling.

Conclusions: Our findings uncover a cardiac metabolic rewiring associated with Pdd1 deficiency, revealing a pattern only partially similar to the metabolic profile observed in the cystic kidney phenotype. These data conceptually expand the understanding of heart dysfunction associated with Pdd1 deficiency and likely ADPKD.

Funding: Government Support - Non-U.S. POI1509

Elevated Expression of CaMK4 Contributes to mTOR-dependent Cell Proliferation and Cyst Growth of ADPKD Cells

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Background: Mammalian target of rapamycin (mTOR), a central integration site for pathways involved in cell growth, is aberrantly activated in renal cyst-lining cells in human ADPKD and PKD mice. mTOR inhibition reduces cell proliferation and cyst growth in PKD mice. A better understanding of the pathways responsible for elevated mTOR expression is important for the development of new therapies. Calcium/calmodulin-dependent kinase type IV (CaMK4) was recently identified as an important upstream regulator for mTOR activation in multiple cells. CaMK4 is fully activated by binding of Ca2+/calmodulin(CaM) and phosphorylation by Ca2+-dependent kinase kinases (βCaMKK). However, the role of CaMK4 on mTOR signaling and cyst growth in ADPKD remains unclear.

Methods: We stained tissue sections of human ADPKD kidneys and normal human kidneys (NHKs) with an antibody to CaMK4. We also analyzed levels of CaMK4 in primary human ADPKD NHK cells, 30-weeks old ADPKD +/-(BALB/c background) and Pkd1RC/RC (normal) mouse kidneys. We determined the effects of W7, a calmodulin inhibitor, STO-690, a CaMKK inhibitor, and KN-93, a CaMK4 inhibitor, on mTOR signaling, cell proliferation, and in vitro cyst growth of ADPKD cells. To confirm a role of CaMK4 on mTOR regulation, we knocked down CaMK4 using a lentiviral shRNA approach in human ADPKD cells.

Results: We found moderate levels of CaMK4 in nuclei of tubule cells in NHK; by contrast, there were elevated levels of CaMK4 in the cytosol and nuclei of cystic epithelial cells in human ADPKD NHK cells, 30-weeks old ADPKD +/-(BALB/c background) and Pkd1RC/RC (normal) mouse kidneys. We also found a 2.8-fold increase of CaMK4 expression in Pkd1RC/RC kidneys compared to normal kidneys. Inhibition of CaMK4 using KN-93 caused a remarkably decreased in levels of P-S6K and P-S6 in a dose-dependent and time-dependent manner. Inhibition of CaMK4 activation using W7 and STO-690 reduced P-S6 in Pkd1RC/RC ADPKD cells. CaMK4 knock down decreased levels of mTOR, P-S6K and P-S6 confirming regulation of CaMK4 on mTOR signaling in ADPKD cells. W7, STO-690, and KN-93 significantly inhibited cell proliferation and in vitro cyst growth of ADPKD cells within a collagen matrix.

Conclusions: The aberrant expression of CaMK4 appears to contribute to elevated mTOR-dependent proliferation of cyst cells and may be a potential target to slow cyst growth in PKD.

Funding: NIDDK Support POI1510

Mechanisms of Tethered-Ligand Mediated Polycystin 1 GPCR Signaling

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Background: Polycystin-1 (PC1) is the most commonly mutated protein in autosomal dominant polycystic kidney disease (ADPKD) thought to function as an atypical GPCR. In vivo studies have demonstrated PC1-regulated G protein signaling is a critical function for preventing renal cystogenesis. Like the Adhesion class of GPCRs, PC1 undergoes auto-catalyzed cleavage at a GPS motif which generates an extracellular N-terminal fragment (CTF) and a transmembrane C-terminal fragment (CTCF). The PC1 CTF is transmembrane domains preceded by an N-terminal extracellular stalk of 25 residues. We previously reported that CTF-mediated signaling to an NFAT promoter-luciferase reporter is dependent on the presence of the stalk, is reduced by ADPKD-associated missense mutations and can be rescued by synthetic, stalk-derived peptides, supporting a tethered ligand mechanism of PC1-G protein signaling. In this study, we have utilized a combination of computational molecular dynamics (MD) simulations and mutagenesis analyses to characterize the mechanism of PC1 signaling.

Methods: A computer model of the human PC1 CTF was generated using the cryo-EM structure of the PC1-PC2 complex (Su et al, 2019) and the I-TASSER protein structure prediction tool. All-atom enhanced simulations (~ 900 ns) using a robust, high-resolution force field were conducted to unravel the molecular mechanisms of CTF-mediated signaling. Key residue interactions between different domains of the CTF predicted from the GaMD simulations suggest an allosteric mechanism for PC1-G protein activation for which mutagenesis and functional signaling and expression assays are underway.

Results: All-atom simulations of the wildtype, ADPKD mutant and stalk-less version of the PC1 CTF reveal a dynamic conformational change and a significant difference in the energetics of the wild-type, ADPKD, and stalk-less versions of the PC1 CTF. The low selectivity for Ca2+ blocked by GSK2193874 exacerbated ARPKD progression leading to a larger kidney body weight ratio, reduced cyst numbers and area when compared to the control. TRPV4 blocker, GSK1016790A for 1 and 2 months treatment reduced ARPKD progression as significant decrease in kidney to total body weight ratio, reduced cyst numbers and area when compared to the control. TRPV4 blocker, GSK2193874 exacerbated ARPKD progression leading to a larger kidney volume and more pronounced cystogenesis. We showed that high K+ intake increased renal PC2 G protein signaling and activity. Consistently, high K+ diet (10% KCl) had similar to GSK1016790A beneficial effects on ARPKD progression. GSK2193874 reversed these effects suggesting their TRPV4-dependent nature. Unexpectedly, high K+ high alkali diet

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(10% K Bicarbonate/Citrate) dramatically accelerated cystogenesis despite augmented renal TRPV4 expression. TRPV4 activity (estimated as a GSK1016790A-dependent increase in [Ca<sup>2+</sup>]) in freshly isolated cyst monolayers from Pck453 rat kidneys) was approximately 2 fold larger in cyst cells from high K<sup>-</sup> diet treated compared to control. Basal [Ca<sup>2+</sup>] and flow-induced [Ca<sup>2+</sup>] levels were also larger on this condition. In contrast, TRPV4 activity was less than 2 fold similar on high K<sup>-</sup> high salt diet.

**Conclusions:** We show a positive correlation between TRPV4 functional status and the time course of ARPKD progression in PCK 453 rats. Chronic alkaline load renders TRPV4 to an inactive state, which contributes to exacerbated cystogenesis in Pck453 rats. Reduced function of TRPV4 promotes cyst growth with high K<sup>-</sup> high salt diet will be instrumental to attenuate the rate of PKD progression in clinical.

**Funding:** Other NIH Support - NIH-NIDDK DK095029 and DK117865 (to O. Pochynyuk), Private Foundation Support

### PO1513

**Abstract Withdrawn**

### PO1514

**Somatic Tubular Epithelial Cell Model of Type II Polycystic Kidney Disease Reveals Phenotypes of Altered Ciliary Length and Polycystin-Somatic Tubular Epithelial Cell Model of Type II Polycystic Kidney Disease**

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**Abstract**

Heterozygous Loss of Pkd2 Accelerates Cystogenesis in Pkd1<sup>RC/RC</sup> Mice

**Background:** Autosomal dominant polycystic kidney disease (PKD) is a life-threatening condition caused by mutations in PC1 and PC2, respectively. The sporadic nature of cyst formation led to the hypothesis that cystogenesis requires a two-hit mechanism, involving PC-1 and PC-2 function in a common pathway and that lowering the expression of the polycystins is sufficient to initiate cystogenesis. We think that the increased progression of cystic disease in Pkd1<sup>RC/RC</sup> mice makes it a promising model for evaluating therapeutic interventions.

**Funding:** NIDDK Support

### PO1515

**Heterozygous Loss of Pkd2 Accelerates Cystogenesis in Pkd1<sup>BCC/MC</sup> Mice**

**Emily A. Daniel,1,2 July P. Metcalf,1,2 Yuqiao Dai,1,2 Yan Zhang,1,3 Darren P. Wallace, University of Washington Medical Center, Kansas City, KS.

**Background:** Autosomal dominant polycystic kidney disease (ADPKD) is caused by mutations in PC1 (-50% of cases) or PC2 (-5%) in the human population. There is no cure for ADPKD patients. The prevalent phenotypic manifestations of ADPKD are polycystin-1 (PC-1) and polycystin-2 (PC-2), respectively. These form a receptor-channel complex in the primary cilium whose molecular function remain uncertain, making it difficult to develop targeted therapeutic.

**Methods:** To establish a somatic cell model of PKD, we generated five clones of proximal tubule cell line (LLC-PK1) completely lacking PCK2 using the CRISPR-Cas system, alongside five isogenic control lines. Mutations were verified for each allele by TOPO cloning and clones were derived from a single subclone to minimize heterogeneity.

**Results:** In the absence of PC, C2, PC-1 steady-state levels, ciliary defects, and cyst formation in low adhesion plates in the presence of cyst activators. Forskolin, 8-BrcAMP and the myosin inhibitor blebbistatin promoted cystogenesis. Transcript analysis indicated that the expression of altered PC steady-state levels was post-transcriptional. Exogenous myc-PC2 rescued PC1 in the PC2 null cells.

**Conclusions:** We have established a somatic tubular epithelial cell model for PKD, which can be rapidly assessed for molecular and cellular phenotypes. This reveals the necessity of PC2 for proper ciliary structure and to prevent the degradation of a protein complex containing PC1 and intraflagellar transport components. Overall the porcine model appears more similar to human cells than mouse. Notably, intraflagellar transport components including ARL13B and IFT88 were also reduced. Cilia in 2D cultures appeared short while in the cystic cells was lengthened. Pharmacologic agents that inhibit the proteasome and the lysosome stabilize PC1 in these cells and rescues the cystic phenotype. Additionally, the drugs reduce cyst size in human PKD organoids lacking Pkd2.

**Funding:** NIDDK Support, Other NIH Support - National Center for Advancing Translational Sciences.

### PO1517

**Characterization of Porcine Models of Autosomal Recessive Polycystic Kidney Disease**

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**Background:** Autosomal recessive polycystic kidney disease (ARPKD), a relatively common form of mainly infantile PKD, is caused by biallelic mutations to PKHD1. The nonsense change, p.T36M, is the most common pathogenic allele (-15% of the total) and associated with severe disease. Mouse and rat models do not display the classical ARPKD presentation of early onset, enlarged, echogenic kidneys. Therefore, to better understand the pathomechanism, we developed and characterized porcine ARPKD models. The pig has a similar anatomy (multi-papillary structure) and physiology to humans, and thus it makes an ideal model system to study disease progression and test treatment options in this disorder.

**Methods:** Using the CRISPR/Cas9 methods and homology directed repair (HDR), we genetically engineered pigs with the p.T36M or null PKHD1 alleles. The following genotypes were breed (WT, T36M/T36M, T36M/KO, KO/KO) and characterized longitudinally to 5-months old (where possible) using MRI and a blood chemistry panel, and analyzed histologically.

**Results:** Two KO/KO pigs were sacrificed at one and two days of age with a phenotype of greatly enlarged cystic kidneys with severe functional loss as well as fibrotic, cystic livers, matching classical human ARPKD. Four T36M/KO pigs were imaged monthly to five months but they only developed a few kidney cysts that did not grow significantly during follow up, and without a decline in function. Similar analysis of two T36M/T36M pigs revealed only occasional kidney cysts.

**Conclusions:** Through gene editing, an authentic porcine model of early onset ARPKD kidney and liver disease was developed that will be valuable for understanding the pathomechanism of neonatal ARPKD. MRI and biochemical assays enabled detailed

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evaluation of functional and morphological changes in the kidneys, liver, and heart of the mice. Genotyping analysis of the p.T36M allele indicates it more functional in pigs, and so associated with a milder phenotype than in humans.

**POI158**

**Cystin Deficiency in Cystic Kidney Disease**

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**Background:** Human ARPKD (MIM 263200) is caused by mutations in PKHD1 (which encodes FPC), yet mouse Pkd1 mutations cause minimal renal cystic disease. By contrast, Cystin-positive (cpk) mice exhibit an ARPKD-like renal phenotype. The function of cystin (encoded by Cyst1) is not fully understood, but the protein is found in the cytoplasm, primary cilium, and nucleus. N-terminal myristoylation enables membrane-association, and the AxEKG motif is necessary for ciliary targeting, suggesting a function for cystin in vesicular trafficking. To examine whether cystin is a trafficking adaptor for transmembrane ciliary proteins, like FPC, we evaluated FPC expression in wild-type (WT) and cpk mouse kidney lines.

**Methods:** Cell lines: Wild-type (WT) and cpk mouse kidney cortical collecting duct cells were generated using mTERT immortalization. We used qRT-PCR, western blotting, immunofluorescence, and RNA sequencing to examine FPC expression in both cell lines. Results: While Pkd1 mRNA levels were similar, FPC protein levels were reduced by 75% in cpk cells relative to WT. In contrast, PC2 protein levels were only reduced by 25% and no differences in acetylated tubulin or other ciliary proteins, e.g. Tg58 or Arl13b, were observed. In cpk cells, both cystin and FPC were absent from primary cilia, but the percentage of cpk cells with primary cilia, ciliary length and thickness were identical to WT cells. These observations suggested that cystin deficiency specifically influences FPC expression and ciliary targeting. Elevated expression of FPC resulted in partial restoration of the cilial Hedgehog signaling protein Arl13b and the intercellular proteins TSG101 and Alix, as well as the transmembrane proteins CD63, CD9, and CD81. Tsc1 deletion resulted in less EVs production and synthesis rate compared to Tsc2 deletion. RNA and protein transfection studies were done to evaluate the role of EVs in disease pathology. Quantitative PCR analysis showed the downregulation of mir-212a-3p and mir-99a-5p in EVs derived from Tsc2 which are sought to contribute the more TS severity as compared to TSC1. In addition, mir-212-3p/mTORC1 and mir-99a-5p/mTORC1 axis are could be a novel therapeutic and biomarker strategy for TSC disease.

**Conclusions:** We used lineage tracing experiments to understand the tubular cell fate, and mutant Tsc2 gene locus disruption and differences in renal epithelial extracellular vesicles.

**Funding:** Other U.S. Government Support

**POI1520**

**Tsc Gene Locus Disruption and Differences in Renal Epithelial Extracellular Vesicles**

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**Background:** The severity of tuberous sclerosis complex (TSC) manifestations seem different depending which TSC locus is affected. This is a puzzling finding, given that the gene product of both loci heterodimerize to regulate mTORC1 activity, so loss of either one releases the repression and results in constitutive mTORC1 activation.

**Methods:** To begin to understand possible mechanisms for this difference, we have used mouse inner medullary collecting duct (mIMCD) cells with either the Tsc1 or the Tsc2 gene disrupted by a CRISP/CAS9 strategy. We have previously characterized the Tsc2-mutant cell line derived EVs, and present here intriguing differences between the extracellular vesicles (EVs) derived from cells with mutant Tsc1 or Tsc2 genes. To characterize the EVs, we used tunable resistive pulse sensing, dynamic light scattering, transition electron microscopy and immunoblot analysis.

**Results:** To characterize the size of the EVs, we used tunable resistive pulse sensing and dynamic light scattering. The EVs were smaller than 153.5 ± 5.7 nm and mutant Tsc1-derived EVs had an average size 131.5 ± 8.3 nm. The surface charge for the two cell lines were -16.3 ± 2.1mV and -19.8 ± 2.7mV respectively. The isolated nanosized vesicle had excellent purity as assayed using transmission electron microscope. Both cell lines had a heterogeneous population of EVs based on size, and more than 90% of the EVs were smaller than 150nm. Immunoblot analysis revealed the presence of ciliary Hedgehog signaling protein Arl13b and the intercellular proteins TSG101 and Alix, as well as the transmembrane proteins CD63, CD9, and CD81. Tsc1 deletion resulted in less EVs production and synthesis rate compared to Tsc2 deletion. RNA and protein transfection studies were done to evaluate the role of EVs in disease pathology. Quantitative PCR analysis showed the downregulation of mir-212a-3p and mir-99a-5p in EVs derived from Tsc2 which are sought to contribute the more TS severity as compared to TSC1. In addition, mir-212-3p/mTORC1 and mir-99a-5p/mTORC1 axis are could be a novel therapeutic and biomarker strategy for TSC disease.

**Conclusions:** We have found that the intercellular communication of EVs has significant differences depending upon which TSC locus is affected, and this difference may be involved in the different phenotypes expressed.

**Funding:** Other U.S. Government Support
POI1522

Description of a Multidisciplinary Model of Care in a French Cohort of Tuberous Sclerosis Complex Adult Patients

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Background: Tuberous sclerosis complex (TSC) is a rare autosomal dominant genetic disorder. Due to the various manifestations of TSC and their potential complications, a multidisciplinary care approach is recommended by consensus guidelines. Our study aimed to give a complete description of our TSC adult cohort and to evaluate the multidisciplinary and interdisciplinary management model.

Methods: Data on each adult patient diagnosed with TSC, including disease manifestations, interventions and outcomes, were collected at baseline and updated annually. A multidisciplinary TSC approach with all the recommended explorations was carried out annually. Quality of life was evaluated by SF36 score.

Results: 90 patients were enrolled in a French hospital, between January 2000 and September 2018. Median age of patients at inclusion was 37 years (range, 27-47). Regarding the occurrence of TSC manifestations, 97% of the patients had cutaneous lesions, 89% had neurological manifestations, 83% had renal manifestations and 100% had dental lesions with pits. More than half the patients had sclerotic bone lesions (68%), TAND (64%) and lymphangioleiomyomatosis (LAM) (59%). A TSC multidisciplinary approach in day hospital was developed including a global follow-up and an evaluation of TAND (64%) and lymphangioleiomyomatosis (LAM) (59%). A TSC multidisciplinary model, involving a global follow-up and an evaluation of TAND (64%) and lymphangioleiomyomatosis (LAM) (59%).

Conclusions: By whole exome sequencing we identified a disease-causing mutation in 62% of families with a diagnosis of NPHP-RC and identified 10 potential novel causative gene candidates.

Funding: NIDDK Support

POI1524

Using Whole-Exome Sequencing to Identify PKD1 and PKD2 in 50,000 UK Biobank Participants

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Background: Studies have demonstrated that genetic testing using whole-exome sequencing (WES) detects undiagnosed monogenic kidney disease in up to 2% patients with predefined clinical phenotypes and/or strong family histories of kidney disease. We aimed to take advantage of newly available datasets with WES and medical information on 50,000 people from UK Biobank (UKBB) to identify PKD1 and PKD2 variants in a sample not selected for kidney disease, to compare their phenotypic features to people with ICD 10 codes for PKD in UKBB.

Methods: We analysed data from the subset of 50,000 individuals from UK Biobank (n=500,000) who have had WES data released. We looked for mutations in PKD1 and PKD2. Our primary analysis involved looking for a subset of mutations, protein-truncating variants, that had a very high likelihood of being disease-causing. We performed standard quality control which included visual inspection and assessing individual mutation on genome databases.

Results: We found 53 protein truncating variants (44 in PKD1 and 9 in PKD2). The Average age for those with mutations was 57, the same as the UKBB population. We excluded 33 variants on the basis that they were either very common in GnomAD therefore unlikely to be pathogenic or did not pass visual inspection on IGV plot. This left 20 likely pathogenic mutations (13 PKD1 and 7 PKD2). An ICD 10 code for PKD on hospital records was found in 8 of those with mutations. The 8 individuals with mutations and a PKD ICD 10 code had a more severe phenotype; 7/8 (88%) were hypertensive compared with 6/12 (50%) in those with mutations but without a PKD ICD10 code. Their renal function was worse (63% vs 15% had CKD eGF 53 < 80, p=0.01) and 1 individual received a renal transplant.

Conclusions: We were able to find disease causing mutations in PKD1 and PKD2 and link this to phenotype in UKBB. People with protein truncating mutations and hospital codes for PKD had independent evidence of kidney disease however those without an ICD 10 code for PKD could either have milder undiagnosed PKD, or non-pathogenic mutations. The genetic complexity of PKD1 and 2, and the difficulty of ascertaining mutations with exome sequencing means that further work needs to be done to see if prevalence of PKD, and in particular undiagnosed mutations, could be assessed using WES from the complete UKBB dataset when available.
PO1525
PKD1 Compared with PKD2 Genotype and Cardiac Hospitalizations in the HALT-PKD Studies
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Background: Polycystin 1 and 2 are expressed in vascular endothelial and vascular smooth muscle cells. While the hallmark of autosomal dominant polycystic kidney disease (ADPKD) is the development and continued growth of multiple renal cysts that ultimately result in loss of kidney function, cardiovascular complications are the leading cause of death. Although hypertension occurs earlier and more frequently in PKD1 vs. PKD2, both genotypes seem to confer equal risk of developing intracranial aneurysms. It is currently unknown if PKD1 vs. PKD2 confers a different risk of cardiovascular events.

Methods: 864 individuals with ADPKD who participated in the 5-year HALT-PKD study A or B and had genotype data with either a PKD1 or PKD2 mutation were included in this analysis. Since the number of cardiac events in the HALT-PKD studies was limited, we determined the association of genotype with the adverse cardiac event with the highest frequency (cardiac hospitalization; defined according to the Common Terminology Criteria for Adverse Events v.4.0 of the National Cancer Institution and adjudicated by an endpoints committee). The association of genotype with cardiac hospitalization was determined using logistic regression.

Results: Among the 864 included participants, individuals with the PKD1 genotype (84%) were slightly younger (42±10 vs. 46±10 years; p=0.001) and had a slightly lower baseline estimated glomerular filtration rate (eGFR; 70±26 vs. 75±26 mL/min/1.73m²; p=0.06). Cardiac hospitalization (n=43) was more common in individuals with a PKD2 genotype (9.2%) compared to a PKD1 genotype (4.1%; p=0.01). After adjustment for age, sex, race, and study randomization, PKD2 was associated with an increased odds of cardiac hospitalization (OR: 2.14, 95% CI: 1.04-4.41 vs. PKD1). This association was slightly attenuated after further adjustment for cardiac history, systolic blood pressure, body mass index, and baseline estimated glomerular filtration rate (OR: 2.12; CI: 0.99-4.52).

Conclusions: In early- and late-stage participants in the HALT-PKD studies, PKD2 genotype was independently associated with increased odds of cardiac hospitalization.

Funding: NIDDK Support

PO1526
A Novel Case of Turner Syndrome and Autosomal Dominant Polycystic Kidney
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Introduction: Turner Syndrome (TS) is a sex chromosome disorder resulting from the complete or partial loss of one of the X chromosomes. Short stature is common in TS patients and is commonly treated with growth hormone (GH). Autosomal dominant polycystic kidney disease (ADPKD) is a multisystem disease that has bilateral renal cysts and is an important cause of end stage renal disease (ESRD).

Case Description: A 5.5-yr-old girl with TS was admitted at 45 DO, treated with GH since the age 2 yr with good clinical response. She presented to nephrology clinic for evaluation of bilateral large kidneys for age (RK 10.0 cm, LK 9.7 cm) per recent renal ultrasound (US). No hypertension was found on her exam. Family History was negative for polycystic kidney disease (PKD), hypertension, renal disease, hemodialysis, renal transplant or intracranial aneurysm. On follow up US 1 year later, a few bilateral cysts measuring < 1 cm and persistent renal enlargement was noted. Due to concerning findings of progressive renal cysts with further growth of the kidneys potentially secondary to GH treatment, her GH treatments was stopped. After 6 months off GH therapy, renal enlargement was unchanged with enlargement of her cysts. Patient get genetic studies for PKD and was found to be heterozygous for pathogenic variant in the PKD1 gene consistent with the diagnosis of ADPKD. Parents both tested negative for PKD1 mutation suggestive of de novo mutation.

Discussion: Patients with TS often have short stature requiring GH treatment in order to achieve intended adult height. TS has multi-organ system manifestations including an increased risk for renal anomalies like simple renal cyst, horseshoe, duplicated, or absent kidney. This case highlights the potential increased risk for patients with TS who are on GH treatment to develop kidney disease. To the best of our knowledge, the association of TS and ADPKD has not been described yet. The current clinical practice guidelines state that patients with known TS should receive a renal US at time of diagnosis with no further follow up renal imaging has been recommended at this time. Given the potential role of GH in cyst proliferation and frequency of GH therapy in this patient population, we recommend reevaluation of current renal screening guidelines for patient with TS. Early diagnosis and treatment could potentially reduce morbidity associated with renal disease and growth hormone.

PO1527
CYP24A1 Mutations Are Associated with Renal Cystic Disease

Background: Loss-of-function mutations in the CYP24A1 gene cause a rare hereditary disease leading to reduced 24-hydroxylase enzyme activity, characterized by increased serum 1,25-dihydroxyvitamin D3 levels, hypercalcemia, hypercalciuria, nephrocalcinosis, and/or nephrolithiasis. Renal cysts in CYP24A1 mutations were first reported in a single case study from our institution. However, to date a possible association between CYP24A1 mutations and renal cysts has not been examined.

Methods: Retrospective review of all patients with confirmed CYP24A1 mutations and complete renal imaging studies at a tertiary academic center between 2010 and 2020. Cyst location, number, and diameter were measured by contrast-enhanced computed tomography (CT), non-contrast CT, ultrasound or magnetic resonance imaging.

Results: Among the 13 patients with CYP24A1 mutation, 46% were male and 38% children. The mean age at diagnosis was 24.7 ± 18.8 years (range 1-60). Medulloblastoma and/or corticomедulillary junction renal cysts were present in all 13 cases (5 with unilateral and 8 with bilateral cysts). The mean age at imaging with first detected cyst was 31.1 ± 20.5 years (range 3-61). The median number of cysts per patient was 3 (IQR 1-8) and 11.9 ± 6.9 mm in size (range 2-30) respectively. All 13 had normal age-adjusted renal size and none had a family history of polycystic kidney disease. The number of cysts (a 5 mm in size) in 63% of adult patients was above the 97.5th percentile of an age- and sex-matched control population (Figure 1).

Conclusions: This study suggests an association between CYP24A1 mutations and cystic kidney disease. Further studies are needed to evaluate the role of CYP24A1 and vitamin D metabolism in renal cyst formation, and whether cysts enhance CKD risk in patients with CYP24A1 deficiency, or modify nephrocalcinosis/urinary stone risk.

PO1528
Collagen Changes Suggestive of a Primary Defect in pkd2+/- Adult Zebrafish Kidney
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Background: Zebrafish are a valuable model for studies of PKD, with conservation of pathways and phenotypes including renal cysts. Pkd2 mutant zebrafish develop dorsal tail curvature (pkd2+/-), which prevents survival. No phenotype has been described in pkd2+/- zebrafish embryos or adults. MRI is useful for analysis of PKD kidney and collagen changes characterize PKD. In this study, we examined collagen changes in pkd2+/- adult zebrafish kidney and MRI in vivo.

Methods: Zebrafish hr4166 pkd2+/- were compared to sibling pkd2+/- (males). Total kidney volume and texture were quantified from MRI in vivo (16m, n=3). Collagen density was quantified from picrosiris red (PSR) stained sections using polarized light microscopy and ImageJ for color thresholding (19m, n=3). Integrity of the collagen triple helix was assessed in kidney frozen sections labeled with collagen hybridizing peptide in zebrafish (1m, n=4) and mouse Pkd1(-/-) (10m).

Results: Kidney volumes were not different; however, texture analysis showed pkd2+/- kidney was more heterogeneous. This was not explained by explants, as none were visible by H&E staining, nor were tubule diameters different. PSA staining showed significantly
more dense collagen, and collagen hybridizing peptide labeling showed more denatured collagen in plak2
zebrafish kidney. Preliminary data from Pkd1
mice show similar patterns of collagen density and denaturation.

**Conclusions:** To our knowledge, this is the first report of any phenotype in plak2
zebrafish (adult or embryo). The presence of a dominant phenotype and a collagen defect suggests conservation of disease etiology. A collagen defect in the absence of cysts indicates independence of collagen changes from cyst formation, suggesting collagen changes may be a primary defect in PKD pathophysiology.

**Funding:** NIDDK Support

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Increased collagen density in kidney of plak2 mutant zebrafish visualized by staining with picrosirius red and imaging using polarized light (left) quantified using image thresholding in ImageJ (right). Pixels are binned by color indicating density as shown.

**PO1529**

Cystic Kidney Disease in Patients with Thin Basement Membrane Disease (TBMD)


**Background:** TBMD is a benign glomerular disease typically manifesting as microscopic hematuria with/without minimal proteinuria and with preserved kidney function. A few reports described the finding of kidney cysts in TBMD patients, but this association remains uncertain.

**Methods:** A retrospective study of patients seen at a tertiary academic center (2009-2019) and had a kidney biopsy with reported diffuse glomerular basement (GBM) thickening was done. The diagnosis of TBMD was confirmed by a careful review of the biopsy findings, including EM images. Patients with clinical and/or pathologic features of Alport disease or with unavailable abdominal imaging were excluded. Cyst number and size were recorded on the first available imaging.

**Results:** Among 49 TBMD patients, 29 (59%) had kidney cysts (cystic), and 20 had no cysts (noncystic). Both cystic and noncystic groups were mostly females (69% vs. 80%). Cystic patients were older at time of biopsy (51 vs 38 yrs) and imaging (51 vs 39 yrs). Hematuria was the major indication for biopsy. Hematuria and dysmorphic RBCs were found in 72% and 41% of cystic patients respectively vs. 80% and 10% in noncystic patients. Cystic patients had lower mean eGFR at time of biopsy (69 vs. 93 mL/min/1.73 m²), higher mean 24-h proteinuria (968 vs. 172 mg/d), and comparable mean GBM thickness (193 vs. 206 nm). 18 (62%) patients had bilateral cysts. Median number of cysts was 3 (IQR 1-5.5). Average sizes of the smallest and largest cysts were 5.1 (± 4.4) and 19.6 (± 24) mm respectively. The number of cysts (±5 mm) in 34% of cystic patients was above the 97.5th percentile of an age-sex-matched control population (Figure 1).

**Conclusions:** Bilateral kidney cysts were found in a large percentage of biopsy-proven TBMD patients. COL4A4 mutations could be a potential etiology of mild cystic kidney disease with hematuria or mild proteinuria.

**PO1530**

COL4A3/COL4A4 as a Cause of Multicytic Kidney Disease

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**Background:** Thin basement membrane nephropathy (TBMN), the most common cause of persistent microhematuria (mH), is due to mutations in genes codifying alpha-3 and alpha-4 collagen IV chains (COL4A3/COL4A4). Initially considered as a benign condition, subsequent studies have shown that an important number of patients develop proteinuria and CKD. We reported in a previous small study the presence of multicystic kidney disease (MCD) in some TBMD patients. In this study we aimed to evaluate the presence of MCD in a larger cohort of TBMD patients and analyze its association with renal outcomes.

**Methods:** We collected 50 patients with a diagnosis of TBMD based on the presence of persistent mH (>5 erythrocytes per high power field in more than 90% of urinary sediments and radiological examinations to exclude other causes of mH) and at least one first-degree relative with persistent mH. TBMD diagnosis was confirmed by renal biopsy (glomerular basement membrane thickness less than 130nm) in 18 patients and by genetic test (pathogenic mutations in COL4A3/COL4A4) in 6 patients. MCD was diagnosed by the presence of uncountable cysts on renal ultrasonography.

**Results:** Mean age at diagnosis was 43.7 years, 34% were males and 18% had hypertension. At baseline, serum creatinine (SCR) was 0.9 mg/dL, proteinuria 0.48 gr/24h and 9 patients (18%) had CKD (estimated glomerular filtration rate eGFR lower than <60 mL/min/1.73m²). 7 patients (14%) had CKD G3 and 2 (4%) CKD G4. Kidney cysts were found in 34 patients (68%) and 19 (38%) met MCD criteria. After a mean follow-up of 14.7±11.5 years, 23 patients (46%) had CKD. Among them, 17 patients (34%) had CKD G3, 2 (4%) CKD G4, and 4 (8%) CKD G5. Hypertension was more frequent among CKD patients as compared with no-CKD patients (39 vs 0%, p 0.00), proteinuria was higher (0.58±0.68 vs 0.39±0.65 g/24h, p 0.05) and MCD more frequent (65.2% vs 14.8%, p 0.00). Patients with MCD had higher Scr (2.1 vs 1.1 mg/dL, p 0.004) and lower eGFR (41.7 vs 77.2 mL/min/1.73m², p 0.08) at the end of follow-up, and MCD was the only risk factor for increased occurrence of CKD (OR 6.49, 95% CI 1.33-31.6) by multivariable analysis that included age, hypertension and proteinuria.

**Conclusions:** MCD is frequently observed in TBMD patients and is a risk factor for the progression of CKD.

**PO1531**

Genotype-Phenotype Correlations in Pediatric Patients with HNF1B Mutations

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**Background:** HNF1B is one of the most common disease-causing genes of CAKUT, especially renal cysts. HNF1B mutations also manifest various renal and extra-renal phenotypes. Fagaer S, et al. proposed HNF1B scoring system in 2014 to screen patients with HNF1B mutations clinically.

**Methods:** A total of 14 patients, who were diagnosed as having HNF1B mutations in the Department of Pediatrics, Seoul National University Children’s Hospital during the period from 1990 to 2019, were recruited in this study, and the phenotypes of the patients were analyzed retrospectively.

**Results:** All 14 patients were male. Initial symptoms of patients revealed incidental abdominal pain (36%), abnormal prenatal USG(29%), etc. The median ages at the onset, at the genetic diagnosis, and at the last follow-up were 0.1 years, 12.8 years, and 20.3 years, respectively. HNF1B genotyping revealed total heterozygous mutation in 43%, truncating mutations in 36%, and missense mutations in 21% patients. The renal image studies revealed multiple renal cysts in 93% patients, renal parenchymal hyperchogenecity in 79%, and unilateral/bilateral renal hypoplasia in 50%. The other renal or extra-renal phenotypes included hyperuricemia in 79% patients and hypokalemia in 57%. During follow-up, 80% patients progressed to CKD, including 36% patients to ESRD. The mean HNF1B score at the time of diagnosis was 14.4±5.8, and all patients except one had a score higher than 8. The score at the last follow-up in ten patients except for 4 patients with transplantation was highest in patients with missense mutations (22.5±5.3) and lowest in those with truncating mutations (14.8±2.9, P<0.040). Hypokalemia was most common in patients with total deletion mutations (83%) and least common in those with missense mutations (0%, P=0.027).

**Conclusions:** HNF1B mutations manifest various renal and extra-renal phenotypes. Most patients (86%) progressed to CKD or ESRD during follow up. The HNF1B scoring system showed high sensitivity, although specificity was not evaluated.
PO1532
Identifying and Assessing the Phenotypic Features of HNF1B Deletions and Duplications in UK Biobank
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Background: Heterozygous mutations of hepatocyte nuclear factor 1β (HNF1B) are the most common known monogenic cause of developmental kidney disease. Renal cysts are the most frequently detected feature. Other features include early-onset diabetes and abnormally low function. It is thought that duplications of HNF1B do not result in strong phenotypic features. The true pathogenicity and penetrance of many rare putative disease-causing copy number variants (CNVs) is uncertain and may be over- or underestimated by clinical ascertainment. We aimed to assess the pathogenicity and penetrance of HNF1B deletions and duplications in UK Biobank (UKBB) and to describe any associated phenotype.

Methods: We used data from 388,714 UKBB participants to assess CNVs of HNF1B in a population-based setting using SNP chip intensity data. We tested the association of these CNVs with diabetes and other clinically-relevant traits. We assessed the UKBB phenotype and biomarker information and correlated these with the deletions and duplications.

Results: We identified 11 individuals with large deletions relating to HNF1B and 106 with duplications. There were no significant difference in the average ages of deletion (53), duplication (56) and UKBB population (57). Of the 11, 3 were reported to have glomerular disease, 1 had haematuria, 1 had a renal transplant, and 6 had diabetes (55% vs. 5% amongst the rest of UKBB; P=2x10^-6). The penetrance of diabetes was 30% and 15% in the UKBB population. Average eGFR was 60 v 71 mL/min/1.73m^2 in UKBB population. There were no significant difference in the average ages of deletion and duplication and diabetes (4.4% vs. 5.3%; P=0.8) or liver function.

Conclusions: HNF1B deletions and duplications can be detected in a large unselected dataset. Deletions are more pathogenic than duplications. However, HNF1B duplications do not result in strong phenotypic features, which has not been previously described. The frequency of both HNF1B deletions and duplications may be higher than previously estimated.

PO1533
Late-Onset Hepatocyte Nuclear Factor 1β-Associated Kidney Disease
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Introduction: Hepatocyte Nuclear Factor 1β (HNF1β) is an important transcription factor for kidney development in the embryo, which has not been previously described. HNF1β-associated kidney disease may not manifest until adulthood. We present a case of an older female with chronic hypomagnesemia and kidney cysts due to a heterozygous deletion in the HNF1β gene.

Case Description: 66 y/o Puerto Rican female with a history of recurrent urinary tract infections, pre-diabetes, hypertension, arthritis, congenital absence of left ovary and baseline SCr 0.9 mg/dL was referred for evaluation of bilateral kidney cysts and chronic hypomagnesemia. Review of magnetic resonance imaging and ultrasound going back to 2003 showed normal sized kidneys and presence of more than 4 cysts in each kidney, some of which were mildly complex. No extrarenal cysts were noted and she denied family history of kidney cysts. Chronic symptomatic hypomagnesemia was present since at least 2015 with serum magnesium ranging from 1.1-1.6 mg/dL, resulting in emergency room visits and hospitalizations. Fractional excretion of magnesium was 29%, consistent with renal magnesium wasting. Serum potassium and bicarbonate were normal. Intact parathyroid hormone ranged from 83-112 pg/mL, but serum calcium, phosphorus, 25 dihydroxyvitamin D were normal. Urinalysis was bland. She was sent for genetic testing and underwent whole exome sequencing. Results demonstrated a heterozygous deletion in the HNF1β gene consistent with HNF1β nephropathy. She was started on amiloride and slow release magnesium supplementation with near normalization of her serum magnesium.

Discussion: HNF1β-associated kidney disease is a challenging diagnosis given extreme variability in phenotypes. De novo mutations occur in up to half of patients. The true pathogenicity and penetrance of many rare putative disease-causing copy number variants (CNVs) is uncertain and may be over- or underestimated by clinical ascertainment. We aimed to assess the pathogenicity and penetrance of HNF1B deletions and duplications in UK Biobank (UKBB) and to describe any associated phenotype.

Methods: We used data from 388,714 UKBB participants to assess CNVs of HNF1B in a population-based setting using SNP chip intensity data. We tested the association of these CNVs with diabetes and other clinically-relevant traits. We assessed the UKBB phenotype and biomarker information and correlated these with the deletions and duplications.

Results: We identified 11 individuals with large deletions relating to HNF1B and 106 with duplications. There were no significant difference in the average ages of deletion (53), duplication (56) and UKBB population (57). Of the 11, 3 were reported to have glomerular disease, 1 had haematuria, 1 had a renal transplant, and 6 had diabetes (55% vs. 5% amongst the rest of UKBB; P=2x10^-6). The penetrance of diabetes was 30% and 15% in the UKBB population. Average eGFR was 60 v 71 mL/min/1.73m^2 in UKBB population. There were no significant difference in the average ages of deletion and duplication and diabetes (4.4% vs. 5.3%; P=0.8) or liver function.

Conclusions: HNF1B deletions and duplications can be detected in a large unselected dataset. Deletions are more pathogenic than duplications. However, HNF1B duplications do not result in strong phenotypic features, which has not been previously described. The frequency of both HNF1B deletions and duplications may be higher than previously estimated.
PO1536
Impact of Long-Term Tolvaptan Treatment for Autosomal Dominant Polycystic Kidney Disease: A Single-Centre Retrospective Japanese Cohort Study
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Background: Several clinical trials have revealed the efficacy of the tolvaptan for autosomal dominant polycystic kidney disease (ADPKD) in the US. Our objective is to verify the impact of tolvaptan in our Japanese ADPKD cohort.

Methods: We retrospectively investigated the efficacy of tolvaptan for ADPKD patients who initiated tolvaptan from June 2014 to March 2020 in Hokkaido University Hospital. Patients treated with tolvaptan for more than one year were included for analyses. Patients never treated by tolvaptan were set as control. Patients in CKD stage 5 or 3D at baseline or post-kidney transplantation were excluded from analyses. We stratified patients by Mayo classification (Class 1A-IE). Analyses included the comparison of the annual changes of eGFR and ΔTKV (mL/min/1.73m²/year) and total kidney volume (ATKV [V/year]) between pre and post-treatment, and ΔeGFR or ΔATKV between tolvaptan-treated and control.

Results: 109 tolvaptan-treated and 139 control patients were included. 24 patients in each group were excluded. About 40% of tolvaptan-treated patients belonged to advanced CKD stage (CKD3-4). Duration of tolvaptan treatment was 3.1±1.3 years. eGFR of tolvaptan group were lower and htTKV of tolvaptan group were higher compared to those of control group at baseline (eGFR: 53.7±22.8 vs 65.7±30.0, p=0.16. htTKV: 1193.9±22.8 vs 829.5±799.5 mL/min, p<0.0001). There was no significant difference in ΔeGFR between tolvaptan and control group (ΔeGFR: -6.9±8.2 vs 0.3±4.3, p=0.19), however in tolvaptan group ΔeGFR improved compared to pre-treatment (-2.9±5.26 vs -4.3±5.52, p=0.027) and this improvement lasted at least for 36 months in 50 patients. AKTV of tolvaptan group was lower than that of control (21.9±9.5% vs 23.0±10.4%, p=0.004), however in tolvaptan group AKTV also decreased compared to pre-treatment (2.19±0.33-4.06 vs 4.67±2.57-6.76, p=0.01).

Conclusions: Tolvaptan treatment had no apparent effect on renal function in this study. However, tolvaptan improved AKTV compared to control. Further large-scale studies are needed to validate the effect of tolvaptan.

PO1537
Canadian Real-World Assessment of Tolvaptan in ADPKD: C-MAJOR Study and Safety Monitoring and Distribution Program
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Background: Tolvaptan is the first and only approved treatment for autosomal dominant polycystic kidney disease (ADPKD) approved in the United States (US). The Food and Drug Administration (FDA) required a Risk Evaluation and Mitigation Strategy (REMS) to mitigate the risk of liver injury. The aim of this interim analysis is to describe baseline characteristics of patients at initiation of tolvaptan through the C-MAJOR study and to report on treatment persistence and liver transaminases elevation rate through the REMS.

Methods: C-MAJOR is a non-interventional, multi-centre study of ADPKD patients treated with tolvaptan. HSMDP ensures tolvaptan is dispensed under controlled liver function monitoring. Patients treated with tolvaptan in the REMS comprised the study population. Mean age at tolvaptan initiation was 46.8 years (standard deviation [SD]: 11.6); 2,751 (51.3%) were female. Of the patients with a known race (n=2,705, 99.2%) 1,256 (46.3%) were white, 1,373 (50.3%) were black or African American, 73 (2.7%) were Asian, 16 (0.6%) were American Indian or Alaskan Native, and 1 (0.04%) were of other race.

Results: 4,355 patients. The mean age at tolvaptan initiation was 48.8 years (Standard Deviation: 12.3), with 51.7% (n=2,251) female. Hypertension was the most commonly observed comorbidity (n=3,520, 80.8%), followed by diabetes (n=273, 6.3%). The distribution of CKD stage, available for 1,566 (36.0%) patients, was: 6.2% (n=97) in CKD Stage I, 13.4% (n=210) in CKD Stage II, 55.2% (n=864) in CKD Stage III, 22.9% (n=359) in CKD Stage IV, and 2.3% (n=36) in CKD stage V.

Conclusions: This is one of the first real-world studies to describe comorbidities and baseline characteristics in ADPKD patients initiating tolvaptan in the US. Stage III was the most commonly reported CKD stage among patients with a known CKD stage during their baseline period. Additional analyses evaluating the real-life impact of tolvaptan on clinical outcomes, healthcare utilization, and quality of life are needed.

PO1538
Early Findings of Patients with Autosomal Dominant Polycystic Kidney Disease Initiating Tolvaptan in the United States: A Claims-Based Analysis
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Background: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease. Tolvaptan (Jynaq®), the first and only approved treatment for ADPKD in the United States (US), has been shown to slow kidney function decline in clinical trials. An understanding of characteristics of the real-world patients initiating treatment with tolvaptan in the US is needed.

Methods: An observational, retrospective analysis assessing baseline measures was conducted among patients with ADPKD who had initiated treatment with tolvaptan from 14 May 2018 through 9 January 2020 in the US. Data were obtained by linking the Symphony Health Integrated Datavverse (IDV), a nationally representative billing database, with Specialty Pharmacy (SP) data from the tolvaptan Risk Evaluation and Mitigation Strategy (REMS), which is a mandatory program for patients prescribed tolvaptan to treat ADPKD. The study index date was the date of first shipment of tolvaptan. Descriptive analyses were conducted on the following baseline measures: demographics, comorbidities, and disease characteristics. All measures were identified within the 6-month period prior to the index date in the Symphony Health IDV.

Results: A total of 5,366 patients who initiated tolvaptan in the REMS comprised the study population. Mean age at tolvaptan initiation was 46.8 years (standard deviation [SD]: 11.6); 2,751 (51.3%) were female. Of the patients with a known race (n=2,705, 99.2%) 1,256 (46.3%) were white, 1,373 (50.3%) were black or African American, 73 (2.7%) were Asian, 16 (0.6%) were American Indian or Alaskan Native, and 1 (0.04%) were of other race.

Conclusions: This is the first descriptive demographic report of real-world ADPKD patients in the US initiating tolvaptan. Based on the data currently available, most patients were between 35-55 years, equally male or female, and were non-Hispanic or non-Latino. Overall, 2,366 (44.1%) tolvaptan initiators had at least 1 year of follow-up after the index date and were included in the treatment pattern analysis. The most frequent dose of tolvaptan was 45/15 milligrams daily (47.5%). The mean MPR was 0.74 (SD: 0.32); mean persistency was 50.4%, the majority were white (n=2,153, 79.6%). Of those with known ethnicity (n=2,705, 99.2%) 1,256 (46.3%) were white, 1,373 (50.3%) were black or African American, 73 (2.7%) were Asian, 16 (0.6%) were American Indian or Alaskan Native, and 1 (0.04%) were of other race.
Benefit of Tolvaptan on Time to ESRD for Patients with Rapidly Progressing Autosomal Dominant Polycystic Kidney Disease (ADPKD): A Disease Progression Model

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Background: The efficacy and safety of tolvaptan in adults with ADPKD was initially established in a 3-year phase 3 clinical trial (TEMPO 3:4; NCT00428948). Tolvaptan was approved in the United States in 2018 for patients with ADPKD at high risk of progression. A published ADPKD progression model predicted longer-term outcomes including eGFR decline and time to ESRD. The model incorporated an equation used to predict eGFR based on Mayo subclasses 1C, 1D, and 1E as indicators of rapid progression. To estimate treatment benefit, long-term outcomes were modelled for patients treated with and without tolvaptan based on the TEMPO 3:4 cohort.

Methods: In the base case, the annual absolute reduction in eGFR decline for tolvaptan versus placebo of 1.2 ml/min/1.73m2 was applied to the predicted rates of eGFR decline in the absence of treatment. Additionally, in a sensitivity analysis based on a post-hoc analysis of TEMPO 3:4, the effect on eGFR decline by subclass 1C, 1D, and 1E was applied. CKD progression and time to ESRD were estimated for both cohorts.

Results: The predicted time to ESRD was longer for all patients in CKD stages 1-3 treated with tolvaptan, with greater estimated absolute benefit when treatment was initiated for patients in early CKD stages (Image). The model estimates that patients treated with tolvaptan versus no treatment spend more time in earlier CKD stages and later onset of ESRD. Results were consistent across CKD stages and Mayo subclasses. Findings highlight the potential long-term value of early intervention with tolvaptan in patients at risk of rapid ADPKD progression.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc.

Conclusions: Patients with ADPKD receiving tolvaptan in the real-world experienced improved clinical outcomes without negative impact on QoL. Additional studies assessing real-world evidence supporting tolvaptan treatment in this population are needed.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization, Inc.

Urinary Lithogenic Risk Profile in ADPKD Patients Treated with Tolvaptan

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Background: Nephrolithiasis is a common health problem in autosomal dominant polycystic kidney disease (ADPKD) and significantly contributes to patient morbidity. Recently, Tolvaptan has been introduced for the treatment of ADPKD, but if it is associated with alterations of the urinary lithogenic risk profile remains unknown.

Results: We conducted an analysis of participants enrolled in the Bern ADPKD registry, a prospective observational cohort study. 24 hour urine analyses were performed at baseline and then at yearly follow-ups. Relative supersaturation ratios for calcium oxalate, brushite and uric acid were calculated with the program EQUIL2. Unadjusted and multivariable mixed-effects linear regression models, adjusted for age, sex, body mass index, eGFR, and glomerular filtration rate, net acid excretion and height-adjusted total kidney volume were used to assess the association of Tolvaptan with urinary parameters relevant for kidney stone formation. Maximum individual follow-up time was 3 years, median follow-up time 1.9 years and cumulative follow-up time was 169 years.

Results: 125 participants (38 with and 87 without Tolvaptan treatment) were included in the analysis. In multivariable analysis, Tolvaptan treatment was associated (adjusted estimate of the difference Tolvaptan vs. no Tolvaptan; 95% CI) with lower urinary relative supersaturation ratios for calcium oxalate (-0.56; -0.82 to -0.3, p < 0.001), brushite (-0.53; -0.54 to -0.11, p = 0.004) and uric acid (-0.62; -0.88 to -0.37, p < 0.001) and with increased urine citrate in mmol/mmol creatinine per day (0.025; 0.050-0.46, p = 0.02) and calcium in mmol/mmol creatinine per day (0.031; 0.090-0.53, p = 0.006) excretion. In addition, Tolvaptan treatment was associated with decreased net acid excretion in mg/mmol creatinine per day (-0.54; -0.90 to -0.17, p = 0.004) and increased net gastrointestinal alkali absorption in mg/mmol creatinine per day (0.57, 0.26-0.88; p < 0.001).

Conclusions: Tolvaptan treatment is associated with a significantly improved urinary lithogenic risk profile in ADPKD patients.

The Effect of Trichlormethiazide in Patients with Autosomal Dominant Polycystic Kidney Disease Using Tolvaptan: A Randomized Cross-Over Controlled Trial

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Background: The vasopressin V2 receptor antagonist tolvaptan has been shown to slow the progression of autosomal dominant polycystic kidney disease (ADPKD). However, some patients discontinue tolvaptan due to severe adverse aquaretic events. This open-label, randomized, controlled, counterbalanced, crossover trial investigated the effects of trichlormethiazide, a thiazide diuretic, on reducing urinary volume and improving tolvaptan tolerability in patients with ADPKD on high-dose tolvaptan, based on the effects of thiazides in patients with nephrogenic diabetes insipidus.

Methods: A total of 10 patients with ADPKD on high-dose tolvaptan (median age, 49 years; 4 males) received antihypertensive therapy with or without trichlormethiazide in random order for 12 weeks. The starting doses for trichlormethiazide were 2 and 4 mg in patients with estimated glomerular filtration rates of <30 and <30 mL/min/1.73 m2, respectively. Target blood pressure range was 110/70-130/80 during the study period. Primary outcomes were 24-hour urine volume and urine osmolality. Secondary outcomes were health-related quality of life (HRQOL) assessed by the Kidney Disease Quality of Life-Short Form questionnaire, rate of decline in renal function, serum/urinary electrolytes, serum/urinary biomarkers associated with chronic kidney disease and ADPKD progression, and office blood pressure.

Results: The urine volume was significantly reduced (3324 ± 614 vs. 4169 ± 729 mL; P < 0.001) along with an increase in urine osmolality (179.0 ± 26.6 vs. 139.1 ± 39.6 mosm; P = 0.001) in patients on antihypertensive therapy with trichlormethiazide. Moreover, trichlormethiazide improved several HRQOL subscales including effects of kidney disease, sleep, emotional role functioning, social functioning, and role/social component summary. There were no significant differences in the slope of estimated glomerular filtration rate assessed by creatinine and cystatin C or serum/urinary biomarkers between the patients on antihypertensive therapy with and without trichlormethiazide. Office blood pressure was not significantly different between the treatment groups.

Conclusions: In patients with ADPKD treated with high-dose tolvaptan, trichlormethiazide may improve tolvaptan tolerability and HRQOL by reducing urinary volume without affecting ADPKD-related parameters.
PO1544
Predictors for Suppressing Polycystic Liver Progression of ADPKD by Tolvaptan
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Background: Polycystic liver disease (PLD) is one of the fatal complications of ADPKD, which leads to abdominal compression, cyst infection, and liver failure. Although PLD progresses after reaching ESKD, few drugs can effectively inhibit its growth. Tolvaptan (TVP), V2 receptor antagonist, has been known to suppress the growing rate of polycystic kidney disease, but the effect on PLD has not been studied yet. In order to evaluate the tolvaptan’s effect on PLD, an observational cohort study was conducted.

Methods: ADPKD patients with PLD taking tolvaptan were enrolled in this study. Total liver volume (TLV) was measured by CT and calculated by automated calculated application, VINCENT®. Annual change of TLV (ΔTLV) was defined by the approximate slope estimated from more than two points. If the patients had some interventions including cyst drainage, surgical fenestration, and transcatheter trans-arterial embolization, the observational period was excluded for one year after such interventions. We compared ΔTLVs before and after TVP initiation, and defined “responder” as patients whose post-ΔTLV were smaller than pre-ΔTLV. Factors associated with “responder” were analyzed by the logistic regression model, adjusting sex, age, BMI, blood pressure, height adjusted total kidney volume(tTKV) and ATLV before taking TVP(preATLV), by using R version 3.4.3.

Results: 85 patients were eligible to this study. Median observational periods were 1.98 and 2.19 year in pre-prescription period and post-prescription period respectively. Median age was 55 years old and 31 cases were female. Median htTLV and htHTK before taking TVP was 1747[557-7432] (ml/m) and 909[226-4152] (ml/m), respectively. The reduction of ΔTLV were observed in 46 cases, who were significantly older, had higher preATLV and had higher rate of taking ursodeoxycholic acid. Logistic regression analysis showed older age (OR 2.69[1.36-5.72],p<0.01) and higher preATLV (OR 1.25[1.12-1.46],p<0.01) were the predictors of the reduction of ΔTLV.

Conclusions: In this study, more than half of ADPKD patients experienced reduction of ΔTLV after taking TVP. Our study suggests that older age and higher pre-ΔTLV would predict the reduction of the progression of PLD after TVP use, though it was reported younger female tend to have larger PLD.

PO1545
Use of Lixivaptan in a Patient with Autosomal Dominant Polycystic Kidney Disease (ADPKD) Who Previously Experienced Liver Toxicity with Tolvaptan
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Introduction: Blockade of the vasopressin V2 receptor has beneficial effects on the renal manifestations of ADPKD, the most prevalent inherited renal cystic disease in humans. Tolvaptan, a vaspressin V2 receptor antagonist, is the only approved pharmacologic therapy for the treatment of ADPKD patients; however, it is associated with potentially serious idiosyncratic liver toxicity. Lixivaptan is a novel, potent antagonist of the V2 receptor in Phase 3 development for the treatment of ADPKD. Evidence from non-clinical and in silico studies predicts that lixivaptan will have a safer liver toxicity profile in patients with ADPKD. Here we provide the first clinical evidence of lixivaptan’s superior liver safety compared to tolvaptan.

Case Description: A female patient with ADPKD presented with severe bilateral, fluctuant flank and abdominal pain. The patient had been treated with tolvaptan previously in an attempt to improve her pain; however, tolvaptan therapy had to be permanently discontinued after the patient developed clinically-meaningful alanine aminotransferase (ALT) elevations on each of three sequential attempts to treat her. The patient was screened and enrolled in an open-label study of lixivaptan under a US IND expanded-access protocol (PA-103). After treatment with therapeutic doses of lixivaptan for 12 months, there have been no elevations of ALT or other liver chemistry tests. Improved pain control has allowed resumption of more normal daily activities and the cessation of use of opioid pain medications. Pharmacodynamic effects including decreases in total kidney volume and liver volume were demonstrated as well as expected changes in eGFR with a vasopressin antagonist. Treatment with lixivaptan continues.

Discussion: This is the first report of successful treatment with lixivaptan of a patient who had previously experienced liver toxicity on tolvaptan. These clinical data highlight the potential for improved liver safety with lixivaptan in a patient at high risk for developing liver toxicity. A larger study (PA-ADPKD-303: The ALERT Study) is starting up to treat ADPKD patients with lixivaptan who previously discontinued tolvaptan because of liver chemistry test elevations.

PO1546
Generation of Collecting Duct Kidney Organoids from Human Induced Pluripotent Stem Cell

Background: Polycystic kidney disease (PKD) is one of the most common human genetic disorders without effective therapy. During its progression, fluid-filled cysts replace normal collecting duct (CD) tubules causing end-stage renal failure. The lack of disease-relevant in vitro models of PKD has hampered early drug discovery and needs more efficient and robust tools.

Methods: Here we modified a previously published protocol [1] and established a high-throughput and highly efficient method for the generation of CD kidney organoids from human induced pluripotent stem cells (hiPSC). We employed a dynamic modulation of cell signaling pathways in combination with 3D extracellular matrix support to induce CXXr4/cit+ ureteric bud (UB) cell progenitors and further UB branching. Results: The UB gives rise to renal collecting ducts and the lower urinary tract. We observed the development of UB-like cytoarchitecture including, bifurcated ureteric tip expressing specific markers (RET, WNT9B, HOXB7). Using single-cell RNA sequencing (scRNAseq) we identified two major cell populations in differentiated CD organoids – collecting duct cells and stromal cells. CD cells express typical markers of UB trunk (CK19), the ureteric epithelium (CDH1, CK8), as well as mature markers (AQ2P, CALB1, MUC1) including principal (AQP3) and intercalated cells (AQP5). Moreover, we identified cilia formation on the inner surface of the luminal cavity of CD tubules. High-order kidney organization was promoted by immunostaining. Cell Stem Cell; 21: 730-746

Conclusions: In conclusion, we provide a robust and highly efficient method for collecting duct marker expressing organoids that may contribute to elucidating the mechanisms of kidney development, disease modeling of the lower urinary tract (polycystic kidney disease), and drug discovery. 1. Taguchi A, Nishinakamura R. (2017) High-order kidney organization in organoids from pluripotent stem cells. Cell Stem Cell; 21: 730-746

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Underline represents presenting author.
PO1548  The Effect of Trehalose on Autophagy-Related Proteins and Cyst Growth in a Hypomorphic Pkd1 Mouse Model of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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Background: There is growing attention on understanding the role of impaired autophagy in ADPKD. Trehalose (TRE) is a natural sugar that is used as a food additive. TRE increases protein stability, aggregate clearance and autophagy in neurodegenerative diseases. TRE treatment in wild type (WT) mice resulted in increased expression in the kidney of Atg12-5 complex and Rab9a (Table), autophagy-related proteins that play a role in the formation of autophagosomes. Thus, the aim of the study was to determine the effect of TRE on cyst growth and autophagy-related proteins, in the Pkd1tm8(sc) (RC) mouse model.

Methods: Autophagy proteins determined by immunoblot analysis. Male RC mice were treated with TRE from 50-120 days of age.

Results: In RC kidneys, expression of the Atg12-5 complex was inhibited by TRE resulting in increased free Atg12. TRE was unable to rescue the deficiency of the Atg12-5 complex. Rab9a was decreased in RC and unaffected by TRE. The TRE-induced increase in p62, a marker of autophagic cargo, that was seen in WT was blocked in RC kidneys. In RC kidneys, there were decreases in autophagy-related proteins (Atg12-5 complex, Atg16L1), decreased Rab9a and increased mTORC1 (serine/threonine kinase 1 (pS6, p-mTOR) proteins. 2 kidney/ body weight ratio (2K/BW), cyst index/count, BUN were not different in TRE vs. Veh treated RC kidneys.

Conclusions: The autophagy phenotype in RC kidneys was characterized by decreases in essential autophagy related proteins. TRE increased Atg12-5 complex, Rab9a and p62 in WT kidneys, but was unable to rescue the deficiency in autophagy proteins or suppress mTORC1 in RC kidneys and did not protect against cyst growth.

Funding: Veterans Affairs Support, Other U.S. Government Support

Densitometry units/GAPDH *P<0.05, **P<0.01, ***P<0.001

PO1549  Suppressed Autophagic Flux in the Heart in a Hypomorphic Pkd1 Mouse Model of ADPKD

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Background: Heart disease is largely unexplored in mouse models of ADPKD. The aim of the study was to determine mTOR signaling and autophagy in the heart in Pkd1RC/RC (RC) mice.

Methods: Proteins were determined by immunoblot analysis. Mice were treated with autophagy inducers 2-deoxyglucose (2-DG) or Tat-Beclin1 peptide (Tat).

Results: There was increased heart weight/body weight ratio (HW/BW) in 180 d old RC mice. In 70 day old RC hearts, there was no increase in mTOR but a large increase in p-AMPK (Thr172), a known autophagy inducer. In 150 day old RC hearts, there was an increase in p-S6, p-Akt (Ser473), p-GSK3β, p-AMPK, p-Beclin, an autophagy regulator and activating molecule in Beclin-1-regulated autophagy (AMBRA1). There was suppressed autophagic flux (lack of an increase in LC3-II, a marker of autophagosomes, with the lysosomal inhibitor bafilomycin-Ba1) in 70 and 150 d old RC hearts compared to an increase in wild type (WT) hearts. In 120 d old RC hearts there was no increase in proliferation (PCNA) or apoptosis (TUNEL). Both 2-DG and Tat treatment increased heart weight and had no effect on kidney weight.

Conclusions: There was a large increase in p-AMPK and suppressed autophagy in RC hearts. Unexpectedly, autophagy inducers increased heart weight.

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Ferroptosis Promotes Cyst Growth in Autosomal Dominant Polycystic Kidney Disease

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Background: Ferroptosis is a newly discovered form of non-apoptotic cell death which is dependent on accumulation of lipid reactive oxygen species (ROS). Recent studies have shown that ferroptosis is involved in the pathophysiological processes of many diseases, such as cancer. However, the roles of ferroptosis in ADPKD remain unknown.

Methods: To evaluate whether ferroptosis occurs in ADPKD, we detected the levels of ROS with C11-BODIPY and 4-HNE staining, and the expression of glutathione peroxidase 4 (GPX4), a key protein in the ferroptotic pathway, by western blot and qRT-PCR in cystic cells and kidneys. To understand the role of ferroptosis in ADPKD, we treated Pkd1 mutant mice with erastin, a ferroptosis inducer, and Ferrostain-1, a ferroptosis inhibitor.

Results: We found that the levels of free radical-induced oxidation and 4-HNE, a byproduct of lipid peroxidation, were increased in Pkd1 mutant renal epithelial cells and tissues as examined by C11-BODIPY and 4HNE staining. Erastin treatment resulted in smaller-than-normal mitochondria with increased density, a morphological feature of ferroptotic cells, in Pkd1 mutant renal epithelial cells under electronic microscopy. We further found that treatment with erastin promotes cyst growth as seen by increased cystic index, kidney weight (KW)/body weight (BW) ratios, blood urea nitrogen (BUN) levels, cyst lining epithelial cell proliferation, and lipid peroxidation in Pkd1tm8(sc) mice (all p < 0.01). In contrast, treatment with Ferrostain-1 delayed cyst growth in early stage Pkd1tm8(sc), Pkd1-Cre mice and Pkd1tm8(sc) mice as seen by decreases in all the parameters observed in erastin treated mice. Treatment with erastin increased the activation of ERK, Stat3, Akt and Rb in Pkd1 mutant renal epithelial cells and tissues. Activation of Stat3 increased the expression of DNA methyltransferase 1 (DNMT1), leading to the binding of DNMT1 to the GPX4 promoter and decreased expression, resulting in the accumulation of ROS species to promote cystic renal epithelial cell ferroptosis. Treatment with Ferrostain-1 reversed all these processes in Pkd1 mutant renal epithelial cells and tissues.

Conclusions: Pkd1 mutation induced the downregulation of GPX4 via Stat3- DNMT1, resulting in cystic renal epithelial cell ferroptosis. Inhibition of ferroptosis in ADPKD may be a viable new therapy for ADPKD.

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Cux1 Regulates Cilia Length in Polycystic Kidney Disease

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Background: Cilia are critical to the pathogenesis of ADPKD, which is one of many ciliopathies that exhibit renal cystic disease. Cux1, a murine homologue of the Drosophila gene Cat, is a cell cycle dependent transcriptional repressor that regulates the cyclin kinase inhibitor p27. Cux1 is highly and ectopically expressed in mice carrying a collecting duct (CD) specific mutation of Pkd1 (Pkd1 knockout) and in human ADPKD cells. Mice carrying mutations in both Cux1 and Pkd1 have reduced cystic disease and an increased life span. A role for Cux1 in regulating genes involved in cilia assembly and function has recently been identified in the Galapagos cormorant, however the role of Cux1 in cilia in the mammalian kidney is not known.

Methods: To begin to determine whether Cux1 regulates ciliogenesis we evaluated cilia morphology and the expression of the ciliary protein, ODF1 (oral-facial-digital-1), in ADPKD.
identified as a Cux1 target in the Galapagos cormorant. Cilia analysis was performed on kidneys isolated from wild type, Cux1 transgenic, Pkd1 knockout, and Pkd1 Cux1 double knock out mice. Cilia morphology was assessed by immunofluorescence labeling of alpha-tubulin, a major component of cilia, and the collecting duct marker dolichos biflorus agglutinin (DBA) to identify cells in which Pkd1 was deleted.

Results: Cilia in Pkd1/Cux1 double knockout kidneys were significantly shorter than cilia in the Pkd1 knockout kidneys alone, consistent with previous studies showing that decreased cilia length corresponds to decreased cystic disease. OFD1 is an inhibitor of ciliogenesis and OFD1 expression in the various mouse models demonstrate that OFD1 expression correlates with Cux1 expression. OFD1 protein levels were the lowest in the kidneys of mice cotransfiently expressing Cux1 and were highest in mice with deletions of Cux1.

Conclusions: Taken together, our results suggest a novel role for Cux1 in regulating ciliogenesis in the kidney and that reduced cystic disease in the Pkd1/Cux1 double mutant mice results from reduced cilia length.

PO1552

Low-Dose Repeated Cisplatin-Induced Renal Injury Promotes Cyst Formation in Both Pkd1 and Pcd2 Mutant Mouse Models

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Background: Multiple renal cystic diseases, including PKD, are caused by dysfunction of the primary cilium on the tubule epithelium. Links between cilia dysfunction, cyst formation, and renal injuries have been reported. In animal models, injury (e.g. ischemia reperfusion) exacerbated the rate of cyst formation. Cisplatin is an established anti-metabolite used in treatment of varieties of malignancies that displays severe nephrotoxic side effects. Here we evaluate whether a second form of renal injury induced by a low dose of Cisplatin also leads to mal-repair of the kidney and to increased cyst formation in mouse models with cilia function perturbation.

Methods: To test the effects of cisplatin-induced renal injury on cyst formation, we utilized a low-dose repeated cisplatin protocol (Cting BW; IP once a week for 4 weeks) on adult-induced conditional IHH8 and PCD2 mutant mice. We performed IP staining for the injury marker klim1 and flow cytometry analysis of immune cells from WT and cilia dysfunctional kidneys 3 days after 2° cisplatin treatment to evaluate renal injury. Cyst index was analyzed at 5 weeks in PCD2 mutant and at 9 weeks in IHH8 mutant after the final dose.

Results: Low-dose repeated cisplatin treatment resulted in increased klim1 expression, mainly in the cortex, compared to vehicle treatment group in both IHH8 mutant and PCD2 mouse sequence compared to control. Analysis of flow cytometry data showed that there was minimal immune cell accumulation, including macrophages, NK, B or T cells, at 3 days after 2° cisplatin injection, similar to that in controls. Additional time points are currently being evaluated. While we did not observe major changes in immune cell response at the earlier time point prior to cyst formation, in both PC2 and IHH8 mutants there was a marked increase in cyst severity, accompanied with massive immune cell accumulation compared to vehicle treated mutants at 5 and 9 weeks after the final cisplatin injection, respectively.

Conclusions: These data indicate cilia function is important in regulating repair processes following injury, defects in which contribute to more aggressive rates of cystogenesis. Additionally, it suggests multiple forms of injury induce cyst formation and that the cisplatin protocol could be used as an alternative approach to IRI to accelerate cyst formation in PKD animal models.

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PO1553

Primary Cilia Defects Reflect Specific Bone Cell Activity in Human ADPKD Osteoblast Cells

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Background: Autosomal dominant polycystic kidney disease (ADPKD) is predominately caused by mutations in primary ciliary genes polycystic kidney disease PKD1 and PKD2. Recent studies show that ADPKD is associated with abnormal bone health with decreased bone formation and low bone serum alkaline phosphatase, even when cilia function is preserved. Knowledge of the regulatory links between ADPKD, cilia, and human bone health is lacking.

Methods: We assessed primary cilia in cultured pre-osteoblasts derived from ADPKD patients with PKD1 or PKD2 mutations, relative to healthy controls and non-ADPKD chronic kidney disease (CKD) patients. Cilia were quantified by immunofluorescence staining of pericentrin and acetylated-tubulin. Cilia responsiveness was examined following treatment with lithium chloride (LiCl), an activator of the canonical Wnt signaling pathway that is known to induce cilia elongation. Biochemical osteoblast analyses included bone turnover by alkaline phosphatase (ALP) activity and mineralization assays. Results: Compared to healthy control cells, ADPKD osteoblasts displayed longer cilia at baseline and were significantly more responsive to elongation with LiCl. In contrast, non-ADPKD CKD osteoblasts had shorter cilia and lacked LiCl responsiveness. Despite similar histological features and adynamic bone characteristics, ADPKD osteoblasts mineralized faster than osteoblasts from non-ADPKD CKD. The ALP activity levels were decreased in ADPKD osteoblast cells, which is consistent with the lowered circulating bone ALP levels.

Conclusions: Together, these data support a model whereby altered cilia responsiveness in ADPKD osteoblasts is linked to bone cell activity and mineralization defects that are distinct from adynamic bone of non-ADPKD CKD patients.

Funding: NIDDK Support

PO1554

Pathobiology of Cyst Progression in Nbc1A1 and Pkd1 (RC/RC) Mouse Models

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Background: The Pkd1(RC/RC) mouse is a hypomorphic model of autosomal polycystic kidney disease (ADPKD) characterized by renal cortical and medullary cysts which increase in size and number with age. The nature of these cysts and how this epithelium differs from normal collecting duct epithelia is currently unknown. Moreover, as the phenotype is variable, the disease progression of any individual mouse is unknown. We also generated an isoform specific Na+/bicarbonate cotransporter knockout (Nbc1A-KO) mouse using TALENs. As with the whole gene knockout, these mice are severely acidic but also present with cortical renal cysts. The nature of these cysts and their connection to Nbc1A1 protein expression is currently unknown.

Methods: We measure mouse (Bk6J) total kidney volume (TKV) using MRI (T1/16T) and ultrasound (US; Sonovol Vega). The Vega system allows 3D renal imaging and cardiac analysis (e.g., heart rate, ejection fraction, cardiac output). We follow renal function using transdermal GFR measurements. Lastly, kidneys are harvested, fixed, followed by immunofluorescence (IF) of cryosections with nephrin segment specific markers or picrosirius red (collagen stain) and paraffin sections.

Results: A longitudinal study of Nbc1A-KO and RC/RC mice shows both models increased TKV (Fig A) measured by MRI or US (Fig BC). Both show lower GFR [WT: 55±4, nbc1A-KO: 42±14; RC/RC: 27±63±5 μl/min (100g bw)]. Ejection fraction and stroke volume were preserved, while heart rate and cardiac output decreased in Nbc1A-KO and RC/RC mice (Fig A). Both Nbc1A-KO (Fig E) and RC/RC mice (Fig F) have collecting duct cysts, positive for AQP2 and cKit. Picrosirius red staining shows that these cystic structures have increased collagen thickening.

Conclusions: Together these data imply that cystogenesis in the RC/RC and nbc1A-KO models have similar pathobiology. Potentially this means that understanding how and why cysts develop in nbc1A-KOs may provide additional mechanistic information in ADPKD.

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PO1555

Characterization of the Nuclear Factor Erythroid 2-Related Factor 2 (Nrf2) Response in Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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Background: Autosomal dominant polycystic kidney disease (ADPKD) is characterized by progressive development and enlargement of bilateral renal cysts. Abnormal epithelial cell proliferation, along with the inability to maintain planar cell polarity, underlies cyst formation and enlargement. Therefore, processes that stimulate renal cell proliferation have the potential to generate the cystic phenotype. Interestingly, an increased nuclear factor erythroid 2-related factor 2 (Nrf2) response has been shown to direct cancer cells into an anabolic mode that favors cellular proliferation, and has been associated with renal cyst formation in experimental and human fumurate hydratase deficiency. However, the Nrf2 response has not been described in ADPKD. We hypothesized that early ADPKD presents with an elevation in the Nrf2 response that favors cellular proliferation and contributes to cystogenesis.

Methods: We sought to longitudinally characterize the Nrf2 response and association with cystogenesis and fibrosis in a slow in progress mouse model of ADPKD (Pkd1lox/lox) and its wildtype controls (n=6 males, 6 females per group). Urine and plasma samples were collected at 30, 60, 120, and 180 days for chemistries and metabolic profiles, and cystic index (CI), and total kidney volume (TKV) were determined from abdominal MRI. Nrf2 levels and related response enzymes, as well as cell proliferation and fibrosis were analyzed using western-blots, immunofluorescence, and assay kits. At 30 days, Pkd1lox/lox mice presented increased CI and TKV/BW. However, serum creatinine and fibrotic markers were not different compared to controls. Pkd1lox/lox mice exhibited elevated Nrf2 expression and immunoreactivity early on that declined as ADPKD progressed from 30 to 180 days and correlated directly with cell proliferation (R=0.693, p<0.05) and inversely with fibrotic markers (R=-0.672, p<0.05).

Conclusions: Our study shows longitudinal changes in the Nrf2 response in Pkd1lox/lox mice that are associated with cystogenesis early on and renal fibrosis at later stages of the disease. These findings have significant implications for the treatment of human ADPKD, and suggest that Nrf2 modulators might represent an advantageous intervention for the disease.

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PO1556

Dietary Protein Load Increases Kidney Macrophage and Accelerates Polycystic Kidney Disease

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Background: The disease severity for autosomal dominant polycystic kidney disease (PKD) is highly variable even among families with the same gene mutation, suggesting factors other than genetics may affect cystogenesis. One factor that accelerates cyst growth in PKD mouse is compensatory renal hypertrophy triggered by unilateral nephrectomy or a high protein diet. We recently reported that unilateral nephrectomy increases kidney macrophages, cytokines and accelerates cystogenesis in Pkd1-knockout mice. We hypothesize that Pkd1-knockout mice fed a high protein diet, similarly increases kidney macrophages and accelerates cyst growth.

Methods: We used adult tamoxifen inducible Pkd1floxflox mice with or without CAGG-cre. After cre induction, mice were fed either a high protein (HP, 60%), a normal protein (NP, 18%) or a low protein (LP, 6%) diet for a total of 1 or 6 weeks. Some mice fed a HP diet were treated with liposomal clodronate (to deplete macrophage) or phosphate buffered saline (intraaperitoneally twice a week) for a total of 6 weeks. Mice were euthanized at the end of the experiment for kidney histology, measurements of cytokine and macrophages by flowcytometry.

Results: Pkd1-knockout mice fed a HP diet for 6 weeks resulted in increased number of kidney resident macrophage (CD11b+ F4/80+), and infiltrating macrophages (CD11b+, F4/80+) compared to Pkd1-knockout mice fed a NP or LP diet. HP diet fed mice resulted in increased kidney pro-inflammatory cytokines, chemokines and severe kidney cysts growth compared to NP or LP diet fed mice. Early after dietary protein modification (1 week), Pkd1-knockout mice fed a HP diet had larger kidneys, higher cystic index and kidney mTOR level compared to LP diet fed Pkd1-knockout mice but there were no differences in the number of macrophages, chemokine and cytokine levels in the kidney. HP diet fed Pkd1-knockout mice treated with liposomal clodronate, resulted in decreased number of macrophages, cytokine and fewer cysts compared to PBS treated Pkd1-knockout mice.

Conclusions: Dietary protein load increases kidney macrophages, inflammatory cytokines, and accelerates cyst growth in adult Pkd1-knockout mice. HP diet stimulates kidney cyst expansion prior to the recruitment of macrophages early on, but subsequent macrophage depletion therapy slowed the acceleration of cyst formation.

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PO1557

Cyst-Lumen Renal Stones in Mice Compound Heterozygous for Hypomophoric Pkd1 and Pkd1Rc Alleles

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Background: Autosomal dominant polycystic kidney disease (ADPKD) patients exhibit a ~2.5-fold higher propensity for renal stone formation compared to that of the general population. However, there are no good mouse models for the analysis of stone formation in ADPKD. We previously reported the presence of cortical renal stones in cystic mice compound heterozygous for hypomorphic alleles Pkd1 and Pkd1Rc (Parnell et al. 2018 J Am Soc Nephrol 29:295). In this present study, the composition and location of the renal stones in this PKD model were determined.

Methods: Pkd1 and Pkd1Rc mice on a C57 background were crossed to produce cystic Pkd1Rc mice. Mice were sacrificed at 3-26 weeks and their kidneys analyzed by Alizarin Red and von Kossa staining. Individual stones were microdissected from cysts and analyzed by μCT and infrared spectroscopic analysis to determine their composition.

Results: Although Pkd1Rc mice were noticeably cystic by 3-weeks of age, stone formation was not obvious until ~13-weeks. Histological sections from 13- and 26-week old mice had regions that stained positive by Alizarin Red and von Kossa in a generally overlapping pattern. In contrast, there were no obvious staining patterns by Alizarin Red or von Kossa in kidneys from 3-week old mice. When kidneys were dissected it became evident that the stones were found almost exclusively within the lumens of cysts (see microdissected cyst with internal stone in Figure 1). μCT and infrared spectroscopic analysis confirmed that dissected stones were comprised of calcium phosphate in the mineral form of apatite, and also rich in protein.

Conclusions: Pkd1Rc mice develop mineralized stone deposits comprised of apatite and protein within the renal cyst lumen. To our knowledge this is the first known instance of renal stones in a mouse model of ADPKD.

Funding: NIDDK Support

Poster

PO1558

Small-Molecule Allosteric Activators of Long-Form PDE4 Enzymes

Suppress Cystogenesis in Models of ADPKD

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Background: In ADPKD, mutations in either Pkd1 or Pkd2 perturb intracellular calcium signalling and drive a chronic elevation of intracellular cAMP through de-suppression of calcium inhibited adenylyl cyclase 5/6. This elevation of cAMP signalling underpins the molecular pathology of ADPKD, promoting widespread cyst formation within the nephron epithelium, ultimately leading to renal failure. Phosphodiesterase 4 (PDE4) enzymes degrade intracellular cAMP in a localised manner, and their activity contributes to the compartmentalisation of sub-cellular cAMP dynamics. By modulating or terminating cAMP mediated signalling events, PDE4A isoforms are placed as a central regulator of many cAMP mediated biological processes. We have previously described the discovery and characterization of novel small-molecule compounds which allosterically activate long isoforms of PDE4A, and here we further describe their therapeutic potential in suppressing the core cAMP drive behind the pathogenesis of ADPKD.

Methods: Biochemical assay, gene expression profiling and genetic manipulation of cell models were undertaken alongside primary human cell 3D-culture experiments and

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Mouse Pkd1ΔCΔC metanephric organ culture to investigate the effects of pharmacological long-form PDE4 activity on intracellular cAMP and cyst dynamics.

Results: Our data show that within murine kidney epithelial cells PDE4 long-form variants from Pde4c and Pde4d predominate and that allosteric pharmacological activation of long-form PDE4 enzymes suppresses intracellular cAMP. We show that the PDE4-inhibited samples have increased expression of mitogen-activated protein (MAP) kinase suppression and increased expression of the transcription factor in translational models of ADPKD, such as in Pkd1ΔCΔC metanephric organ culture and primary human ADPKD cyst culture. This further supports the potential therapeutic benefit of allosteric inhibition of PDE4 in treating ADPKD.

Conclusions: Small-molecule activators of long-form PDE4 enzymes suppress cystogenesis in vivo and increase of amiloride-sensitive transepithelial flux with maximal effect at 50 μM.

Funding: Commercial Support - Sanofi-Genzyme

PO1560 Pharmacological Inhibition of β-Catenin-Activated Transcriptional Slows Cystogenesis in a Postnatal Mouse Model of ADPKD Valerie A. Schubert,1,2 Juny Joan Jung,2 Jordan A. Kreidberg,1,2 (Boston Children's Hospital, Department of Urology, Boston, MA; 2Harvard Medical School, Boston, MA.)

Background: The Wnt signaling pathway has an important role in nephron development and elevated expression of β-catenin, master regulator of the Wnt signaling development and elevated expression of β-catenin-activated transcription slows cystogenesis in a postnatal model of ADPKD.

Methods: To understand the pathological contribution of Wnt signaling to ADPKD, we measured expression of Wnt genes and β-catenin in vivo using a postnatal murine model of ADPKD. We also tested the effect of a selective β-catenin-CBP inhibitor on cyst formation.

Results: We observed both increased expression of Wnt7a and higher levels of β-catenin in cystic kidneys of CAGG-CreERT2;Pkd1ΔCΔC mice. In addition, fibronectin, a known transcriptional target of β-catenin was significantly overexpressed in murine kidney tissues. Using flow cytometry from human samples, we noted increased β-catenin transcriptional activity was required for cystogenesis, we treated CAGG-CreERT2;Pkd1ΔCΔC mice with a small molecule, ICG-001, that blocks the interaction of β-catenin with CBP. We detected significant reduced cyst formation as measured by decreased cyst area and number, decreased cyst area per kidney area, and decreased a significant reduction in fibronectin after ICG-001 treatment. Interestingly, cysts that may have formed prior to the start of the treatment remained large suggesting that ICG-001 may primarily act on inhibiting cyst initiation, rather than inhibiting the enlargement of pre-existing cysts. Importantly, ICG-001 treatment did not affect the growth of the mice.

Conclusions: Our study demonstrates that increased β-catenin transcriptional activity has an important role in cystogenesis and inhibition of the β-catenin-CBP complex by ICG-001 may serve as a new therapeutic modality to decrease cyst formation.

Funding: NIDDK Support

PO1561 Glucosylceramide Synthase Inhibition Preserves Mitochondrial Function and Reduces Reactive Oxygen Damage in the Jck Mouse Model of Polycystic Kidney Disease Tyler Picariello, Kelly A. Rogers, Laurie A. Smith, Christina M. Bracken, Nikolay O. Bukanov, Oxana Beskovrnya, Thomas A. Natoli. Rare and Neurological Disease Research, Framingham, MA.

Background: Glucosylceramide synthase inhibitor (GCSi) treatment blocks disease progression in PKD mouse models. Defective mitochondrial morphology and function are observed in kidneys of ADPKD patient and murine models. We assessed the impact of GCSi treatment on mitochondrial function in the jck mouse model of PKD and jck derived kidney epithelial cells.

Methods: Twenty-six-day-old wt or jck mice were treated with vehicle or 60 mg/kg GCSi (Genentech67161) in food for 38 days prior to tissue harvest. mRNA expression was measured using RT-PCR. protein levels were measured by western blot. Mitochondrial DNA content was measured using real-time PCR. Oxidized DNA was detected using anti-8OHdG antibodies. Oxidized proteins were measured using the Oxylab system (Milipore).

Results: Reductions in electron transport chain and mitochondrial membrane potentials were observed in jck mouse kidneys, as well as GCSi treated samples. Decreased mitochondrial DNA was also observed in jck kidneys with increased levels of oxidized DNA and protein; these changes were mirrored in ADPKD samples. Reduced cyst burden following treatment of jck mice with GCSi was associated with increased levels of mitochondrial DNA, mitochondrial proteins, and induction of mitochondrial biogenesis pathways. GCSi treatment partially reversed antioxidant gene downregulation and normalized oxidized DNA and protein levels in jck tissues. jck cells exhibited decreased mitochondrial number, defective mitochondrial function, and increased protein oxidation consistent with in vivo and ADPKD patient data. GCSi treatment alleviates these defects. This suggests that reduced mitochondrial DNA and increased oxidative stress are primary cellular defects and not a result of cyst formation.

Conclusions: Mitochondrial dysfunction and increased oxidative stress were observed in jck mouse tissues, jck cell lines, and ADPKD patient samples. GCSi treatment inhibited disease progression in jck mice, reducing oxidative stress and correcting mitochondrial dysfunction. Reduced cyst growth following GCSi treatment correlates with preserved mitochondrial function.

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Quantifying Murine Total Kidney Volume with Robotic 3D Ultrasound

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Background: As a potential therapeutic method to halt the progression of polycystic kidney disease, we developed and implanted a computed tomography (CT) image-derived morphometric 3D capsule device to excise a kidney. In this study, the long-term effect of the capsule device on size, function, and histology of polycystic kidneys were assessed using wild-type, Cy/+ and PCK rat models.

Methods: Kidney capsule devices were designed from CT images of rats and surgically implanted on left kidneys, while sham operations performed as controls, in wild-type (n=2), Cy/+ (n=2) and PCK (n=3) rats. After operation, rats were followed to grow. Monthly CT scans were performed and used to measure kidney volume. At the final follow-up, rats were sacrificed and kidney weight, serum BUN and creatinine (Cre) were measured. Histological analyses including cystic area measurement and immunohistochemistry were performed.

Results: In wild-type rats, kidney weights in sham and encapsulated (Enc) rats were similar (Right [R]: 2.2g, Left [L]: 2.1g sham vs. R 2.3g, L 2.2g Enc). In Cy/+ rats survived over 6 months, kidney weights, BUN, and Cre were all lower in Enc rats than those in sham rats (Weight: R 4.7g, L 4.6g sham vs. R 3.6g, L 2.9g Enc (Figure); BUN mg/dL: 113.8 sham vs. 44.9 Enc; Cre mg/dL: 2.06 sham vs. 0.71 Enc). In PCK rats survived over 3 months, kidney weights, BUN, and Cre were all lower in Enc rats than those in sham rats (Weight: R 5.6g, L 5.1g sham vs. R 4.5g, L 3.8g Enc; BUN: 30.6 sham vs. 22.9 Enc; Cre: 0.43 sham vs. 0.36 Enc). Encapsulated kidneys of polycystic rats showed smaller histologic cystic area with reduced cell proliferation and macrophages than unencapsulated kidneys.

Conclusions: Both Cy/+ and PCK rats in long-term follow-ups showed considerable reductions in size of the kidneys that were encapsulated with morphometric 3D capsule devices as well as reduction in BUN and creatinine, demonstrating proof of concept toward a novel potential therapeutic avenue for halting progression of polycystic kidney disease.

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Quantifying Murine Total Kidney Volume with Robotic 3D Ultrasound

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Background: Polycystic kidney disease (PKD) is a genetic disorder characterized by renal cyst formation and kidney enlargement. Noninvasive staging of PKD can be accomplished by measuring total kidney volume (TKV). While TKV has been readily implemented in the clinic, its adoption in preclinical research with small animals has lagged. In this study, a new high-throughput imaging device, based on robotic ultrasound (US), was evaluated as a complementary approach for measuring TKV in murine models and validated against in vivo and ex vivo gold standards (MRI and Vernier calipers).

Methods: Two cohorts of mice were evaluated in a cross-sectional study. Cohort 1 included a range of mature Pkd1(-/-) mice (N = 14 kidneys) that were imaged in 3D with both US and MRI. Cohort 2 included healthy mice (N = 16 kidneys) spanning both sexes and two ages (4k-16 wks). Mice from Cohort 2 were imaged with 3D US in vivo, euthanized, and TKV measured ex vivo with Vernier calipers (length/width). Agreement was assessed with correlation and Bland-Altman (BA) analysis. US images were segmented by 4 independent readers and inter-reader reliability was assessed via intra-class correlation coefficient (ICC).

Results: US-TKV correlated strongly with both MRI and caliper measurements (r² = 0.97 and 0.93, respectively). Against MRI, BA-analysis demonstrated no significant bias and a limit of agreement (LOA) of 70 mm³ between the techniques. Against calipers, a small but statistically significant overestimation was detected of kidney length/width by in vivo US imaging (0.87 mm). Inter-reader agreement for TKV was strong with an ICC of 0.93 (95%CI: 0.83–0.97).

Conclusions: These results show that robotic US, performed by a novice operator, can produce rapid, accurate, and consistent in vivo measurements of TKV in murine models. Future studies will include larger cohort sizes and additional models of kidney disease (e.g. fibrosis) making this approach ideal for therapeutic screening.

Funding: NIDDK Support

Rapid, Quantitative Measures of ARPKD Kidney Disease with Novel Magnetic Resonance Fingerprinting

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Background: Autosomal recessive polycystic kidney disease (ARPKD) is a rare but potentially lethal genetic disorder characterized by diffuse collecting tubule microcytosis. There are currently no disease-specific treatments, although several therapies have shown promise in ARPKD animal models. Clinical trials for ARPKD patients have not been possible due to the lack of sensitive measures of ARPKD kidney disease progression. We previously identified renal T1 and T2 relaxometry as potential imaging biomarkers of ARPKD. The goal of this study was to evaluate a novel, rapid magnetic resonance imaging (MRI) technique, magnetic resonance fingerprinting (MRF), in kidneys of healthy volunteers and pediatric ARPKD patients.

Methods: MRF is a quantitative MRI technique that simultaneously generates maps of multiple MRI parameters (e.g., T1, T2). While also showing resistance to motion artifact, allowing for more rapid and comprehensive assessment of tissue composition and pathology. We developed a kidney MRF acquisition protocol to generate T1 and T2 maps in a single breath-hold (~15 seconds/slice). This MRF method was first validated in vitro using standardized T and T2 phantoms. In vivo kidney T1 and T2 maps were then obtained from 10 healthy volunteers and 3 ARPKD patients.

Results: MRF-based T1 and T2 maps demonstrated good agreement with reference values in standardized phantoms. MRF experiments in healthy volunteers further showed repeatable assessments of the renal cortex (T1: 1318 ± 63 ms; T2: 73 ± 5 ms), consistent with literature values. Repeated kidney MRF scans for 3 ARPKD patients (age 7-13 yrs), estimated glomerular filtration rates 52-97 ml/min/1.73m² on 2 successive days demonstrated good reproducibility (< 3% differences for T1 and T2). Significant differences were seen between the volunteer and ARPKD patient populations for both mean kidney T1 (p<0.007) and T2 (p<0.04).

Conclusions: This novel kidney MRF acquisition protocol provides fast, accurate, and repeatable kidney T1 and T2 maps in pediatric ARPKD patients. The short acquisition times, coupled with resistance to motion artifact, suggest that MRF could allow rapid, quantifiable imaging assessments of ARPKD kidney disease even in younger children, which could be used to identify high risk patients and/or to assess therapeutic efficacy in clinical trials.

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Automated Instance Cyst Segmentation of Polycystic Kidneys in MRIs

PO1566
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Background: Autosomal dominant polycystic kidney disease (ADPKD) is characterized by the development of multiple cysts in the kidneys. Currently, total kidney volume (TKV) is used as the only imaging biomarker to monitor disease progression. However, the ADPKD phenotype can vary widely among patients presenting with similar TKVs. In this study, we developed an MR image analysis method that automatically segments and differentiates individual cysts (i.e. instance-based segmentation) within the kidneys of patients affected by ADPKD.

Methods: A total of 60 T2-weighted MR images representative of different ADPKD stages and phenotypes were identified from our database (TKV range: 299mL-9690mL). The automated 3D instance cyst segmentation model was developed using a convolutional neural network. We reformulated the instance segmentation task by training the model to learn cyst edges and cores separately. The instance labeling was later generated by a combination of connected components and the watershed algorithm. The network was trained on 30 images and validated on 10 images using a 4-fold cross validation technique. The remaining 20 images were used for testing and were compared to manual tracings from two independent readers.

Results: An example of the automated method performance is shown in figure 1A. Quantification of the automatically generated cysts (Fig. 1B.) showed strong correlation with the number of cysts detected by readers 1 and 2 with an R² of 0.96 and 0.88, respectively. The cystic index showed high correlation with an R² of 0.92 and 0.90 for the comparisons between the automated method and readers 1 and 2, respectively.

Conclusions: We developed and tested the first fully automated instance cyst segmentation method for patients affected by ADPKD. The results demonstrate the feasibility and high accuracy of performing cyst counting and measuring total cyst volume and cystic index automatically.

Funding: NIDDK Support, Clinical Revenue Support

Human Factors Impact on the Development of Software as a Medical Device (SaMD): A Case Study Using the System Usability Scale (SUS)

PO1567
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Background: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an inherited, progressive, cystic kidney disease and is the fourth leading cause of end-stage renal disease (ESRD). Total kidney volume (TKV) is the most relevant imaging biomarker for tracking and predicting the natural course of ADPKD. Accurate prognostic tools may help predict outcomes and optimize clinical management to slow the loss of renal function. The ADPKD Progression Management (APM) System is a web-based, clinical-decision support software that offers a consistent method for estimating TKV and aids in the prediction of likely risk of progression. The system helps health care providers (HCPs) automatically calculate TKV, project likely TKV growth, and track eGFR and TKV changes over time. The APM System was evaluated for perceived ease-of-use and user satisfaction utilizing the industry standard System Usability Scale (SUS).

Methods: The SUS was used in 4 human factors studies of the APM System. Participants included nephrologists and radiologists who completed test cases using mock patients and APM data. Participants had no prior experience with the software and received no training on the system. Participants entered clinical information, utilized the automated image measurement to calculate TKV, and generated the automated statistical calculation of predicted growth of TKV, a marker of disease progression. Participants then completed a SUS questionnaire. In each study, a global SUS score was calculated, a total of 79 participants contributed to the global SUS scores: 37 nephrologists, 28 radiologist and 14 nephrologist/radiologist support staff.

Results: APM System received the following SUS scores in studies one through four: 72, 82, 80, and 80. The SUS questionnaire was included in the first four studies.

Conclusions: The SUS results demonstrate the impact of iterative improvements in the design and usability of the APM System. The SUS global scores provide evidence that the perceived usability is above average and comparable to the average SUS score for the top 10 apps across iPhone, Android and tablets.

Cystic Kidney Diseases: Emerging Concepts, Biomarkers, and Clinical Trials

PO1568
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Background: Recent work suggests that dysregulated cellular metabolism plays a key role in autosomal dominant polycystic kidney disease (ADPKD) pathogenesis, with increased glycolytic metabolism (Warburg effect) and impaired oxidative metabolism. The TAME-PKD double-blind, placebo-controlled RCT is underway, testing the safety, tolerability and efficacy of metformin, a regulator of cell metabolism and activator of AMP-activated kinase, in ADPKD patients. The purpose of this study was to analyze the correlation of baseline urinary metabolic biomarkers and metabolic enzymes correlate with ADPKD disease severity parameters in this study population.

Methods: Concentrations of total protein, key metabolites (creatinine, lactate, pyruvate, alanine, and glucose), and key glycolytic enzymes (pyruvate kinase M2 (PKM2), lactate dehydrogenase A (LDHA), and pyruvate dehydrogenase kinase 1 (PDK1)) were measured by ELISA, enzymatic assays and immunoblotting in baseline urine specimens of 95 TAME-PKD participants. These analytes normalized by creatinine were correlated with patients’ baseline height-adjusted total kidney volumes (htTKV) by MRI and estimated GFR (eGFR) by CKD-EPI in unadjusted analyses. Additional analyses were performed adjusting for participants’ age and sex.

Results: As expected, a very significant negative correlation was found between htTKV and eGFR (r = -0.385; p = 0.001) in this population, with a moderately positive correlation between urinary total protein excretion and htTKV (r = 0.201; p = 0.052). None of the metabolites correlated with htTKV or eGFR. Among metabolic enzymes, PKM2 and LDHA both positively correlated with htTKV (r = 0.286; p = 0.005 and r = 0.233; p = 0.012, respectively). All three enzymes detected by readers 1 and 2 were generally consistent in multivariable regression models adjusting for patient age and sex.

Conclusions: To varying degrees, proteinuria, lactate, PKM2, and PD1K1 urinary concentrations correlated with ADPKD severity at baseline in the TAME-PKD study population, consistent with the idea that upregulated glycolytic flux is a feature of ADPKD severity. Future analysis will reveal how treatment with metformin may affect both disease progression and the various urinary metabolic biomarkers in patients throughout the study.

Funding: Other U.S. Government Support

Urine NAG Is an Effective Clinical Parameter to Presume Disease Activity of Autosomal Dominant Polycystic Kidney Disease

PO1569
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Background: Patients with ADPKD are mixed with those who progress to ESRD and those who maintain stability, and should be assessed separately from disease activity shown in rate of kidney volume progression (RKVP), disease progression shown in total kidney volume (TKV), and also renal function shown in eGFR. This is also crucial in considering indication of tolvaptan. However, the evaluation of RKVP requires multiple imaging studies, and problems with costs and complexities. Considering that ADPKD is a disorder primarily affecting tubulo-interstitium, we aimed to examine the clinical potential of urine NAG to evaluate RKVP by retrospective observation.

Methods: Among ADPKD patients treated in our hospital between January 2010 and June 2019, 62 patients who met the conditions of no tolvaptan use, GFR > 30, duration of treatment in our hospital ≤ 1 year, and multiple TKV measurement by CT scanning were included in the analysis.

Results: The mean age was 46.3 years, 62.9% men, the mean baseline eGFR was 64.6 ml/min/1.73 m², the median TKV was 1137 ml, and the median urine NAG index (NAG-to-Cr ratio) was 4.64 ml/mg Cr. In the reduced renal function group (30 < eGFR ≤ 60 ml/min/1.73 m², n=32), we observed a correlation between NAG index and RKVP in single-regression analyses ($R^2 = 0.330, p=0.003$), but not with eGFR and TKV. However, there was no significant correlation between all parameter and RKVP, including NAG index, in the normal renal function group ($eGFR > 60 ml/min/1.73 m², n=30$). Multiple regression analysis showed that NAG index was a predictor of RKVP in the reduced renal function group ($p=0.005$). Based on the approximate equation in the single-regression analyses of NAG index and RKVP (NAG index × RKVP = 1511 X NAG index-2569), the 95% confidence interval for NAG index (5.9-9.40 U/mgCr) in the reduced renal function group, and the corresponding RKVP values (6.16-11.33%year), reasonable cut-off value of NAG index to predict RKVP ≥5% per year might be considered to be 6.0 U/mgCr.
POI570

Overweight and Obesity Are Predictors of Pain in the HALT-PKD Studies

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Background: Pain is a frequent complication of autosomal dominant polycystic kidney disease (ADPKD) and includes back and abdominal pain. Level of pain was previously found to be unrelated to kidney size in participants in the 5-yr HALT-PKD studies. We hypothesized that overweight and obesity would be independently associated with greater self-reported back, abdominal, and radicular pain at baseline and that weight loss would be associated with reduced pain over the follow-up period.

Methods: In a longitudinal study of ADPKD who participated in the 5-yr HALT-PKD study A or B were included in a cross-sectional analysis. The association of baseline BMI with pain was evaluated using multivariable ordinal logistic regression (likert-scale responses). In a longitudinal analysis, the association of annual change in BMI as a time-varying predictor with annual change in pain was evaluated using a generalized estimating equation analysis.

Results: Participants were 43±10 years old and baseline estimated glomerular filtration rate (eGFR) was 71±26 ml/min/1.73m². Back, abdominal, and radicular pain were reported more frequently in individuals with overweight/obesity (p<0.05). After adjustment for demographics, exercise, pain medications, eGFR, and mutations class, overweight/obesity were associated with increased odds of greater back pain and radicular pain, but not abdominal pain. Associations remained similar after further adjustment for baseline height-adjusted kidney and liver volume (Study A only; n=436); back pain: overweight: OR: 2.28 [1.13, 4.60], obese OR: 2.68 [1.25, 5.76]. Longitudinally (n=823), weight loss would be associated with reduced pain over the follow-up period.

Conclusions: After adjustment for demographics, exercise, pain medications, eGFR, and mutation class, overweight/obesity were associated with increased odds of greater back and abdominal pain, independent of total kidney/liver volume. Weight loss was associated with reduced risk of worsening back pain, thus may be an effective strategy to reduce pain symptoms in individuals with ADPKD.

Funding: NIDDK Support

POI571

Asymptomatic Pyuria as a Prognostic Factor in Autosomal Dominant Polycystic Kidney Disease

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Background: Urinary tract infection (UTI) in patients with autosomal dominant polycystic kidney disease (ADPKD) is linked to faster disease progression. The effect of asymptomatic pyuria on ADPKD disease progression is not known.

Methods: Retrospective study of ADPKD patients seen at a tertiary academic center with available urinalysis (UA) and abdominal CT/MR imaging, and without infection or other cause of pyuria. Clinical characteristics of patients with asymptomatic pyuria (AP) (> 10 urinary WBC/hpf without UTI) were compared to the group with no pyuria (NP) (WBC 0-3/hpf). First and last available eGFR and height-adjusted total kidney volume (HTKTV) were obtained to calculate the rate of eGFR and HTKTV change with time.

Results: Female and male patients with AP had similar mean age at UA and baseline eGFR as compared to their counterpart with NP (Table 1). Median baseline HTKTV was similar in NP and AP females (596 vs 550 ml/m², respectively) but higher in AP males as compared to NP males (1132 vs 898 ml/m², respectively). There was no difference between females NP and AP in the median rate of eGFR decline (-2.2 vs -2.0 ml/min/1.73m²/yr) or HTKTV growth (4.4 vs 4.0 %/yr) compared to males NP; males AP had a higher median rate of eGFR decline (-3.8 vs -2.6 ml/min/1.73m²/yr, p=0.04) and a faster median rate of HtKTV growth (12.9 vs 6.7 %/yr, p=0.03).

Conclusions: Asymptomatic pyuria is associated with a faster decline in kidney function and growth of kidney volume in male patients with ADPKD. This could be used as an additional negative prognostic marker.

Table 1: Kidney Function and Height-adjusted Total Kidney Volume by Subgroup

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POI572

Volume Progression and Imaging Classification of Polycystic Liver in ADPKD

Kyongtae Bae,1 Cheng Tao,2 Robert Feldman,3 Alan S. Yu,4 Vicente E. Torres,3 Arlene B. Chapman,4 Ronald D. Perrone,5 Godela M. Brosnahan,6 Theodore I. Steinman,7 William E. Braun,8 Michal Mrug,9 William M. Bennett,10 Peter C. Harris,11 Doug Landsittel,12 Kaleab Abebe.1

Background: While polycystic liver in ADPKD is common and significantly affects the quality of life, volume progression of liver cysts is not well understood. This is in part because previous longitudinal studies focused on the progression of liver volume not liver cyst volume. Thus, the purpose of the study is to evaluate and classify polycystic liver progression in patients with ADPKD based on patient’s age, sex, height-adjusted cystic liver volume (htLCV) and height-adjusted liver volume (htLV) measurements.

Methods: Using longitudinal MRI data (CRISP and HALT studies) from 695 patients with ADPKD over a maximum follow-up of 14.23 years were evaluated to measure LCV and lv. Among them, 258 patients with LCV > 50ml and at least 2 time-points were included in the analysis. Linear mixed models on log-transformed htLCV and htLV were fitted as a function of participant’s age and study as well as a random intercept and slope. The slope coefficient was used to approximate the mean annual rate of change (MAROC) for each outcome. Using the age of 15 years as the hypothetical initial age for LCV or 0, differential growth trajectories were plotted to categorize the participants according to their LCV growth rate and age.

Results: Overall, the MAROC was 10.8% for htLCV and 1.8% for htLV (P<0.0001). 232 participants had net-increases (last measurement > first) on htLCV, while 26 participants had net-decreases (or values remained the same) on htLCV. For the net-increase group, MAROC was 12.7% for htLCV and 2.2% for htLV (P<0.0001). For the net-decrease group, MAROC was -7.3% for htLCV (P=0.0168) and -2.1% for htLV (P=0.1116). According to the annual growth rate, 5 classes (A <5%, B 5-10%, C 10-15%, D 15-20%, E ≥20%) were defined. The numbers for female and male participants in each class were (F/M): A (31/7), B(48/15), C (49/51), D (27/16) E (9/5).

Conclusions: The mean volume growth rate of the liver cyst was 6 times greater than that of the liver. Similar to the kidney imaging classification, the severity of polycystic liver may be categorized on the basis of patient’s age and liver cyst volume. Funding: NIDDK Support, Other U.S. Government Support
Baseline Characteristics and Associations with Renal Function in a Greek Cohort of Polycystic Kidney Disease
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Background: Recent advances in the treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD) highlight the interplay between the clinical and the laboratory profile of the disease. This study aims to present the baseline characteristics of patients followed in a large ADPKD cohort from a single center in Greece, and explore possible associations between demographic, clinical and laboratory parameters.

Methods: Patients followed in a specialized outpatient PKD clinic from December 2018 up to December 2019 were recruited in this study. At enrollment, demographics, medical and family history and laboratory data were recorded using a standardized form. Estimated glomerular filtration rate (eGFR) was calculated and Magnetic Resonance Imaging for total kidney volume (TKV) measurement was performed.

Results: One-hundred three females and 83 males with a mean age±SD of 41.4 ± 13 years (18.8 % < 30 years) were enrolled. Overall, 60.8% of them were classified as Chronic Kidney Disease, (CKD) stage 1 and 2. The ADPKD was diagnosed at a mean age±SD of 26.5±12.5 years. Thirty four percent out of 186 patients were diagnosed before the age of 20 and 9% of them before the age of 10. A positive family history was present in 89% of patients. In this subgro, the median age of the affected parent that reached end stage dialysis was 55 years (range 28-87 y). Hypertension was diagnosed in 89% at a mean age±SD of 37.2± 10.5 years. Hepatic cysts were present in 79.3% of patients, urinary tract infections, nephrolithiasis, macroscopic hematuria and pain in 44.3%, 42.5%, 24.8% and 54.4% respectively. A history of intracranial bleeding in family was present in 21.5%. In multivariable analysis, lower eGFR was associated with younger age (p < 0.08) and greater values of TKV (p < 0.001), height adjusted TKV (ht-TKV) (p < 0.001) and greater values of BMI (p < 0.002) and Body Mass Index (BMI) (p = 0.02). In the patients with ADPKD were diagnosed at a young age and hypertension developed early on the course of the disease. Both these factors together with ht-TKV and TKV were independently associated with low eGFR.

Identification of Factors Associated with Progression, Prognosis, and Tolvaptan Indication in Polycystic Kidney Disease Patients
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Background: The identification of risk factors for the progression of Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an emerging field. The present study explores the associations between epidemiological, clinical and imaging data in a large cohort of ADPKD patients.

Methods: All patients included in the study had a Magnetic Resonance Imaging (MRI) for measurement of Total Kidney Volume (TKV). For all patients, the Mayo Clinic cohort of ADPKD patients explores the associations between epidemiological, clinical and imagining data in a large Dominant Polycystic Kidney Disease (ADPKD) is an emerging field. The present study followed in a large ADPKD cohort from a single center in Greece, and explore possible associations between demographic, clinical and laboratory parameters.

Results: 158 patients in total were included. Based on measurements of height-adjusted TKV (ht-TKV) and age, 5% of the patients were classified as stage 1A, 20% as 1B, 34% 1C, 25% 1D and 16% 1E, MCIC. In multivariable analysis, patients’ age (p<0.01), male sex (p<0.01), parent’s age at time of ESRD registration (p=0.001) and proteinuria (p=0.04) were associated with ht-TKV. Parent’s age at ESRD differed significantly between the MCICs of the offspring (means+SD), 70.83 (12.90) in 1A, 63.79 (11.39) in 1B, 57.32 (10.42) in 1C, 51.42 (18.16) in 1D and 47.94 (5.73) years old in 1E (p<0.001). Similarly, there were differences in the presence and age of hypertension onset (p=0.004 and p=0.003, respectively). In 104 patients eligible for tolvaptan treatment, age at ADPKD diagnosis, age at hypertension onset and parent’s age reaching at ESRD were all significantly lower (p<0.001 for all) when compared to non-eligible patients. Finally, factors associated with the prediction score of ESRD (e-GFR 15ml/min) were hypertension, uric acid and the age at ESRD of the affected parent (p=0.001, 0.02, 0.01, respectively).

Conclusions: The age at which an affected parent had reached ESRD, as heritability estimator, was significantly associated with a worst phenotype, prognosis and tolvaptan indication. Early diagnosis of the disease, hypertension and its early onset, proteinuria and male sex are also possible risk factors for the progression of ADPKD.

POI157

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Background: Most patients with autosomal dominant polycystic kidney disease (ADPKD) do not participate in clinical research. To empower ADPKD patients in the US to participate in research and to encourage the development of optimal prognostic and treatment strategies, the PKD Foundation designed a national ADPKD Registry of patient-reported data.

Methods: The ADPKD Registry is hosted on a secure, online platform (IQVIA, oc-meridian.com/pkdcare). Participants are registered and consented through the online system and asked to complete a series of modules quarterly. The Core Questionnaire asks about diagnosis, latest kidney function lab values, current symptoms, and comorbidities. Participants are also asked about family history, diet and lifestyle, and quality of life.

Results: The ADPKD Registry was launched on September 4, 2019. As of May 2020, 1023 ADPKD patients across the US have registered and completed the Core Questionnaire. Participants have a median age of 52 years, and are 72% female, 94% Caucasian, 4% self-identifying as Hispanic/Latino and 2.4% as African American. 76% have not reached end stage renal disease, 4% are treated with dialysis, and 21% received a renal transplant. A family history of the disease was reported in 79% of participants, 2% of whom had a genetic test for PKD. The majority of patients (91%) have had a vascular aneurysm, as determined by imaging. At the time of entering the registry, 78% reported having hypertension and 62% had liver cysts (although only 28% reported a diagnosis of polycystic liver disease [PLD]).

Conclusions: The ADPKD Registry is a longitudinal research tool intended to capture patient-reported data with respect to ADPKD and is designed to impact research in multiple ways. All participants have consented to be contacted about future clinical trials for which they will likely qualify and a process has been established to enable researchers to submit content for new outcome modules. Thus far modules addressing extra renal complications such as PLD and vascular aneurysms have been developed. In addition, the variety of disease stages reported by participants will allow for a range of research questions related to the clinical management of ADPKD from early stage disease through dialysis outcomes and post-transplant complications.

Funding: Private Foundation Support

First in Canada: A Comprehensive Autosomal Dominant Polycystic Kidney Disease (ADPKD) Patient Registry in British Columbia (BC)
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Background: Early identification, assessment of renal progression and implementation of appropriate treatments are key components of modern ADPKD care. Existing BC Renal programs focus on patients in later disease stages when they access chronic kidney disease clinics, renal replacement modalities, or renal formulary drugs, but data on patients entering the care system is limited. As a comprehensive ADPKD patient registry was created to enhance identification and understanding of ADPKD in BC.

Methods: The registry was created within PROMIS, the dedicated BC renal database. A specific focus was registration of patients seen in nephrologists’ private offices, prior to enrollment in other BC Renal administered services. Minimum registry data set included basic patient name, date of birth, provincial healthcare number and diagnosis. Laboratory and outcome data are captured via existing PROMIS infrastructure. A streamlined registration process was developed with stakeholder feedback. Time-limited reimbursement was provided to nephrologists’ office to support the new workflow of identifying and registering patients.

Results: With the ADPKD registry, the number of ADPKD patients registered in PROMIS has increased from 545 to 1065 between January 2015 to January 2020. The increase in patient registration has been most prominent in early stage patients not on dialysis or transplant (increased from 237 to 703). In those not on dialysis or transplant increase in patients registered was most pronounced in those at earlier CKD stages; from 2015 to 2020, in those with eGFR 15-59ml/min, registration increased from 27 to 54 patients per year. eGFR 15-30ml/min registration increased from 43 to 71, with eGFR 45 to 60ml/min registration increased from 19 to 109, and in those with eGFR >60ml/min, registration increased from 32 to 237 patients.

Conclusions: Through creation of a comprehensive ADPKD registry, greater numbers of ADPKD patients have been identified in BC, particularly patients earlier in their disease course. The registry will continue to build on this with next steps including enhancements to clinical data, patterns of treatment use, quality metrics for care delivery, and clinical outcomes.

Funding: Commercial Support - Creation of the registry was assisted via an unrestricted grant from Otsuka Canada Pharmaceuticals Inc.
PO1577
STAGED-PKD: An Enriched, Seamless, Two-Stage Study for Venglustat Assessment in ADPKD
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Background: Autosomal dominant polycystic kidney disease (ADPKD) occurs due to cyst formation and growth, resulting in increased total kidney volume (TKV) preceding kidney function decline by decades. The natural history of ADPKD complicates testing of new therapies. Venglustat, a glucosylceramide synthase inhibitor, inhibits cyst growth and reduces kidney failure in PKD mouse models. STAGED-PKD determines venglustat safety and efficacy and was designed using enrichment for progression to ESRD and extensive modeling from prior ADPKD trials.

Methods: STAGED-PKD is a two-stage (Phase 2/3), international, double-blind, randomized controlled trial in adults with ADPKD with increased TKV (Mayo Imaging Class 1C–1E) and eGFR 45–90 mL/min/1.73 m². Target enrollment in Stages 1 and 2 is 240 and 320 patients, respectively. Stage 1 randomizes patients 1:1:1 to venglustat dose 1, dose 2 or placebo. Stage 2 randomizes patients 1:1:1 to placebo or venglustat preferred dose based on Stage 1 safety data. Primary endpoints are TKV growth rate over 18 months in Stage 1 and eGFR CKD-EPI Hope over 24 months in Stages 1 and 2 (n=560).

Results: Baseline characteristics for Stage 1 are shown (Table; n=225). Mean patient age is 42.7 years; mean eGFR CKD-EPI Hope over 24 months in Stages 1 and 2 (n=560).

Conclusions: STAGED-PKD enables optimal dose selection and evaluation of venglustat safety and impact on TKV growth and eGFR slope in ADPKD. Stage 1 TKV assessment via a nested approach allows early efficacy evaluation, increasing trial design efficiency.

Funding: Commercial Support - Sanofi Genzyme

Stage 1 Baseline Characteristics

Modeling of the Relationship Between TKV Growth Rate and eGFR Decline

PO1578
STAGED-PKD: Patient Enrichment and Treatment-Driven Efficient ADPKD Trial Design
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Background: Total kidney volume (TKV) and eGFR slope are key endpoints in autosomal dominant polycystic kidney disease (ADPKD) trials, indicative of cyst growth and kidney function decline. To date, unequivocal demonstration of drug effect on these endpoints required two trials. STAGED-PKD assesses the effect of glucosylceramide synthase inhibition with venglustat on both endpoints in one efficient, short-duration trial.

Methods: Retrospective analysis of TKV and eGFR slope data from CRISP (3-yr) and HALT-A combined identified rapidly progressing patients for enrichment. A statistical relationship between TKV growth vs eGFR slope was derived by modeling. Meta-analysis was conducted of randomized clinical trials assessing treatment impact on both TKV and eGFR. These analyses enabled study powering for both endpoints. Comparison of design efficiency was performed vs prior trials.

Results: Retrospective analysis of CRISP and HALT-A confirmed a significant correlation between TKV growth and eGFR slope (correlation 0.346, p<0.0001; Figure). Different statistical approaches showed that in rapidly progressing ADPKD patients, 50% reduction in TKV growth is associated with a ~30% reduction in eGFR slope. Thus, STAGED-PKD is powered to detect 50% reduction in TKV growth and 30% reduction in eGFR slope. STAGED-PKD is highly efficient vs HALT-A and -B, TEMPO 3:4, and REPRISE.

Conclusions: Modeling allowed the design and powering of a two-stage study to assess venglustat impact on TKV growth and eGFR slope. STAGED-PKD improves efficiency via modeling and patient enrichment to reduce patient number and trial duration.

Funding: Commercial Support - Sanofi Genzyme

PO1579
Biological Efficacy and Safety of Niacinamide in Patients with Autosomal Dominant Polycystic Kidney Disease
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Background: Autosomal dominant polycystic kidney disease (ADPKD) is characterized by progressive cyst enlargement, leading to kidney failure. Sirtuin-1 is upregulated in ADPKD and accelerates disease progression by deacetylating p53. Niacinamide is a dietary supplement that inhibits sirtuins at high doses.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Methods: We conducted an open-label, single arm intervention trial (Study 1, N=10), and a randomized, double-blinded, placebo-controlled trial (Study 2, N=36) to assess the biological activity and safety of niacinamide. Patients with ADPKD were given 30 mg/ kg oral niacinamide or placebo, for 12 months. Primary endpoint was ratio of acetylated p53 to total p53 protein in peripheral blood mononuclear cells. Secondary outcomes were change in height-adjusted total kidney volume (ht-TKV) and overall pain and quality of life scores. Other biomarkers of efficacy included serum creatinine, CRP, urine protein/creatinine and urine MCP1/creatinine ratios.

Results: There were no statistically significant differences in the baseline characteristics between placebo and niacinamide arms. There was no statistically significant change in total p53 ratio in either study. In study 1, the ratio was higher at 1 month (p=0.003) but not at 6 and 12 months and no difference was noted between placebo and niacinamide arms in study 2 (p=0.51). There was no difference in the change of ht-TKV from baseline to 12 months in niacinamide and placebo. Ht-TKV increased slightly from 1049 to 1082 ml/m² (p=0.71) with small eGFR decline from 83.6 to 81 ml/min/1.73 m² (p=0.84) in niacinamide treated patients (combined study 1+2). Furthermore, there was no statistically significant difference in urine MCP1/creatinine, urine protein/creatinine and quality of life scores over time. Niacinamide was generally well-tolerated. Most common adverse effects were nausea, diarrhea, gastroesophageal reflux (combined GI symptoms:70% in study 1, 78% in study 2 niacinamide treatment arm and 58% placebo), headache and acneiform rash with no difference in their incidence between niacinamide and placebo.

Conclusions: Niacinamide is safe and well-tolerated in ADPKD patients. However, we were unable to detect a sustained inhibition of situtation activity over 12 months of treatment, and there was no signal to suggest a beneficial effect on any efficacy measure.

Funding: Other NIH Support - Pilot and Feasibility Clinical Research Grants in Kidney or Urologic Diseases R21 (DK104086). Frontiers Pilot and Collaborative Studies Funded Program funded by an NIH Clinical and Translational Science Award grant (UL1 TR000001, formerly UL1RR033179) awarded to the University of Kansas Medical Center.Kansas Institute of Precision Medicine (P20 GM130423)

PO1580
Curcumin Therapy to Treat Vascular Dysfunction in Children and Young Adults with Autosomal Dominant Polycystic Kidney Disease (ADPKD): Design and Baseline Characteristics of Participants
Heather Farmer-Bailey, 1 Melissa A. Cadinapornrach, 2 Zhiling You, 1 Diana George, 1 Wei Wang, 1 Anna Jovanovich, 1, 3 Danielle Soranno, 4 Berta Roca, 1 Kelly Q. Nowak, 1 University of Colorado Denver - Anschutz Medical Campus, Aurora, CO, 2 Rocky Mountain Pediatric Kidney Center, Rocky Mountain Hospital for Children at Presbyterian St. Luke's Medical Center, Denver, CO, 3 Rocky Mountain Regional V4 Medical Center, Aurora, CO, 4 Children's Hospital Colorado, Aurora, CO.

Background: Complications of ADPKD begin in childhood. While the hallmark of the disease is the development and continued growth of multiple renal cysts that ultimately result in loss of kidney function, cardiovascular complications are the leading cause of death. Vascular dysfunction (endothelial dysfunction and large elastic artery stiffness) is evident from a very young age and appears to involve increased oxidative stress and inflammation. Treatment options to prevent cardiovascular disease in adults with ADPKD are limited; thus, childhood may represent a key therapeutic window.

Methods: Curcumin is a safe, naturally occurring polyphenol found in the Indian spice turmeric, with the unique ability to activate transcription of key antioxidant enzymes, suppress inflammation, and reduce proliferation. We are conducting an ongoing randomized, placebo-controlled, double-blinded clinical trial to assess the effect of curcumin therapy (25 mg/kg/d) on vascular function (brachial artery flow-mediated dilation [FMD] and aortic pulse-wave velocity [apWV]); co-primary outcomes) and kidney growth (change in height-adjusted total kidney volume [ht-TKV]) in children/young adults 6–25 yrs with ADPKD.

Results: The study is fully enrolled. Of the 68 screened participants, all 68 were randomized to receive either the curcumin or placebo. Participants ranged in age from 6-25 yrs, n=25 (37%) were children <18 yrs, and mean±S.D.estimated glomerular filtration rate was 71±16 ml/min/1.73 m². FMDₐ was 9.3±0.5%, apWV was 553±30 cm/sec, and median (IQR) ht-TKV was 333 (234, 475) ml/min. In the sub-group of young adults who received a supraphysiological infusion of ascorbic acid to inhibit vascular oxidative stress (n=24), FMDₐ improved vs. isovolumetric saline (13.6±5.2% vs. 11.3±4.3%), indicating baseline vascular oxidative stress. Greater baseline apWV was independently associated with larger baseline ht-TKV.

Conclusions: The trial will be completed in December of 2020. This study has the potential to establish a novel, safe, and facile therapy for the treatment of arterial dysfunction, and possibly renal cystic disease, in an understudied population of children and young adults with ADPKD.

Funding: NIDDK Support, Other NIH Support - National Center for Advancing Translational Sciences, Commercial Support - Verde Sciences (provided curcumin and placebo), Private Foundation Support

PO1581
End-of-Study Results from ACQUIRE: A Study Measuring Quality of Life, Treatment Preference, and Treatment Satisfaction of Autosomal Dominant Polycystic Kidney Disease Patients in Europe
Dominique Joly, 1 Helen Doll, 2 Anne De Jong-Laird, 3 Madhusudan Kabra, 2 Nephrology Department, Necker Hospital, Paris, France, 1 Clinical Outcomes Solutions Ltd, Folkestone, United Kingdom; 2Otsuka Pharmaceutical Europe Ltd, Wexham, United Kingdom.

Background: Little is known about health-related quality of life (HRQoL) and patient (pt) reported outcome (PRO) measures in early autosomal dominant polycystic kidney disease (ADPKD), and longitudinal studies are lacking.

Methods: ACQUIRE (NCT02848521) was a prospective, non-interventional, real-world observational study in pts with early and rapidly progressing ADPKD (chronic kidney disease [CKD] stages 1–3) across 7 European countries. The primary objective was to measure changes in Physical Health Composite Scale (PCS) scores of the 12-item Short Form Health Survey (SF-12) over 18 months. Other objectives included changes in SF-12 Mental Health Composite Scale (MCS) scores, ADPKD-specific PROs including the ADPKD-impact Scale (IS), -Urinary Impact Scale (UIS) and -Pain & Discomfort Scale (PDS), and treatment satisfaction questionnaire (TSQM-9).

Results: Patient demographics were previously reported. Overall 305/403 (75.7%) were included in the PRO analysis set. Changes from baseline in SF-12 (PCS and MCS), ADPKD-IS (Physical and Emotional domains) and TSQM-9 (Global Satisfaction) through Month 18 are presented in Figure 1. CKD-1 pts and pts not receiving telaprevir reported the lowest treatment satisfaction. No consistent changes were observed for ADPKD-UIS and ADPKD-PDS (not shown).

Conclusions: Over an 18-month timeframe, pts reported reduced scores in the PCS component of SF-12, deterioration in the physical components of ADPKD-IS and reduced treatment satisfaction. These data suggest that continued disease progression negatively impacts the HRQoL of pts with early stages of ADPKD and implies there may be current unmet treatment needs in this pt population.
**Methods:** ESRD patients treated with dialysis or transplant with at least one ADPKD diagnosis code and a reported ADPKD service date from January 1, 2014, to December 31, 2016, in the US Renal Data System (USRDS) were included. Mortality rates were estimated overall, by sex, by race, and by age group (with a patient’s follow-up potentially spanning two age groups). Both unadjusted mortality and adjusted mortality by 2016 US population age distributions for 65 years and older were computed.

**Results:** Of 3,208,884 ESRD patients in the USRDS database, 76,428 patients (2.4%) had ADPKD and of those 14,756 were aged 65 years and older in the study period. Among elderly ADPKD patients, mean age was 70.8 years and overall mortality was 99.8 per 1,000 patient-years (129.9 age-adjusted).

**Conclusions:** These findings fill an important gap in the literature on ADPKD mortality in the US.

**Funding:** Commercial Support - Osaka Pharmaceutical Development & Commercialization, Inc.

**Mortality (Deaths per 1,000 Patient-Years) Among Elderly Patients with ADPKD in ESRD**

<table>
<thead>
<tr>
<th>Age-adjusted Mortality</th>
<th>Population of Patients (Counts)</th>
<th>Mortality (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>65</td>
<td>603,109 (402,550–814,116)</td>
</tr>
<tr>
<td>By age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>25%</td>
<td>151,555 (108,292–214,054)</td>
</tr>
<tr>
<td>70-79</td>
<td>30%</td>
<td>191,084 (139,138–242,762)</td>
</tr>
<tr>
<td>80+</td>
<td>45%</td>
<td>195,961 (137,212–258,221)</td>
</tr>
</tbody>
</table>

*Patient demographics at study entry.*

**PO1583**

**Risk of Severe Herpes Zoster Infection in Patients with Polycystic Kidney Disease: A Nationwide Cohort Study with Propensity Score-Matching Analysis**

**Background:** Polycystic kidney disease (PKD) should be considered as a systemic disorder rather than only a kidney disease. Significantly lower lymphocyte cell counts, including B and T lymphocyte counts, is noted in patients with PKD. This lymphopenia poses a risk of viral infection. Data to elucidate the herpes virus infection risk in patients with PKD are lacking; therefore, we conducted a national-wide population-based cohort study to investigate the herpes virus risk in PKD patients.

**Methods:** Patients who were hospitalized at least once with a diagnosis of autosomal dominant PKD were defined as PKD patients; patients without any diagnosis of PKD during the study period were grouped into the non-PKD cohort. The index date was set as the date when the patients were newly diagnosed with PKD. All study patients were followed up until the occurrence of herpes zoster infection, herpes simplex infection, death, withdrawal from the National Health Insurance Research Database for other reasons, or until December 31, 2013.

**Results:** We included 4358 PKD patients and 4338 non-PKD patients. The incidence rate and the risk of developing herpes zoster and herpes simplex were estimated using multivariate stratified analyses. PKD patients had an overall 2.43-fold risk of herpesvirus infection (aHR = 2.43, 95% CI 1.47–4.04) and 2.36-fold risk of herpes zoster (aHR = 2.36, 95% CI 1.34–4.13) in subgroup analysis compared with the non-PKD cohort. PKD patients without any comorbidities had a significantly higher risk of herpes zoster or herpes simplex (aHR = 3.38, 95% CI 1.51–7.56).

**Conclusions:** This is the first study to reveal the severe risk of herpes zoster infection in patients with PKD. High index suspicion of severe herpes zoster infection should be maintained in clinical professionals. Whether patients with PKD should be prophylactically universally with anti-varicella-zoster virus vaccine needs to be investigated in the future.

**PO1584**

**The Use of a Visual-4-Scoring Scale Improves the Yield of [18F]-FDG PET-CT Imaging in the Diagnosis of Cyst Infection in Patients with Autosomal Dominant Polycystic Kidney Disease**

**Background:** [18F]FDG PET/CT imaging helps in the diagnosis of CyI in ADPKD patients, and the use of a 4-point scoring of [18F]FDG uptake improves its yield, with positive and negative predictive values of 78.3% and 78.4% respectively.

**Methods:** All ADPKD patients who were hospitalized between January 2017 and March 2019 for suspected CyI and who underwent an [18F]FDG PET/CT were included. [18F]FDG PET/CT was diagnosed in case of (i) homogeneous or (ii) heterogeneous [18F]FDG accumulation in cyst wall, or (iii) diffuse [18F]FDG accumulation within the cyst. Next, the uptake of [18F]FDG of the suspected CyI was scored in comparison to blood pool and liver activities. An accumulation of [18F]FDG around the cyst equivalent or inferior to the blood pool was scored as 1. If it was superior to the blood pool but inferior or equal to the hepatic [18F]FDG background, it was scored as 2. If it was slightly superior to the liver, it was scored as 3. If it was largely superior to the hepatic [18F]FDG activity, it was scored as 4.

Using a 4-point scoring, authors identified 60 patients (45% with CyI, 55% without CyI). Sixty [18F]FDG uptake was performed for suspected CyI in 38 ADPKD patients: 29 episodes met the gold-standard criteria for CyI. The visual assessment of PET/CT images reached a sensitivity of 73.1% and a specificity of 70.6%. The pattern of [18F]FDG accumulation around or within the suspect cyst was not discriminant. By contrast, the 4-point scale improved the diagnostic yield (specificity of 85.3%) with a diagnostic threshold of [18F]FDG uptake ≥3, i.e. higher than the hepatic background.

**Conclusions:** [18F]FDG PET-CT imaging helps in the diagnosis of CyI in ADPKD patients, and the use of a 4-point scoring of [18F]FDG uptake improves its yield, with positive and negative predictive values of 78.3% and 78.4% respectively.

**PO1585**

**Liver Cyst Infection After Hepatic Transcatheter Arterial Embolization in Patients with Autosomal Dominant Polycystic Kidney Disease**

**Background:** Hepatic transcatheter arterial embolization (TAE) is a non-surgical treatment to reduce the volume of enlarged liver in patients with autosomal dominant polycystic kidney disease (ADPKD). The incidence of liver cyst infection after hepatic TAE is not known.

**Methods:** Patients with ADPKD who underwent hepatic TAE between January 2014 and July 2019 in Toranomon Hospital Kajigaya to reduce the volume of enlarged liver were retrospectively analyzed for their history of liver cyst infection before and after hepatic TAE.

**Results:** 107 patients were included in the study. The mean ± standard deviation (SD) of age and height-adjusted total liver volume was 53.9 ± 9.6 years and 5,048 ± 2,124 mL, respectively. 26 patients (24%) were men, and 36 patients (34%) were on renal replacement therapy. Seven patients (7%) had a history of liver cyst infection before hepatic TAE. During the follow-up period, 16 patients (15%) experienced 20 liver cyst infections in total after hepatic TAE, and only one of them had a history of liver cyst infection before hepatic TAE. The mean ± SD of the follow-up period was 714 ± 601 days. Median [interquartile range] of 467 [225–1,078] days. 10 out of 16 patients were on renal replacement therapy, which were all hemodialysis. Four out of 20 liver cyst infections occurred within three months of hepatic TAE. The incidence rate of liver cyst infection after hepatic TAE was 96 cases per 1,000 person-years.

**Conclusions:** This is the first report on the incidence of liver cyst infection after hepatic TAE. Although comparison with a control group without hepatic TAE is necessary to evaluate the risk of liver cyst infection caused by hepatic TAE, setting a control group with a similar background is difficult and remains a research question.

**PO1586**

**3D Facial Gestalt Analysis of Individuals with Mutated PKD1 and PKD2 Genes in Polycystic Kidney Disease: Results of a Czech Pilot Study**

**Background:** Pathogenic variants in PKD1 and PKD2 genes cause autosomal dominant polycystic kidney disease (ADPKD) that can also manifest in the liver, pancreas or cardiovascular system. Nonetheless, association of ADPKD with 3D facial gestalt has not been studied SO far. Here we present our first results of 3D facial morphometry in a Czech ADPKD patients.

**Methods:** Thirty ADPKD cases were enrolled and analyzed by the 3DMd Face System. 3D morphometric analyses were performed using the Morphome3cs software by comparing cases versus age and sex matched controls.

**Results:** We observed that 3D facial gestalt in ADPKD patients differs from controls. ADPKD patients have more prominent nasal region, most significantly in the area of the tip of the nose. In addition, there is retrusion of the eyebrows area, midface-zygomatic prominence and retrusion of the lateral buccal region. Most of the ADPKD cases have thin and prominent nasal region, most significantly in the area of the tip of the nose. In addition, there is retrusion of the eyebrows area, midface-zygomatic prominence and retrusion of the lateral buccal region. Most of the ADPKD cases have thin

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

Underline represents presenting author.
PO1587
Increased Phosphorylation of ACTN4 Leads to Podocyte Dysfunction and Focal Segmental Glomerulosclerosis Mimicking Disease-Causing Mutations
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Background: Genetic mutations in ACTN4 have been linked to focal segmental glomerulosclerosis (FSGS) in humans through cytoskeletal disruption and impairment in podocyte response to mechanical stress. ACTN4 is phosphorylated at S159 in podocytes, but the effect of this post-translational modification on podocyte and kidney function is not known.

Methods: We used phosphomimetic ACTN4 to investigate the effects of this phosphorylation in vitro and in vivo. The effect of phosphorylation on the interaction between ACTN4 and F-actin was assessed through F-actin bundling assays, and the effect on F-actin alignment was assessed by immunofluorescence staining and quantified using autocorrelation analysis. Microfluidic organ-on-a-chip technology was used to measure the rate of podocyte detachment when simultaneously exposed to fluid flow and cyclic strain. A phosphomimetic mouse model was generated, subjected to subtotal nephrectomy (to simulate glomerular hyperfiltration), and assessed for renal injury. Targeted mass spectrometry was used to determine whether injurious stimuli to podocytes increased ACTN4 phosphorylation.

Results: Compared to wild type (WT) ACTN4, phosphomimetic ACTN4 led to increased FRAP.4 Phosphorylated podocytes demonstrated nearly a 3-fold higher rate of detachment (28/154 podocytes, 18.2%) in comparison with WT (12/170 podocytes, 7.1% p<0.05). Phosphomimetic Actn4 mice developed proteinuria and glomerulosclerosis after subtotal nephrectomy. Finally, phosphorylation of ACTN4 at S159 in podocytes was stimulated by high extracellular glucose and TGF-

Conclusions: Increased phosphorylation of ACTN4 at S159 leads to biochemical, cellular, and renal pathology that is similar to pathology resulting from human disease-causing mutations in ACTN4. Stimulation of this phosphorylation by glucose and TGF-B suggests potential mechanisms of ACTN4-mediated kidney disease that extend beyond its original genetic etiology.

Funding: NIDDK Support

PO1588
Toward a Molecular Mechanism for Low-Molecular-Weight Proteinuria in Dent Disease
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Background: Dent disease is a progressive X-linked disorder caused by loss of function of the CI/H+ exchanger CLC-5. Early symptoms include low molecular weight (LMW) proteinuria resulting from inefficient recovery of filtered proteins by megalin and cubilin receptors in the proximal tubule (PT). Knockout of CLC-5 in mice recapitulates the LMW proteinuria observed in human disease and decreases protein (but not mRNA) levels of megalin and cubilin. How loss of CLC-5 leads to reduced receptor expression remains unknown. Previous gene expression studies in Clcn5 KO mice suggest there are alterations in cholesterol and lipid metabolism. Elevated cholesterol levels have been demonstrated to alter the organization of the endocytic pathway and impair receptor recycling in cultured cells. We hypothesize that altered cholesterol metabolism impairs megalin traffic through the recycling pathway and promotes its degradation.

Methods: We used siRNA knockdown (KD) and CRISPR-Cas9 knockout (KO) and rescue approaches in an opossum kidney (OK) cell culture model that recapitulates morphologic and functional features of the PT in vivo to study the role of CLC-5 in the endocytic pathway. Additionally, we assessed PT function, megalin/cubilin expression, and cholesterol distribution in these generated CRISPR/Cas9 KO and rescue cells.

Results: KD or KO of CLC-5 resulted in significantly decreased endocytic uptake of fluorescently labeled albumin that was fully rescued by heterologous expression of wild-type human CLC-5. Additionally, the half-life of megalin was reduced in Clc-5-deleted cells. We confirmed LMW proteinuria in the KO mice. Heterozygous females also had reduced PT uptake and megalin expression. We observed an accumulation and a redistribution of cholesterol in PTs of heterozygous mice and in Clc-5 KO cells.

Conclusions: Our new cellular models for Dent disease should enable us to identify the molecular mechanism that results in reduced megalin/cubilin expression and determine whether altered cholesterol metabolism contributes to the LMW proteinuria observed in Dent disease.

Funding: NIDDK Support

PO1589
Super-Resolution Imaging of the Filtration Barrier Suggests a Role for Podocin R229Q in Genetic Predisposition to Glomerular Disease
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Background: Breakdown of the three-layered glomerular filtration barrier is a leading cause of end-stage kidney disease. Whereas extensive research led to a growing understanding of hereditary glomerular diseases in children, most adult patients lack a genetic diagnosis. p.R229Q is a common missense variant in NPHS2, the gene encoding podocin, and it is associated with albuminuria in the general population. However, epidemiological studies suggest that p.R229Q is only disease causing in trans-association to additional genetic alterations.

Methods: We assessed the predisposition of p.R229Q to glomerular disease by introducing the equivalent point mutation in mice using CRISPR/Cas9-mediated genome editing. By applying super-resolution STED microscopy and functional measurements, we characterized the phenotype of Podcn229Q mice. Additionally, we evaluated the podocin229Q protein stability in human cultured podocytes.

Results: Although Podcn229Q mice do not develop overt glomerular disease, super-resolution microscopy and morphometric analyses revealed ultrastructural alterations that were previously been linked to disease predisposition. Ultrastructural alterations were even more prominent in homozygous Podcn229Q mice resulting in microalbuminuria in aged mice. Consistent with a recently published study, the slit diaphragm length correlated significantly with levels of albuminuria. Podocin229Q protein levels decreased in Podcn229Q mice and decreased further in Podcn229Q mice expressing the variant. Mechanistically, increased proximal degradation resulted in a decreased protein stability of podocin229Q in human cultured podocytes.

Conclusions: Collectively, our data suggest that podocin R231Q may contribute to genetic predisposition in adult patients.

PO1590
Reduced Glomerular and Nephron Injury due to Albumin Knockout in the Heavily Nephrotic, Polymerization-Defective GBM Laminin B2-Def44 Mutant Mice
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Background: Increased proteinuria is associated with adverse outcomes in chronic renal disease. Much evidence indicates that increased albumin filtration through the glomerular filtration barrier exacerbates nephron injury, but in vivo evidence is conflicting. Although it was previously shown that Nagase anabuminicane rats exhibit little or no increase in renal injury following multiple insults, Alport mice lacking albumin were previously shown to have dramatically increased lifespan with delayed injury to glomeruli and nephrin epithelium.

Methods: We mated CRISPR-meditated, albumin-knockout mice with laminin B2-Def44 mice, which exhibit heavy albuminuria, but delayed foot process effacement and fibrosis. Mice were monitored until their natural deaths or euthanized at 9, 10, or 11 months for analyses. Plasma was analyzed for BUN. Glomeruli were analyzed by electron microscopy to determine foot process effacement. Nephron epithelium was analyzed by immunofluorescent microscopy to determine status of injury markers.

Conclusions: Albumin-Def44 mice exhibited a significantly increased lifespan (6-month vs 9-month average), with significantly reduced BUN at all ages. Similar to Alport mice, foot process effacement in albumin-Def44 double mutant mice
was decreased at younger ages. Nephron tubule epithelium exhibited reduced KIM-1 expression at early ages, indicating delayed injury.

**Conclusions:** Similar to Alport mice, the absence of albumin in Lamb2-Del44 mice resulted in increased lifespan with delayed renal injury. These data support a significant role of albumin in nephron injury in murine models of nephrotic syndrome.

**Funding:** NIDDK Support

**PO1591**

**Klotho Improves Renal Function in Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD-UMOD)**

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**Background:** Heterozygous Uromodulin (UMOD) mutations cause ADTKD but no therapies are available. We tested if Klotho improves renal function in a murine model for ADTKD-UMOD.

**Methods:** To generate a stronger phenotype we crossed homozygous mutant UmodC93F/C93F mice with Klotho-overexpressing (TgKl) mice. We studied wild-type (WT), TgKl, UmodC93F/C93F and TgKl/UmodC93F/C93F mice at 6 and 13 months. For quantitative proteome analysis (LC-MS/MS) we harvested kidneys at 3 months. UmodC93F/C93F and TgKl/UmodC93F/C93F mice at 6 and 13 months. For quantitative proteome analysis (LC-MS/MS) we harvested kidneys at 3 months.

**Results:** 1. Compared to UmodC93F/C93F mice, TgKl/UmodC93F/C93F animals had significantly lower serum BUN, creatinine, cystatin C (see Figure 1), PTH, FGF23 values, significantly lower serum BUN, creatinine, cystatin C (see Figure 1), PTH, FGF23 values, osteoglycin/mimecan in TgKl/UmodC93F/C93F and osteoglycin/mimecan in TgKl/UmodC93F/C93F mice by increasing UMOD expression at early ages, indicating delayed injury.

**Conclusions:** To generate a stronger phenotype we crossed homozygous mutant UmodC93F/C93F mice with Klotho-overexpressing (TgKl) mice. We studied wild-type (WT), TgKl, UmodC93F/C93F and TgKl/UmodC93F/C93F mice at 6 and 13 months. For quantitative proteome analysis (LC-MS/MS) we harvested kidneys at 3 months. UmodC93F/C93F and TgKl/UmodC93F/C93F mice at 6 and 13 months. For quantitative proteome analysis (LC-MS/MS) we harvested kidneys at 3 months.

**Funding:** NIDDK Support, Other U.S. Government Support, Private Foundation

**PO1592**

**Spectrum of Mutations in 106 Chinese Patients with Gitelman Syndrome**

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**Background:** Gitelman’s syndrome (GS) is an rare, autosomal recessively inherited salt-losing tubulopathy(SLT) characterized by hypokalemic metabolic alkalosis. GS is caused by the mutations in SLC12A3 gene encoding for the thiazide-sensitive NaCl cotransporters (NCC). However, the sensitivity of genetic sequencing was low. No large genomic rearrangements in Chinese patients with GS was previously identified.

**Methods:** Targeted gene sequencing (TES) by next generation sequencing associated with SLC12A3 was performed for patients suspected of GS. Then, a search for large genomic rearrangements by ligation-dependent probe amplification (MLPA) assay was performed in patients with heterozygous for point mutations and patients with homozygous mutations without consanguinity history.

**Results:** Fifty-nine patients(56.67%) were female, the age was (34.87±15.23) years, serum potassium level was (2.68±0.13) mmol/L, serum magnesium level was (0.58±0.13) mmol/L, ninty-four patients(88.68%) had hypomagnesemia, seventy-nine patients(81.44%,79/97) had hypocalciuric. Eighty-three different mutations in SLC12A3 were identified within these 106 GS patients, including 32 novel mutations and 4 recurrent ones,5 large genomic rearrangements. Recurrent mutations were p.T60M(22.86%),c.965-1_976delGCGGA CATTTLTTGnsACCGAAAATTIT(6.19%),p.D486N(4.76%), p.C539K(4.76%). Triple mutations was identified in 8 patients, compound heterozygous mutations were identified in 70 patients, homozygous mutations were identified in 18 patients, whereas 10 patients had only one heterozygous mutations. The 5 large genomic rearrangements were exon deletion, including E7,E8 deletion, E8,E23 deletion, E20,E24 deletion, E8 deletion,E14,E6 deletion. The sensitivity of genetic testing sequencing was 90.57%.

**Conclusions:** We identified 83 mutations related to GS, containing 32 novel variants and 4 high-frequency ones, 5 large genomic rearrangements. TES combined with MLPA significantly increased the sensitivity of genetic sequencing and facilitate more accurate diagnosis of GS.

**Funding:** Government Support - Non-U.S.

**PO1593**

**Glucosylceramide Synthase Inhibition with Venglustat in Classic Fabry Disease Patients Leads to Progressive Reduction of Endothelial Cell Globotriaosylceramide Inclusion Volume**

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**Background:** Fabry disease (FD) is a rare disorder caused by mutations in the gene for the lysosomal enzyme alpha-galactosidase A (αGal-A). Progressive accumulation of globotriaosylceramide (GL-3) in vascular endothelial and other cell types leads over decades to renal, cardiovascular, and other severe clinical manifestations. In a phase 2 study, glucosylceramide synthase inhibition with venglustat led to reduction in microscopic (LM) scores of lysosomal GL-3 inclusions in skin capillary endothelial cells (EC) after 3 years, although not after 6 months. We applied quantitative unbiased stereological methods to better characterize the effect of venglustat on skin EC GL-3 inclusions.

**Methods:** Skin biopsies were obtained from classic male Fabry disease patients (N = 11) at baseline and during daily treatment with venglustat (NCT02228460, NCT02489344). Images from at least 50 randomly selected superficial skin capillaries per biopsy were obtained using transmission electron microscopy (EM) at 7,500 X magnification. The fraction of the volume (Vv) of EC cytoplasm occupied by GL-3 inclusions [Vv(Inc/Endo)] was estimated using point counting by a masked reader. Two-sided paired t tests were used to evaluate changes from baseline to post-treatment values at each time point.

**Conclusions:** We identified 83 mutations related to GS, containing 32 novel variants and 4 high-frequency ones, 5 large genomic rearrangements. TES combined with MLPA significantly increased the sensitivity of genetic sequencing and facilitate more accurate diagnosis of GS.

**Funding:** Government Support - Non-U.S.

**Schematic diagram of mutations in 106 ChineseGS patients**
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**Results:** Venglustat therapy led to a significant reduction from baseline in VvInc/Endo of 0.062 (p=0.001) after 6 months and 0.119 (38.7%; *p=0.001) after 2 years of treatment.

**Conclusions:** Treatment with venglustat led to reduction in skin capillary GL-3 inclusion fractional volume which was detectable after 6 months using precise quantitative histological methods, but not by LM scoring. This was followed by further reduction over the next 2 1/2 years. We posit that, in the absence of otgal-A activity, inhibition of GL-3 production with venglustat allowed other enzymatic or non-enzymatic mechanisms to progressively reduce EC lysosomal GL-3 content. Long-term venglustat therapy may therefore prevent or reverse progressive tissue injury in Fabry disease.

**Funding:** Commercial Support - Sanofi Genzyme

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**PO1594**

**The Role of Claudin Variants in the Formation of Kidney Stones**

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**Background:** Genetic risk factors contribute to the formation of calcium-based kidney stones. The majority of calculus is reabsorbed via paracellular transport through tight junctions along the human nephron epithelium where Claudin proteins are expressed. Claudins determine the selectivity and permeability of different nephron segments. Studies have shown that CLDN gene sequence variants are associated with kidney stones. I hypothesize that sequence variants in Claudin genes that regulate paracellular renal transport of calcium will be associated with the formation of kidney stones.

**Methods:** Patient DNA was analyzed by Fluidigm Next Generation Sequencing and short-read analysis by Sanger sequencing. Rare variants (MAF<1%) were compared to the gnomAD database. In silico prediction software was used to predict the impact of the amino acid change. Human kidney variants were generated by site-directed mutagenesis and cloned into a mammalian expression vector, pEGFP. Immunofluorescence was performed on HEK293 cells that were transiently transfected with both variant and WT sequences.

**Results:** Ninety adult patients (45 females, 45 males) with recurrent calcium-based kidney stones were recruited from one urologist’s kidney stone clinic. Seventy-two percent (n=90) of the patients self-defined as Canadian-European. Sixty-two percent (56/90) of the patients presented with the first kidney stone less than 40 years of age. Four novel heterozygous missense variants were identified in the following: CLDN11 S157F, CLDN16 R129S, CLDN17 A94V, and CLDN17 H121D. Nine rare variants include CLDN4 A113T, CLDN8 V45M, CLDN9 D27N, CLDN12 M25V, CLDN23 A90T, and CLDN24 V97L. CLDN4 A28T, CLDN8 A94V, CLDN11 S157F, and CLDN17 A94V are predicted to be deleterious. HEK293 cells were transiently transfected with CLDN4 A28T and the mutant protein was unable to localize to the tight junction, unlike the WT CLDN4 protein which did co-localize with ZO-1 by immunofluorescence as expected (n=3 independent experiments). Other Claudin variants are under evaluation.

**Conclusions:** The rare heterozygous variant, CLDN4 A28T is located at the second 5' end of mRNA of these cells by using rapid amplification of cDNA ends (5' RACE) gene and then examined identified yet.

**8-24 exists and it works partially as a 5-phosphatase. However, such isoform has not been
clarified until now, but it is suspected that an isoform consisting of exon
functions by the regulation of inositol phospholipids. The molecular mechanism by which
that acts on phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) and is related to cellular
was observed in the tubules. There was no significant finding in the immunofluorescence
and no electron dense deposits was detected by electron microscopy. Although
cyst-like expansion of the tubules was not clear, tubular atrophy was dominantly found
in the distal tubules by CK7 staining. Then, we performed genetic analysis of
NPHP1 gene, and found complete deficiency of NPHP1 gene, leading to definitive diagnosis of
juvenile NPHP.

**Discussion:** NPHP is often progress to ESRD at an average age of 13-14 years old. Thus, it is exceedingly rare to find NPHP in adult. Although present case did not show the typical histological abnormalities, such as cyst-like expansion of the tubular lesion, we could diagnose by genetic analysis of NPHP1 gene. In patients with renal failure and interstitial disease dominantly in distal tubule, it is necessary to discriminate NPHP even in the adult case.

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**PO1595**

**Elucidation of Molecular Pathogenesis of Lowe Syndrome and Dent Disease-2**

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**Background:** Lowe syndrome and Dent disease-2 (Dent-2) are both X-linked kidney diseases caused by OCRL gene abnormalities. However, the severity of these diseases are quite different. Genetic studies have shown that patients with truncating mutation in exon 1-7 of OCRL gene were diagnosed with Dent-2, and those with truncating mutations in exon 8-24 were diagnosed with Lowe syndrome. OCRL protein encodes a 5-phosphatase that acts on phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) and is related to cellular functions by the regulation of inositol phospholipids. The molecular mechanism by which different isoforms of this protein exerts its functions by the regulation of inositol phospholipids has not been clarified until now, but it is suspected that an isoform consisting of exon 8-24 exists and it works partially as a 5-phosphatase. However, such isoform has not been identified yet.

**Methods:** We extracted mRNA from cultured urine derived cells of healthy controls and Dent-2 patient with truncating mutation in exon 9-48 of OCRL gene and then examined 5’ end of mRNA of these cells by using rapid amplification of cDNA ends (5’ RACE) method. We also prepared three types of OCRL protein expression vector: wild type model, Dent-2 model and harboring truncating mutation in exon 4 and 7, and Lowe syndrome models harboring truncating mutation in exon 16 and 22. These vectors were transfected into Hela cells and analyzed the protein expression and 5-phosphatase activity.

**Results:** As a result of 5’ RACE, the 5’ end starting from Exon 6 was detected in both cells of healthy control and Dent-2 patient. In fluorescent immunostaining of transfected Hela cells, strong protein expression was observed in the wild type model, relatively weak expression was observed in Dent-2 models and no expression was observed in Lowe syndrome models. Western blot analysis detected two bands of 105kDa and 90kDa in the wild type model, single band of 80kDa in Dent-2 models, and no bands in Lowe syndrome models.

**Models:** 5-phosphatase activity of Dent-2 models was 59.85% that of wild type model, whereas, it was less than 2% of that of wild type model.

**Conclusions:** An isoform OCRL protein with 5-phosphatase activity is synthesized by alternative transcription of OCRL gene. This isoform contributes to the mild clinical phenotype in Dent-2.

**Funding:** Government Support - Non-U.S.
PO1598
Clinical and Genetic Features of Autosomal Dominant Alport Syndrome
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Background: Alport Syndrome is the second most frequent genetic kidney disease, accounting for around 2% of patients with end-stage kidney disease. It is caused by pathogenic variants in COL4A3, COL4A4 and COL4A5 genes. The aim of this study was to evaluate the clinical and genetic spectrum of patients with autosomal dominant Alport syndrome.

Methods: Retrospective cohort study of 82 families (252 patients) with autosomal dominant Alport Syndrome. Clinical, genetic, laboratory and pathological data were collected. Renal survival, estimated glomerular filtration rate (eGFR) decline, genotype-phenotype correlation and extrarenal features were analyzed.

Results: A pathogenic DNA variant in COL4A3 was identified in 106 patients (34 families) while 134 harbored a pathogenic variant in COL4A4 (44 families). Complex digenic inheritance was observed in 12 patients without clear genotype-phenotype correlation. Overall median renal survival was 67 years (95% CI, 58–75), without significant differences related to gender, causative gene or type of variant (p = 0.85, p = 0.28 and p = 0.81 respectively). Microhematuria was the most common renal manifestation (93%) while extrarenal features were rare. The results of kidney biopsies ranged from normal to focal segmental glomerulosclerosis. Hypertension was common and the temporal pattern at its diagnosis correlated with age at end-stage kidney disease (p < 0.01). The slope of eGFR decline was −1.66 mL/min/1.73m² per year (−1.9 to −1.42) for the overall group, with no significant differences between COL4A3 and COL4A4 genes (P=0.60).

Conclusions: This study shows that autosomal dominant Alport Syndrome patients present a wide spectrum of symptoms ranging from asymptomatic to end-stage kidney disease, regardless of the affected gene or type of variant. This broad phenotype contributes to underdiagnosis in clinical practice and makes autosomal dominant Alport Syndrome diagnosis very challenging.

Funding: Government Support - Non-U.S.

PO1599
Beneficial Effect of Oxalobacter formigenes Treatment on Nephrocalcinosis in a Rat Model of Primary Hyperoxaluria
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Background: Hyperoxaluria leads to urinary calcium-oxalate supersaturation and crystal retention in renal tissue (nephrocalcinosis). In case of primary hyperoxaluria (PH), increased hepatic oxalate production because of a rare genetic defect often leads to severe nephrocalcinosis and early ESRD. Secondary hyperoxaluria is generally less severe, however more common and often related to intestinal oxalate hyperabsorption. Current therapy is often unsatisfactory. Oral administration of Oxalobacter formigenes (Oxf), an oxalate-degrading bacteria, is thought to reduce intestinal oxalate absorption and to derive oxalate from systemic sources by inducing enteric oxalate secretion. Here, the ability of Oxf treatment to prevent or reduce PH induced nephrocalcinosis, by using an ethylene glycol (EG) rat model to mimic increased hepatic oxalate production, was investigated.

Methods: Eighteen rats were administered EG (0.75% in drinking water) for 6 weeks, of which 9 were treated by oral gavage with Oxf and 9 received vehicle. Five control rats did not receive EG/Oxf. Plasma and urinary oxalate levels, calcium-oxalate crystalluria, urinary volume, fluid intake, and serum creatinine were monitored during the study period. At sacrifice, nephrocalcinosis was quantified.

Results: Vehicle treated EG animals showed clear hyperoxaluria, hyperoxaluria, calcium-oxalate crystalluria and nephrocalcinosis. In Oxf treated EG animals the plasma oxalate levels were lower compared to vehicle-treated ones (significant at week 4: 47.6±20.9 vs 88±8.9 µM). Nephrocalcinosis was completely absent in the EG/Oxf group. Urinary output of oxalate (crystals) was similar in Oxf and vehicle treated EG animals which indicates that, taking into account the absence of crystals in renal tissue of Oxf treated EG animals, the amount of oxalate offered to the kidney for excretion was higher in the EG/vehicle group. EG administration significantly increased urinary volume, renal mass and fluid intake, most probably due to osmotic diuresis and partially reversed by Oxf. Serum creatinine levels of EG animals (both vehicle/Oxf) stayed at baseline levels throughout the study.

Conclusions: This study shows a beneficial effect of Oxf treatment on the development of PH-induced hyperoxaluria, hyperoxaluria, and nephrocalcinosis, pointing to Oxf reducing enteric oxalate elimination.

Funding: Commercial Support - Oxthera

PO1600
The Knockdown of RPL36A Downregulates GLA Expression Associated with Fabry Disease In Vitro Model
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Background: Mutations in the galactosidase alpha (GLA) locus can cause Fabry disease. The GLA locus is mapped in the reverse strand of the RPL36A-HNRNPH2 readthrough locus. The study aimed to show the influence of the siRNA downregulation of the RPL36A expression (the first gene in the RPL36A-HNRNPH2 locus) on the GLA expression.

Methods: The siRNA method was used to downregulate the expression of RPL36A in HEK293 cells. The expression of the two genes RPL36A and GLA in vitro was analyzed by RT qPCR. The protein products of the two genes were analyzed by ELISA and Western blot.

Results: The RT qPCR results of the RPL36A knockdown by siRNA showed a significant decrease not only for RPL36A expression but also for GLA expression (p<0.05) compared with the results of the untreated HEK293 cells. ELISA and Western blot assays showed a decrease in the GLA protein following knockdown of the RPL36A gene, but the two assays did not show a decrease in the expression for RPL36A protein. Alignment analysis by EMBOSyzer Matcher showed RPL36A protein amino acid sequence (Length: 106, Mass (Da): 12,441) is 99.1% like RPL36AL protein amino acid sequence (Length: 106, Mass (Da): 12,469). Intriguingly, the sequence of mRNA transcripts of both genes showed an 85.3% similarity. The designed siRNA was specific to RPL36A transcript NM. 021029.6 and not to RPL36AL transcript NM. 001001.5, which may explain the RT qPCR results.

Conclusions: The data provided evidence that malfunction in the expression of the RPL36A locus located at the start of the RPL36A-HNRNPH2 readthrough locus can cause an error in the expression of GLA. These findings revealed the importance of the RPL36A-HNRNPH2 readthrough region in Fabry disease. The work was supported by Sanofi-Genzyme Project GZ-2017-11708.

Metabolic State Modeling of Kidney Single Nuclei Data Reveals Cell-Specific Signatures at Baseline and in Disease

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Background: The kidney is a metabolically active and cellularly diverse organ. Perturbations in metabolic pathways, such as lipid metabolism, is a well-established sequela of chronic kidney diseases, such as diabetic nephropathy. Single cell RNA sequencing has allowed for an unprecedented understanding of the kidney’s transcriptomic complexity. However, until now, understanding the diverse metabolic states of the kidney has been limited to either expression analysis of single metabolic enzymes or bulk metabolomics experiments. Given the highly interconnected nature of metabolic networks and the kidney’s cellular complexity, integrating a systems-level understanding of metabolic perturbations with single cell sequencing has the potential to reveal previously unappreciated metabolic cell states and disease perturbations.

Methods: We have applied the newly developed Flux Balance Analysis (FBA) algorithm for single cell sequencing data, Compass (doi: 10.1101/2020.01.23.917217), to a dataset of 36,560 single nucleus transcripts from mouse kidney comprised of three healthy mice and three mice with CoQ-deficiency proteinic kidney disease.

Results: First, Compass correctly predicted well-established cell-specific kidney transport processes. Next, when comparing proximal tubule cell clusters, corresponding to S1, S2 and S3 segments, the S3 segment was found to have both high activity of branched chain amino acid (BCAA) metabolism and high activity of fatty acid oxidation (FAO). This previously unknown link between BCAAs and FAO in the kidney is of particular interest as cellular metabolism was the most highly downregulated. Downstream and downstream and metabolic disease. Finally, when comparing transcriptomes between disease and healthy mice, podocyte-specific changes in FAO and steroid metabolism were observed which correlated with podocyte cytoskeletal regulation, a hallmark of podocyte injury.

Conclusions: In conclusion, the combination of an enhanced resolution of single nucleus transcriptomics with a systems-level analysis of metabolic networks in the kidney have revealed cell-specific metabolic states at baseline and in disease. Future application of this analysis to human data will provide important validation for the generalizability of these findings and further insight into metabolic perturbations in human disease.

Funding: NIDDK Support

PO1603
Metabolic Dysfunction of Glomerular Endothelial Cells in Alport Syndrome

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Background: Glomerular endothelial dysfunction plays a key role in the development of chronic kidney disease (CKD), but its impact on Alport syndrome (AS), characterized by progressive chronic kidney disease (PKD), has not been fully elucidated. We previously shown that glomerular endothelial cells (GEC) are damaged in AS mice, manifested by enlarged fenestrations and alteration of the glyocalyx in the early stage of disease. In the present study we report the early transcriptional changes in AS GEC as an indication of endothelial dysfunction and contributing factor to disease progression.

Methods: We generated endothelial aTomato reporter AS mice and isolated GEC at 4 month of age by FACS. We studied islet specificity in GEC by flow cytometry, WB, and by monophoton and confocal microscopy, and their transcriptome by RNA-seq analysis. The transcriptional changes were compared to WT-GEC in terms of their morphology and differential gene expression. Tissue samples with patients with AS were used to confirm observations from mice to that of in human by immunohistochemistry.

Results: Comparative transcriptomics showed high enrichment of differentially expressed genes associated with cellular metabolism, with lipid metabolism being among the top five most enriched biological processes in GEC. In particular, genes associated with fatty acid uptake, synthesis and oxidation were significantly downregulated. Among the differentially regulated genes, PGC-1α, genes associated with fatty acid transport, (CD36, FATP-1, FATP-2, Fabp3), fatty acid synthesis (fatty acid synthase), fatty acid oxidation (Acox1, Bdh2, Ec23, Abcd2), and antioxidant enzymatic scavenger proteins (Gpx3, Gpx6, Gsta3, sod2) were also downregulated. We observed similar findings in human biopsy samples from AS patients by histology.

Conclusions: In sum, for the first time a lipoprotein metabolic dysfunction in Alport glomerular endothelial cells. Therefore, better understanding of the functional patients by histology. Also, downregulated. We observed similar findings in human biopsy samples from AS, genes associated with fatty acid transport, (CD36, FATP-1, FATP-2, Fabp3), fatty acid metabolism (Acox1, Bdh2, Ec23, Abcd2), and antioxidant enzymatic scavenger proteins (Gpx3, Gpx6, Gsta3, sod2) were also downregulated. We observed similar findings in human biopsy samples from AS patients by histology.

Funding: Private Foundation Support

PO1604
NPHS1 Variants Can Cause Persistent Asymptomatic Proteinuria: Genetic and Clinical Characteristics of Patients with NPHS1 Variants in Japan

Tomohiko Yamamura,1 Tomoko Horinouchi,1 Shinya Ishikso,2 Yuya Aoto,3 Nana Sakakibara,1 China Nagano,1 Takeshi Ninchoji,1 Yuko Shimada,1 Koichi Nakashima,1 Kandai Nozu,1 Kazumoto Iijima,1,2 Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan; 2Department of Pediatrics, Wakayama Medical University, Wakayama, Japan; 2Department of Child Health and Welfare (Pediatrics), Graduate School of Medicine, University of the Ryukyus, Nishihara, Japan.

Background: NPHS1 gene, which encodes nephrin, is known as a causative gene of congenital nephrotic syndrome (CNS). In addition, recently, it had been recognized that NPHS1 variants present with childhood steroid resistant nephrotic syndrome (SRNS) or focal segmental glomerular sclerosis (FSGS). However, it is not well known that this gene variants account for more milder phenotypes such as asymptomatic proteinuria.

Methods: 347 unrelated patients with CNS, infantile nephrotic syndrome, FSGS and asymptomatic proteinuria were screened for podocyte related genes including NPHS1 by using targeted exon sequencing. A retrospective review of clinical information was conducted for the cases with pathogenic variants in NPHS1.

Results: We identified 15 NPHS1 autosomal recessive pathogenic variants in 15 cases including 2 siblings. Regarding clinical manifestation, 6 cases showed CNS, 5 cases showed SRNS and 4 cases showed only asymptomatic mild to moderate proteinuria. The median age developing proteinuria in cases with SRNS and asymptomatic proteinuria was 6 years old. Pathological evaluation for 12 cases revealed that 11 cases showed minor glomerular abnormality and 1 case showed findings resemble membranous nephropathy. Genetic analysis revealed the variants c.2464G>A p.(V822M) and c.2515del were variational hot spots in the Japanese population and all 6 cases having V822M showed milder phenotypes such as SRNS (n=2) or asymptomatic proteinuria (n=4) and no one showed CNS.

Conclusions: In this study, NPHS1 variants were detected not only in cases with CNS and SRNS, but also in cases with asymptomatic proteinuria. Shono et al. have previously reported that V822M was a causative variant in cases with familial nephrotic syndrome who showed complete remission and functional analysis revealed that this variant leads to milder phenotype through mechanisms of (1)mild reduction of cell surface expression, (2)motion and trafficking restriction on surface and (3)interfering with assembly of microdomain on surface (Hum Mol Genet. 2009). Our study confirmed this variant leads to very mild phenotypes of SRNS or even the asymptomatic proteinuria and broadened the understanding of clinical manifestations of cases with NPHS1 variants.

PO1605
Ckd. Qld fabry Epidemiology (aQuIRE) Study: Fabry Disease Prevalence Amongst Patients with CKD

Andrew J. Mallett,2 Phoebe J. Kearvy,3 Anne Cameron (Salisbury),1 Helen G. Healy,1 Charles P. Denaro,1 Mark A. Thomas,1 Vincent W. Lee,4 Maria Fuller,1 Wendy E. Hoy,1 aQuIRE Study Team 1Royal Brisbane and Women’s Hospital, Herston, QLD, Australia; 2The University of Queensland Faculty of Medicine, Herston, QLD, Australia; 3Royal Perth Hospital, Perth, WA, Australia; 4Westmead Hospital, Westmead, NSW, Australia; 5Genetics and Molecular Pathology Laboratory, SA Pathology, Adelaide, SA, Australia.

Background: Fabry disease (FD) is a rare, genetic disorder resulting in absence or deficiency of alpha-galactosidase A (α-Gal A), leading to accumulation of α-galactosylceramide (αGC) in macrophages and tissues. Accumulation of αGC is due to renal, cardiac, and cerebrovascular manifestations. General population prevalence is ~0.0025%. Dialysis population prevalence is estimated at 0.12-0.36%. Little is known about the prevalence of FD amongst wider chronic kidney disease (CKD) populations. Through FD G1-X-linked, affected females can have variable disease manifestations. Prevalence amongst women is unclear.

Methods: A prospective cross-sectional study of FD prevalence amongst CKD patients in public Queensland nephrology services was undertaken across 7 sites Oct 2017-Aug 2019. Patients with all stages of CKD including Stage 5D/5T were eligible to participate, irrespective of prior CKD aetiology or diagnosis. 3,000 CKD patients were screened using dried blood spot (DBS) testing. Repeat DBS and/or Lyso-GB3 testing was performed. All newly diagnosed cases were male with two being CKD Stage 5T, and one being CKD Stage 5D. One case was in a participant who identified as Indigenous in the first known case in this population. In total, an additional 28 at-risk family members were identified who may benefit from family screening. No readily identifiable pattern of symptoms was identified.

Conclusions: Our results support the potential feasibility and utility of a cascade testing strategy principally using DBS, as a primary screening method for FD in adult patients with CKD. Further, this was consistent with a significant proportion of prevalent cases of FD amongst those with CKD remains undiagnosed.

Funding: Commercial Support - Sanofi-Genzyme

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
**PO1606**

Systems Analyses of Renal Fabry Transcriptome and Response to Enzyme Replacement Therapy (ERT) Identifies a Cross-Validated and Druggable ERT-Resistant Module

Oystein Eikrem,1,2 Nicolas Delaleu,1,4 Philipp Strauss,1 Miroslaw Sekulic,3 Camilla Tender,1 Sabine Leh,1,3 Einar Svarstad,1 Rannevig Skrnes,2 Albina Nowak,3,5 Elena-Emanuella Rusu,3 Tarig A. Osman,1 Hans-Peter Marti,1,5 Renal Research Group Bergen 1University of Bergen, Bergen, Norway; 2Haukeland University Hospital, Bergen, Norway; 32C SysBioMed, Contra, Renal Research Group Bergen

**PO1607**

Circular RNA-Based Biomarker Profile of Patients with Fabry Disease

Albina Nowak1, George Haddad,2 Andreas D. Kistler,1 Steller Nlandu khodo,4 Rudolf P. Wuthrich,3 Johan M. Lorenzen,2 Malte Kölling,1,2 University Hospital Zurich - Department of Endocrinology, Zurich, Switzerland; 3University Hospital Zurich - Department of Nephrology, Zurich, Switzerland; 4Cantonal Hospital Frauenfeld - Department of Medicine, Frauenfeld, Switzerland; 1University of Zurich - Institute of Physiology, Zurich, Switzerland

**PO1608**

Outcome of Primary Hyperoxaluria Type 3: Clinics, Diagnostics, and Follow-Up

Cristina Martin Higuera,1 Sander F. Garrelfs,3 Bodo B. Beck,3 Marcin Zaniek,4 Pzenyšlav Sikora,3 Bernd Hoppe,4 Dept. Ciencias Médicas Básicas, Fac. Medicina, Universidad de la Laguna, Tenerife, Spain; 2Amsterdam Medical Center, Amsterdam, Netherlands; 3Institute of Human Genetics, University Hospital Cologne, Cologne, Germany; 4University of Zielona Gora, Zielona Gora, Poland; 1Department of Pediatric Nephrology, Medical University of Lublin, Lublin, Poland; 2German Hyperoxaluria Center, Bonn, Germany

**PO1609**

Patient Journey in Alport Syndrome

Mariah Lopshire,1Dhivat Joshi,1 Rebecca Gould,2 Emily Wu,2 Daniel Day,2 Ali Hariri,2 Sanofi Genzyme, Cambridge, MA; 1Fulcrum Research Group, Waltham, MA.

**Background:** Fabry nephropathy (FN) is caused by mutations in the α-galactosidase A gene and can be managed with ERT. Via understanding the molecular basis of FN and long-term ERT impact, we aim at a framework for selection of biomarkers/drug targets.

**Methods:** Obtained from normal controls and two independent FN-cohorts, mRNA isolates from archival kidney biopsies (n=41) taken prior and up to 10 years of ERT were subjected to RNAseq and partly IHC. Combining pathway-centered analyses with network-science allowed computation of transcriptional landscapes from glomeruli, proximal/distal tubuli & arteries and integration with existing proteome and drug::target network-science allowed computation of transcriptional landscapes from glomeruli, proximal/distal tubuli & arteries and integration with existing proteome and drug::target networks.

**Results:** Despite inter-cohort heterogeneity, FN seemed well controlled, esp. via early introduced ERT. Pathways consistently altered in both FN-cohorts pre-ERT vs. controls were limited to glomeruli and arteries and commonly pertained to same biological themes. While glomerular keratinization-related processes were ERT sensitive, via early introduced ERT. Pathways consistently altered in both FN-cohorts pre-ERT vs. controls were limited to glomeruli and arteries and commonly pertained to same biological themes. While glomerular keratinization-related processes were ERT sensitive, via early introduced ERT. Pathways consistently altered in both FN-cohorts pre-ERT vs. controls were limited to glomeruli and arteries and commonly pertained to same biological themes. While glomerular keratinization-related processes were ERT sensitive.

**Conclusions:** Transcriptional landscapes of kidney compartments reflected differences in FN-cohorts. ERT can revert FN molecular state to closely match controls. We identified and cross-validated ERT-resistant modules, when leveraged with external data, allowed estimating their suitability as biomarkers and targets for adjunct treatment.

**Funding:** Government Support - Non-U.S.

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**Figure 1.** Target::Drug interactome. Node color target: green=glomerular target, blue=arterial target.

**Methods:** A genome-wide circular RNA expression analysis was performed in blood of 58 genetically diagnosed patients with Fabry Disease and 14 age- and sex matched healthy controls. Most highly increased circular RNAs were validated by quantitative real-time PCR. A disease control cohort of 109 patients with acute kidney injury was included. Linear regression analyses were performed for validated circular RNAs and clinical patient characteristics.

**Results:** A distinct circular RNA transcriptome signature identified patients with Fabry Disease. Circular RNAs hsa_circ_0008553, hsa_circ_0083766 and hsa_circ_002397 distinguished patients with Fabry Disease from healthy controls and patients with acute kidney injury. Furthermore, a female-specific circular RNA expression pattern. Circular RNA level were significantly related to galactosidase α gene mutations, early symptoms, phenotypes, disease severities, specific therapies and long-term complications of Fabry Disease.

**Conclusions:** The discovery of circular RNA-based and Fabry Disease specific biomarker may advance future diagnosis and therapeutic monitoring to diminish long-term complications of Fabry Disease.

**Funding:** Commercial Support - Shire

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**Funding:** Commercial Support - Shire
Males recorded hearing loss more than females (2/3 vs. 1/3 respectively) and at earlier ages. Hearing impairments in males were consulted a nephrologist earlier than females (median age: 12 vs. 28) and were diagnosed –15 years earlier than females (median age=16, females=31). The median delay in diagnosis from first symptom onset was 15 years (males=11, females=26). Two-thirds of patients were diagnosed with genetic testing. The rarer condition was diagnosed by an array of testing criteria (16 genetic, 16 biopsies, 9 others). Patients on delayed diagnosis sometimes receive inconclusive or no biopsy results. Based on current standard of care, dialysis or transplant is seen as inevitable future outcome. The same population included patients with hereditary kidney disease (P/LP) (n=5) experienced participants perceived transplant as an improvement of renal symptoms compared to dialysis.

Conclusions: Diagnosis can take years. Initial symptoms such as hematuria alone would not raise the suspicion for AS. Delays in diagnosis have significant psychosocial impact on patients and caregivers. While dialysis and transplant are considered inevitable outcomes of the disease, patients and caregivers recognize the unmet need for future disease specific treatments.

Funding: Commercial Support - Sanofi Genzyme

PO1610

Multidisciplinary Renal Genetics Clinics: Family Perspectives and Preferences
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Background: Multidisciplinary renal genetics clinics (RGC) comprising nephrologists, clinical geneticists, and genetic counsellors operate in 15 public hospitals across Australia with the goal of providing family-centred care and definitive molecular diagnoses to patients. However, little is known about family perspectives of multidisciplinary clinics or of undergoing genomic testing in this context.

Methods: Patients having genomic testing were surveyed following initial RGC attendance and after results disclosure. We explored patient experiences of the clinic, perceived impact of the disease on the family and reproductive planning, understanding of the test, and hopes and expectations relating to testing. Surveys included the Decision Readiness and Genetic Counselling Outcomes scales.

Results: Of 221 respondents to the baseline survey (RR=72%), most preferred the multidisciplinary clinic model to seeing specialists in separate clinics (n=145, 70%). A better understanding of the condition and implications for relatives were most commonly ranked as the most important advantages of the multidisciplinary clinic (n=27, 47%). Of 206 respondents to the follow-up survey (RR=67%), the majority preferred the multidisciplinary clinic model to seeing specialists in separate clinics (n=124, 79%) and a better understanding of the condition and implications for relatives were most commonly ranked as the most important advantages of the multidisciplinary clinic (n=27, 47%). Respondents agreed they received enough information during pre-test counselling (n=180, 92%) and had the opportunity to ask questions (n=181, 94%). The majority of respondents understood that the test analyses many genes (n=115, 59%), causative variant(s) may not be identified (n=143, 73%), and results may be of uncertain significance (n=142, 73%). Despite this, 44% of respondents thought the test was likely / highly likely to identify the cause of the condition (n=85).

Conclusions: Understanding patient and family experiences and opinions, and the short- and long-term impacts on families will guide the design and delivery of RGCs and associated genomic testing programs. A full author list is available online at www.kidgen.org.au.

PO1611

Autosomal Recessive Renal Tubular Dysgenesis Caused by a Founder Mutation of Angiotensinogen (AGT)
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Background: The International Society of Nephrology recommends the adoption of genetic testing with a goal of providing precision medicine based on individual risk. A recent whole-exome sequencing study showed that genetic inheritance may be responsible for up to 10% of CKD diagnoses. We designed a gene panel to prospectively provide genetic testing in a subset of patients with CKD.

Methods: Reata Pharmaceuticals is partnering with Invitae on KINDEYCODE, a US program that provides no-charge genetic testing using next generation sequencing (NGS) to enable diagnosis of a subset of rare monogenic causes of CKD: Alport syndrome (AS), autosomal dominant polycystic kidney disease (ADPKD) due to PKD2 variants, focal segmental glomerulosclerosis (FGS), and autosomal recessive PKD due to PKHD1 variants. Invitae’s renal disease panel includes 17 genes (ACTN4, ANLN, CD2AP, COLA43, COLA44, COLA45, CRB2, HNF1A, IN2, LMX1B, MYO1E, NPHS1, NPHS2, PAZ1, PKD2, PKHD1, and TRPC6). Patients at risk for hereditary CKD (eGFR ≥ 90 mL/ min/1.73m² plus hematuria or a family history of CKD) or known or suspected AS or FGS are eligible. Family members of those with known or suspected AS or FGS are also eligible.

Results: Of 455 test results, a genetic variant was reported in 278 patients. Of those, 206 patients had 219 variants in COL4A3, 4 or 5 genes [112 Pathogenic/ Likely Pathogenic (P/LP), 107 Variants of Uncertain Significance (VUS)], 87 patients had 95 variants in PKD1 (P/LP, VUS), 62 patients had 63 variants in PKD2 (P/LP, VUS), and 8 patients had variants in PKHD1 (4 P/LP, 4 VUS). Of the 109 patients with P/LP COL44A4 variants, 51 reported a previous diagnosis of Alport syndrome. Other diagnoses in patients with P/LP COL4A4 variants included FSGS, thin basement membrane disease, familial hematuria, hereditary nephritis, IgAN, diabetic CKD, hypertensive CKD, and ADPKD. Hearing loss was reported in 34, and eye disease was reported in 2 of the 109 patients with P/LP COLA4 variants.

Conclusions: Initial results with the KINDEYCODE panel demonstrate the utility of NGS. Combining genetic testing with clinical presentation and medical history can improve the accuracy of diagnosis of hereditary CKD.

Funding: Commercial Support - Reata Pharmaceuticals

PO1613

Very Rare Mutation Identified in Female Patient with Multisystemic Fabry Disease in the United States
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Introduction: Fabry disease is an X-linked lysosomal storage disorder characterized primarily by kidney, cardiac and central nervous system dysfunction. Over a 1000 mutations have been identified to be associated with disease. We describe a patient with biopsy confirmed Fabry disease identified to have very rare mutation not listed in genetic databases.

Case Description: A 48 year old female with past medical history of chronic kidney disease G4A3 (previously biopsy proven Fabry disease), dilated cardiomyopathy, atrial fibrillation, previously treated breast cancer, was referred to our clinic by a nephrology group given progressive worsening of kidney function and consideration for migalastat. Patient was diagnosed with Fabry disease at the age of 32 (normal renal function at the time), and subsequently received agalsidase beta for a period of 3 years thereafter. However, therapy was ceased due to insurance issues. In the interim, patient has progressive decline in renal function (creatinine 2.5 mg/dL on referral), worsening proteinuria, along with development of dilated cardiomyopathy and neuropathy. We proceeded with genetic testing to identify mutation of galactoside A (GLA) gene and kidney biopsy(image 1). Genetic testing revealed a novel mutation variant c.282G>C(p.Gly74Asp) (74%) to be heterozygous and of unknown significance by the laboratory. Kidney biopsy revealed classic finding of glomerular inclusions (podocyte and mesangium) with diffuse renal parenchymal scarring. Patient was eventually prescribed agalsidase beta, given non amenability to migalastat.

Discussion: This case highlights identification of a very rare mutation of the GLA gene that appears to have late onset manifestations. Pursuing genetic testing in patients with Fabry disease has become more important with the introduction of novel therapy migalastat, which may not be compatible with numerous pathogenic mutations.


PO1614
A Unique Case of COL4A3/4 and ACTN4 Mutations Combined
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Introduction: Alport syndrome is due to mutations of the COL4A gene. Males with COL4A mutations present with proteinuria and CKD, hearing impairment and anterior lenticonus. Disease in women ranges from mild hematuria and proteinuria to a syndrome similar to that of X-linked males. Patients in families with mutations of the Alpha-actinin-4 gene (ACTN4; autosomal dominant inheritance) present histologically and clinically with focal segmental glomerulosclerosis. We present the first ever-reported case of a patient with both COL4A4 and ACTN4 mutations

Case Description: Family pedigree is shown in the figure. Subject II:1 is a female with Alport’s syndrome diagnosed by kidney biopsy, CKD3 (in her 50’s) had genetic testing showing a COL4A3 mutation. Her husband (II:2, in his 70’s) had ESRD presumed to be secondary to diabetes (DKD). Given concerns for possible disease in their 2 sons, genetic testing was performed. The oldest son (III:1, in his 30’s) showed the same COL4A3 mutation as II:1 but an additional ACTN4 mutation. He has microalbuminuria (90mg/g) and GFR >90 ml/min. The younger son (III:2; in his 20’s) showed the ACTN4 mutation but no COL4A4 mutation. (clinical tests are pending). Given the ACTN4 mutations in the sons, subject II:2 was tested, showing an ACTN4 mutation (suggesting DKD was not the single etiology of his ESRD). Family history showed both paternal grandparents had ESRD, unknown etiology for I:4 (died in her 70’s) and presumed to be due to DKD for I:3 (died in his 80’s)

Discussion: ACTN4 and COL4A4 mutations have not been reported in a single patient before. The identification of 2 mutations known to be associated with CKD will allow for early intervention with management of comorbid conditions like hypertension, obesity and diabetes and use of RAAS inhibitors. Distinct disease patterns may emerge associated with specific genetic abnormalities allowing a more personalized treatment. Genetic testing should be considered for all patients presenting with proteinuria as findings may dictate changes in management

PO1615
Kidney Tubuloids Model Cystinosis and Allow Drug Screening
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Background: Cystinosis causes progressive damage to the kidney and other organs. In cystinosis, a CTNS mutation causes lysosomal cystine accumulation and other metabolic abnormalities including alfa-ketoglutarate (aKG) accumulation in patient cells and serum. Excess KG associates with aggravated apoptosis, abnormal autophagy and proximal tubule dysfunction, suggesting a key role in cystinosis pathology ( Jamalpoor et al. BioRvX: 2020). Current treatment with cysteamine reduces cystine and delays, but does not stop, progression of renal insufficiency nor restores tubular dysfunction. Therefore, new therapies are needed. Here, we use patient kidney tubuloids to model cystinosis and to test the efficacy of a novel drug combination.

Methods: Tubuloids were grown from primary renal cells from the urine of two cystinosis patients and compared with two healthy controls. Tubuloid origin and composition were assessed by qPCR and stainings. The effect of cysteamine and/or bicalutamide treatment was studied by a large-scale metabolic screen using LC-MS. Potential toxicity of bicalutamide was tested by measuring ATP levels as proxy for tubuloid viability at increasing doses.

Results: Urine-derived tubuloids consisted of kidney cells (PAX8+;p63-) and not urothelium (PAX8-p63+). Tubuloids contained proximal tubule, loop of Henle, distal tubule and collecting duct epithelium. Patient tubuloids showed hallmark cystine accumulation (1.25 ± 0.12 yr. 0.16 ± 0.01 mmol/mg protein in controls, p<0.05). Although cysteamine normalized cystine levels, it failed to restore aKG accumulation. The novel combination of cysteamine with bicalutamide more potently lowered cystine and reduced aKG in tubuloids (aKG peak area reduction of 16-28% with bicalutamide and 21-37% with the combination, both p<0.05). Finally, the used bicalutamide dose did not compromise the viability of cystinotic tubuloids.

Conclusions: Tubuloids model cystinosis in vitro and allow personalized drug screening. Moreover, tubuloids show that the combination of cysteamine and bicalutamide is more effective in normalizing the metabolic abnormalities in cystinosis than cysteamine alone.

Acknowledgements This work is supported by the partners of RegMedX, powered by Health Holland, Top Sector Life Sciences & Health and the Dutch Kidney Foundation (grant 150KG19).

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PO1616
Case Report: Familial FSGS Associated with a Novel Variant of WT1
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Introduction: The underlying causes of Familial FSGS are currently being elucidated by exome sequencing. WT1 has been reported in association with Fraser Syndrome, Denis-Dreah syndrome and isolated nephrotic syndrome. WT1 variants have emerged as a common cause of autosomal dominant FSGS.

Case Description: We report a case of a 22 year old male who presented at age 17 with nephrotic range proteinuria progressing to ESRD over 4.5 years. His renal biopsy at that time revealed FSGS andExome sequencing (Next Generation Sequencing) demonstrated a WT1 variant of uncertain significance. Family history was significant for the following: mother with microalbuminuria (229mg/24hr on spot protein) and hypertenison (onset 2 years prior to proteinuria); maternal uncle with congenital unilateral renal agenesis and later End Stage Kidney Disease requiring transplant at age 29 years; and maternal grandfather who died in his 60s on dialysis for unknown reasons. Genetic analysis in the patient and mother revealed the same heterozygous variant in WT1 (c.1078G>T, p.Gly360Cys).

Discussion: WT1-related renal disease is associated with autosomal dominant inheritance. We strongly suspect the WT1 variant described was pathogenic, as evidenced by a family history of both FSGS and geneticinurinary tract malformations. We review the association of WT1 with nephropth and postulate a potential interaction with NY karyotype, similar to other WT-1-associated disease. Disclosure: The views expressed are those of the authors and do not reflect the Department of Army or U.S. Government.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Positive Identification of Genetic Causes of FSGS Increases with Proper Patient Selection

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Background: FSGS is a histological lesion with diverse pathogenesis, commonly divided into primary, secondary (maladaptive, virus or drugs), and genetic forms. Differentiation of these forms is challenging but important for management and prognosis. We aimed to identify clinicopathologic factors that could be predictive of finding a genetic diagnosis in individuals with unknown forms of FSGS.

Methods: Cohort study included 51 FSGS patients with either a secondary or primary form of FSGS without an identifiable cause or with presumed “primary” FSGS who failed to respond to immunosuppressive therapy (IS). Seven patients with primary FSGS in remission following IS served as negative control. Patients were classified as having pathogenic/likely pathogenic variants (Group 1a), relevant variants of uncertain significance (relevant VUS; Group 1b), and no relevant variants (Group 2). Clinicopathologic characteristics are presented in Table 1.

Results: A pathogenic/likely pathogenic genetic variant or relevant VUS was found in 41.2% (n=21/51) and in 11.8% (n=6/51) of the patients, respectively. 55.6% were in CD2AP (43.3% in podocyte genes [INF2/NPHS2/TRPC6/NPHS1], and 11.1% in other genes [DLC1/SMARCAL1/UMOD]). Family history of kidney disease was present in 75% (n=19/25) of the patients in Group 1a, 16.7% (n=1/6) in Group 1b, 20.8% (n=5/24) in Group 2 and 0% (n=0/7) in the negative control. There was a negative correlation between proteinuria and the probability of finding a genetic variant. Severe foot-process effacement on EM and nephrotic syndrome were significantly more common in the negative control group compared to Group 1a.

Conclusions: Over 50% of adult patients with FSGS who could not be categorized into primary or known secondary forms were found to have a genetic diagnosis. Positive family history and absence of nephrotic syndrome increased the likelihood of identifying a pathogenic/likely pathogenic variant. Genetic testing is therefore highly recommended in such population.

Table 1

<table>
<thead>
<tr>
<th>Disease</th>
<th>Group 1a</th>
<th>Group 1b</th>
<th>Group 2</th>
<th>Posterior</th>
<th>Group 2a</th>
<th>Group 2b</th>
<th>Group 2c</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients with family history</td>
<td>70.7% (19/27)</td>
<td>18.5% (5/27)</td>
<td>0% (0/7)</td>
<td>0.017</td>
<td>6.4% (1/16)</td>
<td>0.4% (1/24)</td>
<td>0% (0/7)</td>
</tr>
<tr>
<td>% of patients with IS response</td>
<td>50.0% (13/26)</td>
<td>70.9% (7/10)</td>
<td>0% (0/7)</td>
<td>0.103</td>
<td>62.5% (5/8)</td>
<td>50.0% (12/24)</td>
<td>0% (0/7)</td>
</tr>
<tr>
<td>% of patients with ESRD at diagnosis</td>
<td>23.1% (6/26)</td>
<td>0% (0/10)</td>
<td>0% (0/7)</td>
<td>0.003</td>
<td>41.7% (4/9)</td>
<td>25.0% (6/24)</td>
<td>0% (0/7)</td>
</tr>
<tr>
<td>% of patients with remission</td>
<td>50.0% (13/26)</td>
<td>70.9% (7/10)</td>
<td>0% (0/7)</td>
<td>0.103</td>
<td>62.5% (5/8)</td>
<td>50.0% (12/24)</td>
<td>0% (0/7)</td>
</tr>
</tbody>
</table>

A Rare Case of Nephrotic Syndrome Associated with Dent Disease

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Introduction: Dent’s disease is a rare X-linked condition caused by a mutation in CLCN5 or OCLR gene, which impair the megalin-cubilin receptor-mediated endocytosis in kidney’s proximal tubules. Thus, it may manifest as nephrotic-range low-molecular-weight proteinuria (LMWP). On the other hand, glomerular proteinuria, indicative of glomerulopathy, is usually not found in Dent’s disease. In this patient, glomerulopathy and the Dent’s disease existed separately in this patient. In such a case of combined LMWP and glomerular proteinuria, the U/J2/UP can be used to monitor the relapse of NS. We should perform renal biopsy in patients with sudden onset of edema and hypoalbuminemia even those who have a congenital proteinuria.

Figure 1 (Left) A glomerulus in PAS staining showed there were no cellular crescents and no proliferation of mesangial cells. (Right) Von Kossa staining showed renal medulla with calcifications (arrows) was observed in the medullary interstitium.

Figure 2 The patient treatment course

Mitochondriopathy Manifesting as Inherited Tubulointerstitial Nephropathy Without Symptomatic Other Organ Involvement

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Introduction: Mitochondrial dysfunction has been previously described in cases of human chronic kidney disease (CKD), and subjects affected by primary systemic mitochondrial disease develop CKD. Importantly, examples of mitochondrially inherited tubulointerstitial kidney disease in subjects with no other symptomatic organ involvement have been recently reported, suggesting the possibility of a single-organ mitochondrial disease.

Case Description: A 12-year-old boy presented with short stature, low body weight, increased serum creatinine (1.9 mg/dL) and increased blood urea nitrogen (30 mg/dL). Blood analysis showed anemia, vitamin D deficiency, hyperparathyroidism and negative antinuclear antibodies (ANA) and antineutrophil cytoplasmic antibodies (ANCA). Ultrasound showed small kidneys (< 5th percentile). A kidney biopsy showed mild, non-specific, chronic tubulointerstitial nephropathy on light microscopy. Immunofluorescence was negative. Electron microscopy showed markedly enlarged and dysmorphic mitochondria. Given this striking histopathologic finding, genetic testing was performed. Next generation sequencing of mitochondrial DNA from the tissue biopsy showed the presence of a homoplasmic, single, missense mutation in position 616 (m.616T>C) of the mitochondrially encoded transfer RNA phenylalanine (tRNA(phe)) gene. Analysis of blood derived mtDNA from mother and maternal uncle, who were on dialysis since their 30s, confirmed the same homoplasmic mitochondrial mutation, supporting our hypothesis.

The renal biopsy findings, genetic findings, and pattern of inheritance were strongly suggestive of a diagnosis of mitochondrially inherited tubulointerstitial kidney disease. Notably, no additional symptomatic organ involvement was present in these subjects.

Discussion: Our case supports and reinforces the possibility of a single organ-limited mitochondrial disease, regardless of the systemic mitochondrial DNA mutation status, potentially radically changing management and prognosis of these patients. Careful analysis of mitochondria by electron microscopy should be performed in patients with tubulointerstitial nephropathy and family history of kidney failure.
PO1620
Discovery of CHK-336: A First-in-Class, Liver-Targeted, Small Molecule Inhibitor of Lactate Dehydrogenase for the Treatment of Primary Hyperoxaluria
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Background: Primary hyperoxalurias (PH) 1-3 are autosomal recessive disorders involving excessive hepatic oxalate production resulting in frequent kidney stones, progressive CKD and ESRD. Few therapeutic options currently exist for these patients. Lactate dehydrogenase (LDH) catalyzes the final and only committed step in hepatic oxalate synthesis and represents a potential therapeutic target for all forms of PH. Herein we describe the profile of a potent and selective LDH inhibitor.

Methods: CHK-336 was evaluated in LDH activity assays and in an AGXT knockout mouse model. Additional characterization of drug properties was performed.

Results: CHK-336 demonstrates potent and selective inhibition of LDH in enzyme assays (IC50 = 0.4 nM) and hepatocyte assays (IC50 = 80-142 nM). To minimize the potential for extra-hepatic LDH inhibition, a liver-targeted tissue distribution profile was engineered into the molecule. CHK-336 demonstrates exceptional liver-targeting across species mediated by OATP-uptake into hepatocytes and tight binding to LDH resulting in a long liver half-life that supports once-daily oral dosing. In a PH1 mouse model, CHK-336 produced significant and dose-dependent reductions in urinary oxate to levels observed in wild-type mice. Wide safety margins were established in rodent toxicity studies to support continued development of CHK-336.

Conclusions: By potently blocking LDH, the terminal step in hepatic oxalate synthesis, along with engineering of liver-targeted tissue distribution, CHK-336 is a promising oral small molecule development candidate with the potential to treat patients with hyperoxaluria.

Funding: Commercial Support - Chinook Therapeutics Inc.

PO1621
Disease Manifestations, Treatment, and Healthcare Resource Use (HRU) in Primary Hyperoxaluria Type 1 (PH1): An International Online Chart Review Study
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Background: Few multinational studies have examined the clinical burden of PH1. This online retrospective chart review evaluated disease manifestations, treatments, and HRU in a large international sample of PH1 patients.

Methods: Nephrologists in the US, Canada, UK, France, Germany, and Italy provided data from PH1 patients in their care via an online platform. Eligible patients had PH1 confirmed by genetic testing or liver biopsy and ≥2 office visits from 2016-2019. Data on disease manifestations, treatment and HRU were collected.

Results: Overall, 86 patients (56% from North America; 63% female) from 41 unique providers were analyzed. Mean age at diagnosis was 21.2±11.6 yrs, with a mean of 6.7±9 yrs to diagnosis from first symptoms. Mean age at index (first office visit in past 3 yrs) was 25.3 yrs; 71% had stage ≥3 CKD at index (median eGFR: 44mL/ min/1.73m2). Mean follow-up was 1.6±1 yrs. The most common PH1 manifestations during follow-up were uro-/nephrolithiasis (57.1%) and urinary tract infection (UTI; 56.9%). Additionally, 29.8% of patients had ≥1 acute renal decline episode, of which 53% resulted in lasting renal function loss. In total, 11.6% of patients had ESKD at or before index, and 8.1% developed ESKD post-index; 2.3% had ESKD with timing not noted. Dialysis and transplant (liver and/or kidney) at any time were reported in 22.2% and 0.6% of PH1 patients, respectively. In terms of HRU, the following patients required ≥1 stone removal procedure ( lithotripsy: 38%; ureteroscopy: 28%; percutaneous nephrolithotomy: 9%). Hospitalization and ER visits were required by 85.9% and 84.6% of patients, respectively, where data was reported (n=73).

Conclusions: There is significant delay between PH1 presentation and diagnosis. Patients with PH1 suffer progressive renal function decline, with many progressing to ESKD. During follow-up, almost all patients required ER visits and hospitalization, and most had stone episodes and UTIs and required stone removal procedures. These findings highlight the ongoing, high-risk profile of acute events that contribute to ongoing morbidity, HRU, and impaired quality of life, underscoring the need for early intervention with effective PH1 treatment.

Funding: Commercial Support - Alynyum Pharmaceuticals

PO1622
Recurrent SLC12A3 Mutations in Taiwanese Families with Gitelman Syndrome: A Rapid Detection for the Higher Prevalence Shih-Hua P. Lin,1 Sung-Sen Yang,1 Chih-Chien Sung,1 Min-hua Tseng,2 1Division of Nephrology, Tri-Service General Hospital, Taipei, Taiwan; 2Division of Pediatrics, Taoyang, Taiwan.

Background: Recurrent mutations in SLC12A3 gene responsible for autosomal recessive Gitelman syndrome (GS) are reported to be common with uncertain prevalence. Rearrangement detection of the recurrent hotspots may help early diagnosis of GS but remain challenging. We aim to investigate the prevalence of recurrent SLC12A3 mutations in a large Taiwan cohort of GS families and develop a simple, novel, and rapid method to detect recurrent SLC12A3 hotspots.

Methods: One hundred and ninety-four index patients with genetically-confirmed GS were enrolled from different regions of Taiwan were consecutively enrolled to define recurrent SLC12A3 hotspots and determine their prevalence. Using Tagman MGB probe-based real-time primer chain reaction (RT-PCR), hotspots-based mutational detection platform was designed and optimized to recognize all hotspots. We validated this mutational detection plate and also tested the feasibility in 12 newly-diagnosed GS patients.

Results: A total of 57 mutations in SLC12A3 gene were identified from our cohort and 22 different mutations including two deep intronic mutations were found in at least two unrelated families, comprising 87.5% of all allelic mutations including biallelic triple mutations. These 22-hotspots-based detection plate was fully validated with excellent sensitivity and specificity in GS patients carrying biallelic SLC12A3 mutations and healthy subjects. In the clinical validation, recurrent mutations were recognized in 87.5% of all mutational mutations of 12 newly-diagnosed GS patients with 4 hours and all confirmed by direct sequencing.

Conclusions: Recurrent SLC12A3 mutations are very common in Taiwanese GS patients. This novel hotspots-based detection plate may be time, cost, and labor saving to rapidly identify the recurrent hotspots and provide an early molecular diagnosis of GS in patients with chronic hypokalemia.

Funding: Commercial Support - Alynym Pharmaceuticals Inc.

PO1623
AVR-RD-01, an Investigational Lentiviral Gene Therapy for Fabry Disease, Reduces Gb3 Substrate in Endothelial Cells of Renal Peritubular Capillaries Mark A. Thomas,1 Mirjam Traune,2 Chris Mason,3 Birgitte Volek.2 1Royal Perth Hospital, Perth, WA, Australia; 2AVROBIO, Cambridge, MA.

Background: Lysosomal disorders are attractive candidates for ex vivo gene therapy based on the potential to transform a patient’s own cells into a drug product to deliver sustained functional enzyme after a single treatment. Fabry disease (FD) is caused by mutations in the GLA gene that result in functional deficiency of the lysosomal enzyme, α-galactosidase A (AGA), which leads to pathological accumulation of substrates and metabolites, including globotriaosylceramide (Gb3) and globotriaosylphosphoinositol (lyso-Gb3). Significant morbidity and early mortality result from damage to kidneys, heart, and brain. Objective: AVR-RD-01 is an investigational ex vivo gene therapy that involves transplantation of autologous stem cells genetically modified with a lentiviral vector which inserts into the human genome a complementory deoxyribonucleic acid (cDNA) sequence that encodes for functional human AGA.

Methods: In a Phase 1 trial of AVR-RD-01, 5 patients, previously on enzyme replacement therapy (ERT), after gene therapy demonstrated increases in plasma and leukocyte AGA activity and decreases in substrate (Gb3) and metabolite (lyso-Gb3) in plasma, now sustained up to 32 months. A Phase 2 clinical trial in 8-12 treatment-naive male and female patients (70 years) with classic FD investigated the safety, tolerability, and efficacy of AVR-RD-01, including its effect on substrate accumulation in the kidney after 48 weeks. Kidney biopsy results for the first patient in the Phase 2 clinical trial demonstrated reduction in renal peritubular capillary (PTC) Gb3 inclusions, quantitatively assessed by the Relative Inclusion Density (RID). At 48 weeks, Gb3 inclusions were reduced from an average of 3.55 to 0.47 per PTC corresponding to an 87% reduction versus baseline (BL). Leukocyte and plasma Gb3 activity increased, associated with declines in plasma and urine Gb3 and lyso-Gb3, including an 87% reduction in plasma lyso-Gb3 at 48 weeks versus BL. Adverse events were as expected with the particular conditioning regimens

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: As of May 2020, 16 participants were enrolled (13 PH1, 3 PH2) in this study. Total exposure (based on 15 participants) to monthly dosing of nedosiran has exceeded 3 years based on the cumulative duration of patient participation in the trial. Seven participants have had exposure to at least 3 monthly doses of nedosiran. Treatment-emergent adverse events (AEs) were observed in 11 participants. Seven participants experienced 33 AEs considered related to study drug administration, including redness, pain, and swelling at the injection site, and one participant experienced injection-site reactions (defined as occurring 4 hr or more after injection). All drug-related AEs were mild. There were no drug-related serious AEs. Six out of the 7 participants who have had exposure to at least 3 monthly doses of nedosiran showed normalization or near-normalization of urinary oxalate excretion (defined as ≥0.46 mmol/24 hr/1.73 m² and ≥0.46-0.60 mmol/24 hr/1.73 m², respectively) on at least 2 visits after the first dose.

Conclusions: Nedosiran has shown an acceptable safety profile in the interim analysis. This and the sustained reduction of urinary oxalate excretion are encouraging signs of potential long-term safety and clinical benefit of a multidose regimen of nedosiran.

Funding: Commercial Support - Dicerna Pharmaceuticals, Inc.

PO1626

A Case of De Novo X-Linked Alport Syndrome Treated by Kidney Transplantation from the Patient’s Healthy Mother

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Introduction: X-linked Alport syndrome is a hereditary nephratitis that leads to end-stage kidney failure by 40 years of age in most affected males. Although kidney transplantation is considered.

Methods: We present a case of a patient with X-linked Alport syndrome that was diagnosed at a young age. The patient was a 38-year-old man. Microhematuria had been present during his early childhood and had been diagnosed with Alport syndrome based on the results of a kidney biopsy at five years of age. He developed bilateral sensory deafness at 20 years of age and started hemodialysis due to end-stage kidney failure at 28 years of age. Although an X-linked mode of inheritance was suspected, none of the patient’s relatives, including his mother, had kidney disease. Since his mother had normal urinary results, living kidney transplantation from his mother was performed when he was 34 years of age. A genetic diagnosis at a later date revealed a splicing variant at c.3107-2A>G in COL4A5 of the patient, confirming that the patient had a de novo mutation.

The kidney function of both the patient and his mother was stable at 4 years after transplantation.

Discussion: For transplantation in cases of hereditary nephritis, it is preferable to avoid transplantation from an affected individual or the gene carrier. The kidney prognosis of female X-linked gene carriers is reported to be worse than expected. Although there was no genetic mutation in the donor in the present family case, if an X-linked form is suspected, a genetic diagnosis of the donor candidate should be performed before kidney transplantation is considered.

Funding: None

PO1627

Clinical and Economic Impact of Primary Hyperoxaluria: A Retrospective Claims Analysis

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Background: This retrospective study analyzed claims from IQVIA PharMetrics® Plus (1/2014-12/2019). PH cohort inclusion was an ICD-10 code for PH (E72.53) and no evidence of secondary hyperoxaluria (SH). A random 5% sample from the same database of patients without PH or SH served as a control cohort (non-PH). Clinical outcomes, including kidney transplantation, were compared between the cohorts for a 12-month period. The Charlson Comorbidity Index (CCI) was used to characterize comorbidities.

Results: The annualized median and mean costs per patient for the PH cohort (n=52; median $1,070; mean $9,910) were significantly higher (p<0.001) than the non-PH cohort (n=2,579,352; median $1,079; mean $5,041). Costs were significantly higher for PH patients across age groups (see table) and care settings, including inpatient/outpatient visits (p<0.001). The majority of PH patient cost (62%) was associated with outpatient visits. The PH cohort saw significantly higher use of specialists compared to non-PH patients (p<0.001), including nephrologists (19% vs 1%) and urologists (66% vs 3%). Over one year, 80% of the PH cohort had at least one kidney stone. The CCI scores for the PH and non-PH cohorts were 0.79 and 0.22, respectively.

Conclusions: The median cost increase for the PH cohort was 10 times higher than the non-PH cohort over all age groups annually, and the PH cohort showed substantially greater HCRU compared to the non-PH cohort. Additional research is required to better understand these costs in an effort to enable more efficient healthcare utilization and improve care delivery to these at-risk patients.

Funding: Commercial Support - Dicerna Pharmaceuticals
PO1628
Identification of Genetic Drivers of Age-Related Renal Histopathology
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Background: Studies to understand age-related changes in the human kidney have been performed by measuring kidney function and damage markers in the urine. These studies have provided valuable information, including clear genetic components underlying kidney disease. However, due to the highly invasive nature of kidney biopsies, it is not possible to identify early causal changes in humans by histological analyses that are hypothesized to precede changes in function and renal damage. However, mouse models provide access to kidneys at specific time points enabling us to conduct histological analyses across lifespan. We established the Aged Mouse Kidney Resource, which consists of kidneys from 600 genetically diverse mice (males and females) at three ages (6, 12, and 18 months). Scanned PAS slides for all mice are publicly available at korstanjelab.jax.org, as well as gene expression, protein expression, and DNA methylation data for a subset of kidneys.

Methods: Renal histology has been mostly a qualitative or semi-quantitative discipline. We leveraged new approaches to image analysis and machine learning and demonstrate the feasibility of quantification on entire sections of mouse kidneys (pathomics) from a large number of animals. We have developed a pipeline that uses machine learning on scanned slides, which allows us to automatically segment glomeruli and quantify mesangial matrix expansion (MME) in a high-throughput fashion.

Results: Applying our pipeline on the 12-month kidneys from our Resource shows an estimated heritability (h²) of 0.76 for MME and genetic analysis identifies three significant loci with 4cfa14 and 12f as strong candidate genes for two of these loci. On the other hand, we find that the heritability drops to 0.61 and no significant loci were found in the 18-month old kidneys. We hypothesize that this is caused by the increasing effect of environmental variation with age and death before 18 months of animals with fast age-related renal functional decline that reduces the genetic variability and mapping power in the population.

Conclusions: Our results demonstrate the importance of genetic factors contributing to histological phenotypes and the power of combining pathomics and genetics to identify genes involved in age-related histological changes.

Funding: Other NIH Support - National Institute on Aging

PO1629
Epigenome-wide Association Study of Kidney Function
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Background: DNA methylation regulates gene regulation and may influence estimated glomerular filtration rate (eGFR).

Methods: The study included over 13,000 participants from multi-ethnic studies for discovery and replication. We tested the associations between whole blood DNA methylation and eGFR using normalized beta values from Illumina 450k or EPIC arrays. Analyses were performed in study- and race-stratified samples using linear mixed models and adjusting for age, sex, and study-specific and technical variables. Study-specific meta-analyses were meta-analyzed, and findings were assessed using integrative epigenomics methods and pathway analyses.

Results: The study identified 93 DMPs genome-wide significantly associated with eGFR, of which 35 replicated in independent samples. We also replicated 6 previously published DMPs including the ZNF20-ZNF788 locus. Identified DMPs showed significant overlap enrichment with DNAs 1 hypersensitive sites in kidney tissue, sites associated with the expression of genes in cis, and transcription factor motifs, in addition to pathways associated with kidney development. Among main findings, we identified a DMP at the KANK1 gene, which has been previously associated with podocyte dysfunction and nephrotic syndrome.

Conclusions: We identified DMPs associated with eGFR and uncovered associations with genomic regions related to regulatory function in kidney tissue. These findings shed light on epigenetic mechanisms associated with kidney function, bridging the gap between eGFR-associated DNA methylation and tissue-specific chromatin context.

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PO1630
Generation of Monogenic Candidate Genes in Humans of Nephrotic Syndrome via Three Independent Approaches
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Background: Steroid-resistant nephrotic syndrome (SRNS) is a frequent cause of chronic kidney disease in childhood. The finding of ~60 single-gene causes of SRNS, mainly through whole-exome sequencing (WES), has contributed to the understanding of its disease mechanisms. Whereas in ~12-30% of cases with onset <25yo, a monogenic cause is detected, most cases remain molecularly unsorted. This indicates that additional monogenic causes of SRNS may exist.

Methods: We generated 3 independent lists of candidate genes: 1) 63 published monogenic mouse models of nephrotic syndrome (NS) or proteinuria, obtained from stringent review of published databases and literature; 2) 64 genes, whose podocytic expression is regulated by WT1 (Lefebvre Kidney Int 88:321, 2015); and 3) a discovery set of 120 candidate genes that we generated by WES analysis of 1,382 NS families over 12 years. We first validated candidate lists 1) and 2) for overlap with 63 known human SRNS genes. We then overlapped candidate lists 1) (mouse genes) and 2) (WT1-regulated genes) with our 120 WES-derived candidate genes (3), in order to identify potential novel genes that may cause monogenic NS.

Results: Twelve of the 63 NS mouse models (1) and 5 of the 64 WT1-regulated genes (2) overlapped with the control set of 63 known human SRNS genes, indicating relevance of the 2 candidate gene lists. When we evaluated for overlap with our 120 WES-derived candidate genes, 6 overlapping mouse genes (1) and 1 WT1-regulated gene (2) overlapped with the control set of 63 known human SRNS genes, indicating relevance of the 2 candidate gene lists. When we evaluated for overlap with our 120 WES-derived candidate genes, 6 overlapping mouse genes (1) and 1 WT1-regulated gene (2) overlapped with the control set of 63 known human SRNS genes, indicating relevance of the 2 candidate gene lists. When we evaluated for overlap with our 120 WES-derived candidate genes, 6 overlapping mouse genes (1) and 1 WT1-regulated gene (2) overlapped with the control set of 63 known human SRNS genes, indicating relevance of the 2 candidate gene lists.

Conclusions: We identified 2 gene candidate sets with a set of 120 genes resulting from WES analysis in 1,382 families with NS, we identified STX38 to be a potential novel monogenic cause of NS.

Funding: NIDDK Support

PO1631
An International Cohort Study of Mutations in Renin Causing Autosomal Dominant Tubulointerstitial Kidney Disease
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Background: There have been few clinical reports of Autosomal Dominant Tubulointerstitial Kidney Disease due to REN mutations (ADTKD-REN), limiting clinical characterization.

Methods: We formed an international collaboration that identified and characterized 111 individuals from 30 families with heterogeneous REN mutations.

Results: Sixty-nine (62%) individuals had a REN mutation in the signal peptide region (signal group), 27 (24%) in the prosegment (prosegment group), and 15 (14%) in the mature renin peptide (mature group). Laboratory investigations revealed that REN signal peptide mutations prevent prosegment and translocation of the endoplasmic reticulum (ER), prosegment mutations led to abnormal deposition of prerenin and renin in the ER Golgi intermediate compartment (ERGIC), and mutations in mature renin led to deposition of prorenin and renin in the ER. Signal and presegment patients were most severely affected, often presenting at <10 years (see Table 1) with anemia, hyperkalemia, and acute and chronic kidney disease. While eGFR was approximately normal in children not receiving erythropoietin was 9.6 ± 1.1 ml/min/1.73m² and children <10 y not receiving erythropoietin was 9.6 ± 0.3 ml/min/1.73m², indicating that these patients have a likely extrarenal cause for chronic kidney disease. The serum potassium values decreased and
bicarbonate values increased in 9 patients taking fludrocortisone (4.77±0.55 mEq/L vs. 4.37±0.56 mEq/L, p<0.001) and in 5 patients with mutations in mature renin presented (20±1 with and 23±1 with AT1R) overlapped with all three candidate gene lists, i.e., the 123 RCR candidates, the 30 sRNA-seq candidates, and the 114 EIAKI candidates. Within the 8 (10) remaining candidates the strongest mutation was detected in the NEK3 gene (NIMA Related Kinase 3). By WES we had identified a homologous truncating mutation, p.N90Kfs*121, in a family of two siblings. We present data on the cell biological role of NEK3 in podocytes.

Conclusions: Utilizing two independent non-overlapping candidate lists, we established 10 potential novel candidate genes for human SNRs.

POI1634
Generating Monogenic CAKUT Candidate Genes from Existing Single-Cell Transcriptomics Data of Human Fetal Kidney

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Background: Congenital anomalies of the kidneys and urinary tract (CAKUT) are the most frequent birth defect and the most frequent cause of chronic kidney disease in the first 3 decades of life. Discovery of >34 monogenic causes of human CAKUT has helped mapping pathogenic pathways of CAKUT in humans (JASN 29:36, 2018). We hypothesized that genes specific to pathogenic pathways of CAKUT may show a temporo-spatial single-cell mRNA expression pattern in human fetal kidney tissue, and that highly expressed genes may represent novel CAKUT candidate genes.

Methods: First, we evaluated 34 monogenic human genes involved in CAKUT pathways for clustering in a temporo-spatial mRNA expression pattern by using the single-cell mRNA sequencing dataset of human fetal kidney at week 17 (Hochane, PLoS Biol 21:17, 2019 and week 16 (Lindstrom, Dev Cell 45:651, 2018). 86 novel CAKUT candidate genes were generated by Whole Exome Sequencing (WES).

Results: The evaluation of the 34 known CAKUT pathway genes showed that genes involved in the FRAS/FREM, RA signaling and BMP signaling pathways did not cluster in either mRNA dataset. However, genes involved in the pathogenesis of branchootorectal (BOR) syndrome (ETYA, SIX1, SIX2, SIX3) clustered in nephron progenitor cells (NPCs) in both datasets, which supports the hypothesis that BOR is a novel CAKUT pathway. Based on the outcome of this first step, to prioritize potential novel CAKUT genes, we then generated and overlapped two lists of independent candidate genes: i) 86 novel single CAKUT candidate genes derived from WES in 1,380 patients and ii) the 100 highest expressed genes in each NPC type a, b, c and d according to Hochane (PLoS Biol 21:17, 2019). This overlap of lists i) and ii) resulted in 20 candidate genes of interest (CHRM5, FGF15, Familin Member 19), which is therefore considered as a novel candidate gene for human CAKUT.

Conclusions: Genes of the BOR pathway are co-expressed in a temporo-spatial way and expressed in a time-specific and cell-type-specific manner throughout human renal development. Single-cell mRNA expression data from human fetal kidney can be used to prioritize WES-derived CAKUT candidate genes.

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POI1635
CHRM5 Mutations as a Potential Cause of Neurogenic Bladder

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Background: Neurogenic bladder is caused by disruption of neuronal pathways that regulate bladder relaxation and contraction. In severe cases, neurogenic bladder can lead to vesicoureteral reflux, recurrent urinary tract infections, and even chronic kidney disease and renal failure. These symptoms overlap with the manifestations of congenital anomalies of the kidneys and urinary tract (CAKUT). Animal models of bladder dysfunction suggest that neurogenic bladder can be caused by single gene mutations (PNAS96:5746, 1999). To identify novel monogenic causes of neurogenic bladder we applied whole exome sequencing (WES) to our worldwide cohort of families with CAKUT.

Results: By WES, we discovered a homozygous missense variant (p.Gln184Arg) in the CHRM5 (cholinergic receptor, muscarinic 5) gene in a patient with neurogenic bladder who presented with dysuria, incontinence, severe hydronephrosis, frequent UTI, and Down triad. The receptor CHRM5 is shown to be expressed in murine and human bladder wall. We propose CHRM5 to be involved in bladder tone regulation and that the molecular defect of our patient causes neurogenic bladder with secondary symptoms as CAKUT. This is similar to CHRN43, which we published as the first gene to cause neurogenic bladder (JHIG 105:186, 2019). Bowman et al (FISB 3.12:2003, 2018) demonstrate that Chrm5 knockout mice show symptoms of bladder overactivity. Functional studies testing the effect of the variant p.Gln184Arg on CHRM5’s receptor function are pending.

Conclusions: We identified a recessive mutation in CHRM5 as a potential cause of neurogenic bladder in humans.

Funding: Other NIH Support - R01 - DK088767

PO1632
Clinical Manifestations and Mutation Analysis of Idiopathic Renal Hypouricemia

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Background: Idiopathic renal hypouricemia (RHUC), was thought an autosomal recessive inheritance disorder, characterized by impaired uric acid (UA) reabsorption in the proximal tubule and subsequent profound hypouricemia, caused by mutations in SLC22A12 or SLC2CA9. Most cases of RHUC were reported in Japan, only a few have been detected in China. A retrospective analysis was performed in this study to report the clinical manifestations and genetic information of RHUC patients in China.

Methods: The medical history, clinical manifestations, biochemical and genetic data, clinical outcomes of Chinese patients with RHUC were collected in this study.

Results: Seven male and two female patients were diagnosed with idiopathic RHUC according to the criteria: serum uric acid(SUA) >6.0 μmol/L, fractional excretion of uric acid (FEUA) >10%, and exclusion of other diseases that present hypouricemia as a symptom. The median age of onset were 30 (11–48) years old. The median levels of SUA was 83 (50–74) μmol/L, the median FEUA was 29(11.5%–346.83%). Homozygous SLC24A12 mutations were identified in two male patients, heterozygous mutations in SLC22A12 in two patients, compound heterozygous mutations in SLC22A12 in one patient, heterozygous mutations in SLC22A12 in four patients. Exercise-induced acute kidney injury (EIAKI) developed in six patients, including the two patients with mutations in SLC24A12, the patient with compound heterozygous mutations in SLC22A12, one patient with homozygous mutations in SLC22A12, two patients with heterozygous mutations in SLC22A12. The two female patients were asymptomatic and the patients with EIAKI were all male. Two patients with heterozygous mutations in SLC22A12 had nephrolithiasis. Two patients had nephrolithiasis and subsequent profound hypouricemia, caused by mutations in SLC22A12.

Conclusions: SLC22A12 mutations were more common than SLC2CA9 mutations in Chinese patients with RHUC. EIAKI only developed in male patients. Heterozygous mutations in SLC22A12 also resulted in hypouricemia. The prognosis of RHUC was favorable.

Funding: Government Support - Non-U.S.

PO1633
RhoA-Rac1-CDC42 Regulators as Candidates for Monogenic Nephrotic Syndrome

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Background: Steroid resistant nephritic syndrome (SRNS) frequently causes chronic kidney disease in children. 58 monogenic SRNS genes are known to cause 11%-29.5% of SRNS in children. These genes map to 12 distinct pathogenic pathways, including Rhos-Rac1-CDC42 regulators (RCRC). Genetic data indicate that many additional monogenic SRNS genes exist.

Methods: To search for additional monogenic SRNS genes, we generated two lists of independent functional candidate genes: i) 123 genes involved in the RCR pathway, which has been implicated in the pathogenesis of nephritic syndrome (Nat Commun 9:1960, 2018), and ii) 30 genes from a single-cell RNA sequencing (sRNA-seq) dataset (JASN 29:2060, 2018).

Results: First, we validated the candidate status of both candidate lists by overlapping them with the 58 known SRNS genes, 12 of the 123 RCR candidates from list i) overlapped with the 58 known SRNS genes (20.6%). Likewise, of the 30 genes from list ii) that were most strongly expressed in podocytes (sRNA-seq), 9 overlapped (30%) with the 58 known SRNS genes (15.5%), thereby validating both functional candidate lists as relevant for SRNS pathogenesis. We then evaluated for overlap of both candidate gene lists [list i) RCR and list ii) sRNA-seq] with 114 candidate gene lists that we identified by whole exome sequencing (WES) in 1,382 families. We found that 10 RCR candidates (8.1%) overlapped with the 114 WES candidates (8.7%). Interestingly, 2 genes (CHRNA5 and CHRNA4) overlapped with all three candidate gene lists, i.e., the 123 RCR candidates, the 30 sRNA-seq candidates, and the 114 WES candidates. Within the 8 (10) remaining candidates the strongest mutation was detected in the NEK3 gene (NIMA Related Kinase 3). By WES we had identified a homologous truncating mutation, p.N90Kfs*121, in a family of two siblings. We present data on the cell biological role of NEK3 in podocytes.

Conclusions: Utilizing two independent non-overlapping candidate lists, we established 10 potential novel candidate genes for human SNRS.
Whole-Exome Sequencing Reveals a Monogenic Cause of Disease in 23.1% of 276 Families with Steroid-Resistant Nephrotic Syndrome

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Background: Steroid-resistant nephrotic syndrome (SRNS) overwhelmingly progresses to end-stage renal disease. To date, more than 59 monogenic genes have been identified to cause SRNS. We previously detected causative mutations in whole exome sequencing (WES) and in several SRNS patients with SRNS using targeted panel sequencing (Sadowski JASN 13:53, 2018) and in 29.5% of patients with SRNS using targeted panel sequencing (Sadowski JASN 26:1279, 2015). However, whole exome sequencing (WES) has become more accessible, with the advantage of detecting not only known monogenic causes of SRNS, but also novel candidate NS-causing genes.

Methods: We employed whole exome sequencing (WES) to detect monogenic causes of SRNS in a large international cohort of 276 families with nephrotic syndrome (NS).

Results: Samples were recruited from April, 1998 to December, 2018 (21 years). WES was performed at the Yale Center of Mendelian Genomics. First, we examined the WES data for mutations in 59 known genes to cause SRNS. In 64/276 families (23.1%), we identified mutations in 22 of the known genes. There were also 7 genes that were identified as phenocopies of, e.g., COL4A3. In 42 families (15.2%), we have identified mutations in a potential novel candidate gene for SRNS. We found a 39.5% solve rate in consanguineous individuals and 10.8% solve rate in non-consanguineous individuals, recapitulating similar solve fractions to what has been previously published (Sadowski 2015; Warezko 2017).

Conclusions: This study confirms that in ~23% of families in our cohort, NS is due to monogenic causes. WES is a viable way to diagnose the underlying cause of NS in children and young adults, and to suggest novel monogenic candidate genes of NS.

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Recovery from Dialysis in Responsive Primary Hyperoxaluria Type 1 (PH1) Patients After Initiation of Pyridoxine

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Introduction: PH1 is a genetic disorder characterized by hepatic overproduction of oxalate and eventual end-stage kidney disease (ESKD). The only established treatment to reduce hepatic oxalate production is the use of pharmacologic doses of pyridoxine in responsive patients including those with G170R mutations, though emerging therapies to block specific hepatic enzymes are under clinical trial and appear promising. However, whether reducing oxalate production can result in recovery of kidney in a subset of patients with advanced chronic kidney disease (CKD) is unknown. Here we report a series of three G170R homozygous patients with ESKD who experienced recovery of kidney function that allowed dialysis discontinuation following treatment with pyridoxine.

Case Description: Data from the Rare Kidney Stone Consortium PH Registry was reviewed. Among the 41 G170R homozygous patients, 23 progressed to ESKD, including those who are the subject of this report. Median age at initiation or resumption of pyridoxine treatment following ESKD among these 23 patients was 37 years (range 20-53), POx was 8.8 mg/kg/d (range 6.8-14.0 mg/kg/d). Median duration of dialysis prior to renal recovery was 10 months (range 5-19). Plasma oxalate (POx) improved after recovery of renal function even while still on dialysis. At a median of 3 months (range 2-46) following discontinuation of dialysis, estimated glomerular filtration rate was 34 ml/min/1.73 m2 (range 23-52), POx was 8.8 mmol/L (range 6.8-14.0 mg/kg/d). Kidney function was maintained during a median of 3.2 years (range 1.3-8.3) of follow-up.

Discussion: Our findings challenge the conventional wisdom that ESKD in PH1 is always irreversible. Rather, in selected PH cases advanced CKD could potentially be reversed if hepatic oxalate production is reduced promptly after dialysis initiation. Thus new or emerging treatments may prevent the need for kidney transplantation in a subset of PH1 patients, even after ESKD ensues.

Baseline characteristics of G170R homozygous PH1 patients who recovered renal function after treatment with pyridoxine

APOL1 Risk variant frequencies by study region

APOL1 Cytotoxicity Is Variant and Dose Dependent

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Background: Two coding renal risk variants (RRVs) of APOL1 gene (G1 and G2), are associated with large increases in chronic kidney disease (CKD) rates among populations of recent African descent, but the underlying molecular mechanisms are unknown. In vitro mammalian cell cultures models are widely used to study cytotoxicity of RRVs, but results have been contradictory. It remains unclear whether cytotoxicity is RRVs dependent or driven solely by variant-independent overexpression. It is also unknown whether the reference APOL1 allele, G0 could prevent cytotoxicity of RRVs.

Methods: We generated tetracycline-inducible APOL1 expression in HEK293 cells and examined the effects of increased expression of APOL1 (G0,G1,G2, G0G0,G0G1 or G0G2) on known cytotoxicity phenotypes including reduced cell viability, increased cell swelling, cellular potassium loss, aberrant protein phosphorylation, and dysregulated energy metabolism. Furthermore, whole genome transcriptome analysis was performed to discover deregulated canonical pathways.

Results: At moderate expression, RRVs but not G0 caused cytotoxicity. RRVs-induced cytotoxicity is dose-dependent and is not reduced by co-expression of G0. RRVs also have dominant effects on canonical pathways relevant for cellular stress response.

Conclusions: In HEK293 cells, RRVs have dominant gain-of-toxic function that worsens with increasing expression. These observations suggest that high steady state levels of RRVs may underlie cellular injury in APOL1 nephropathy, and that interventions that reduce RRVs expression in kidney compartments may be effective for mitigating APOL1 nephropathy.

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Underline represents presenting author.

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PO1640
Mapping the Genetic Susceptibility of HIV-Associated Nephropathy in a Mouse Model
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Background: We studied the genetic determinants of nephropathy in HIV-1 transgenic (Tg) mice, a model that displays all the clinical and molecular signatures of collapsing FSGS. On the FVB/N background over 80% of the Tg-FVB mice develop significant glomerulosclerosis, however F1 hybrids with both inbred strains of mice demonstrate variable penetrance from completely resistant to highly sensitive.
Methods: Tg-FVB mice were crossed with 20 different inbred strains of mice to generate F1 hybrids. At 8 weeks of age, we evaluated the severity of nephropathy by histology, BUN, and proteinuria, hematuria and NGAL was analyzed in the urine. To map loci predisposing to HIVAN, we performed a GWAS using a mixed linear model method.
Results: Six strains (AJ, C3H/HeJ, DBA/1J, KK/J, WSB/EiJ, and LP/J) were highly sensitive to the Tg resulting in severe glomerulosclerosis, 9 strains (129S1/SvImJ, Balb/CJ, C57BL/6J, C57BL/6NJ, C57BL/10J, C3H/HeJ, C578/J, CAST/EiJ and NZB/BINJ) were resistant to the Tg resulting in limited to no glomerulosclerosis, and 5 strains were (CBA/J, DBA/2J, NOD/ShiLtJ, NZO/HlLtJ and FVB/NJ) had intermediate glomerulosclerosis. The glomerulosclerosis score correlated with the presence of casts, interstitial fibrosis and tubular atrophy, interstitial inflammation, proteinuria, elevated plasma BUN, and the detection of urine NGAL. A GWAS searching for haplotype distribution patterns that matched the high/low strain sensitivity pattern identified a genome-wide signal on Chr 13 within a previously known QTL for HIV AN. The interval contains Snhp2, encoding a DNA binding protein that stabilizes transcriptional complexes to prevent proteasomal degradation. Snhp2 is highly expressed in podocytes.
Conclusions: Our data demonstrates differences the susceptibility of inbred strains to the HIV-1 transgene and suggest Snhp2 as a culprit in producing susceptibility to HIVAN in the mouse. Future studies will evaluate the role of Snhp2 in vitro and in Snhp2 null mice.
Funding: Other U.S. Government Support

PO1641
One Disease Cannot Exclude the Other: The Coexistence of IgA Nephropathy and Alport Syndrome
Introduction: Alport syndrome and IgA nephropathy (IgAN) have shared clinical characteristics such as persistent hematuria, proteinuria, and progressive renal failure. We describe a case that histologically was diagnosed as IgAN, genetic testing and segregation analysis confirmed the coexistence of Alport. The additional diagnosis came to light when the daughter, a kidney donor candidate presented with persistent microscopic hematuria (MI).
Case Description: A 61-year-old female with diabetes, hypertension and ESRD presented for evaluation of transplant candidacy. The patient was diagnosed with IgAN after a biopsy at age 50. A second biopsy at the age of 61 years, showed granular mesangial and para-mesangial IgA staining, foot process effacement and irregular thickening of the glomerular basement membrane (GBM). Her daughter presented for evaluation as a live kidney donor and reported MI. She had normal renal function and imaging. Cystoscopy, and urine cytology were negative. To evaluate the hematuria further, her mother was first screened with a renal genetic panel, KidneySeq™ which demonstrated a likely pathogenic variant in the COL4A3 gene, c.361 G>A, p. Gly121Ser. The donor underwent focused screening and was positive for this familial variant. Subsequently obtained FH revealed that a maternal aunt had early onset deafness, and another had CKD. The donor’s daughter was found to have MI. The results suggested that both the transplant candidate and her daughter had a genetic diagnosis consistent with Alport type nephropathy.
Discussion: Pathogenic or likely pathogenic variants in COL4A3 and COL4A4 cause FSGS and AR and AD Alport syndrome. Up to 50% of causal variants are a substitution of glycine in the Gly-X-Y repeat sequence disrupting the triple helical structure of the collagen IV α3(B3) chain causing anomalies in the GBM. Hematuria due to these variants may also manifest with thin basement membrane disease. In this transplant candidate with IgAN and GBM abnormalities, the relative contribution of the COL4A3 variant to her CKD cannot be ascertained. Consequently, the daughter’s long-term renal outcome cannot be predicted. The co-existence of both IgAN and Alport syndrome is rarely described in the literature and the importance of the consideration of genetic renal disease is emphasized here in the context of living donor safety.

PO1642
Discovery of Genetic Modifiers in Thin Basement Membrane Nephropathy (TBMN) by Using Pedigree-Based Whole-Exome Sequencing
Background: TBMN is caused by heterozygosity in COL4A3 or COL4A4, and is the carrier state of autosomal recessive Alport syndrome (ARAS). TBMN is less severe than ARAS, but its phenotype can range from asymptomatic microscopic hematuria and/or grade proteinuria, focal segmental glomerulosclerosis, to end-stage renal disease (13-25% in patients >60 years). The cause of phenotypic heterogeneity in TBMN is unknown. Previously, we found an autosomal dominant pattern of transmission of isolated microscopic hematuria and low-grade proteinuria in two large pedigrees in Utah with ARAS, which led us to hypothesize that genetic modifiers may affect the severity of TBMN.
Methods: Based on pedigree analysis, 64 participants from two large families with characterized COL4A3 mutation were recruited for WES. In order to identify candidate disease-modifying genes, we filtered the VCFs to identify variants (pVAAST) (pVAAST) a probabilistic algorithm for disease gene prioritization that uses pedigree information to perform linkage analysis. Candidate modifying genes were analyzed using Phevor, an algorithm that performs reprioritization based on information about phenotype, gene function, and disease.
Results: We found 17 candidate modifier genes that co-segregated with hematuria, proteinuria and renal dysfunction (Figure). Of note, GRIP1 co-segregated with the Alport allele, hematuria, proteinuria, renal dysfunction (P=9.4E-04), and had a high biologic correlation score (Phevor score=4.1).
Conclusions: GRIP1 is involved in cell adhesion to extracellular matrix proteins, crucial for kidney morphogenesis, and compound heterozygosity in GRIP1 causes renal agenesis and Fraser syndrome. Whole-exome sequencing in large pedigrees reveal 17 candidate disease-modifying genes in TBMN. Validation studies will be needed to ascertain their role in TBMN.
Funding: Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1644
Extreme Rare Variants in Four Complement Genes Contribute to Genetic Susceptibility to Atypical Hemolytic and Uremic Syndrome

Armance Assil, Julia Mezzadri, Yoann Robert, Sarah Noguez, Nisreen Al-Tamimi, et al.

PO1645
Whole-Exome Sequencing Identifies Likely Causative Variants in Four Candidate Genes in 16 Families with Spina Bifida

Chunjie Wang, Wei Chen, Xiaofei Wu, et al.

PO1646
Results from the Ongoing Phase 2 Open-Label Extension Study of Lumasiran, an Investigational RNAi Therapeutic, in Patients with Primary Hyperoxaluria Type 1 (PH1)

Sally B. Hultin, Julie Arthurs, et al.
 Genome-wide Association Study of Lupus Nephritis in Chinese Han Population

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Background: Lupus nephritis (LN) is one of the most common and serious complications of systemic lupus erythematosus (SLE). The genetic factors play a vital role in the pathogenesis of LN. The purpose of this study was to screen for susceptible variants of LN in Chinese Han populations in whole genome.

Methods: A genome-wide association study (GWAS) was performed in 592 LN patients and 453 SLE patients without LN. Fifty-six single nucleotide polymorphisms (SNPs) in 34 loci were selected for replication in independent cohort of 188 LN and 171 SLE without LN patients. Besides, gene-based analysis of selected loci was performed in the enlarged population (2336 LN and 2466 SLE without LN patients) based on exome Asian array data.

Results: We identified 9 SNPs suggesting a correlation with LN (P<10^-6). The most significant SNP was rs12606116 (18p11.32) with P=6.75×10^-9. The rest SNPs were rs11826924 (11p15.2, INSC), rs10151371 and rs17124022 (14q31.3, GPR65), rs10455744 (9p21.4, CD274), rs203359 and rs435091 (12q24.23, CFI), rs7157731 (14q23.2, WDR25), rs2372192 (5p14.1, MAGI1). Gene-based analysis results showed 11 suggestive LN related genes in 11 loci (P<0.05): GPR139 (16p12.3), TH (11p15.5), TGM1 (14q32.2, WDR25), rs2372192 (3p14.1, MAGI1). Gene-based analysis results showed 11 suggestive LN related genes in 11 loci (P<0.05): GPR139 (16p12.3), TH (11p15.5), TGM1 (14q32.2, WDR25), rs2372192 (3p14.1, MAGI1). Gene-based analysis results showed 11 suggestive LN related genes in 11 loci (P<0.05): GPR139 (16p12.3), TH (11p15.5), TGM1 (14q32.2, WDR25), rs2372192 (3p14.1, MAGI1).

Conclusions: Association Analysis of LN was performed in Chinese Han SLE patients for the first time. Multiple susceptible genes were identified moderately associated with LN which may advance our understanding of the genetic basis of LN.

Funding: Government Support - Non-U.S.

PO1649

Copy Number Variation Analysis Increases Diagnostic Yield of Exome Sequencing and Sequences the Identification of Genetic Causation for Congenital Anomalies of the Kidneys and Urinary Tract (CAKUT)

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Background: Congenital anomalies of the kidneys and urinary tract (CAKUT) are the most common cause of chronic kidney disease in children and adults under the age of 30 years. In a previous study, we detected by whole exome sequencing (WES) a causative mutation in a known gene for isolated or syndromic CAKUT in 13% of 232 families with CAKUT (JASN 29:2348, 2018). However, WES will not detect the presence of causative copy number variations (CNV), and CNVs have been detected in up to 16% of CAKUT (AJHG 9:987, 2012).

Methods: We performed a genome-wide single nucleotide polymorphism (SNP)-based CNV analysis on the same cohort of 232 families with CAKUT in which we previously conducted WES analysis (JASN 29:2348, 2018). We evaluated the CNVs with the published predefined criteria (Nat Genet 51:957, 2019).

Results: In a subcohort of 170 families of the 232 family CAKUT cohort (JASN 29:2348, 2018) in whom sufficient DNA was available, we detected in 9 families (5.29%) a pathogenic CNV known to cause CAKUT. There was no competing variant by genome-wide CNV analysis, and there was no conflicting variant by WES analysis. In addition, we identified likely pathogenic CNVs in 1.76% of cases, potentially increasing the CNV diagnostic rate to 7.05%.

Conclusions: CNV analysis in this subcohort of 170 CAKUT families increased the diagnostic rate for genetic causes of CAKUT from 13% to 18% - 20%. We also identified three candidate loci that may cause CAKUT.

PO1650

Genotyping of Renal Transplant Patients

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Background: There is an increasing recognition that though individual inherited kidney diseases are rare, when considered as a single cohort inherited forms of kidney disease may account for up to 10% of CKD. This can have implications for potential living kidney donors who are often related to the recipient and at higher lifetime risk of kidney failure. We sequenced patients undergoing renal transplantation to assess what proportion of kidney failure was caused by monogenic kidney disease.

Methods: We identified adult patients undergoing living or deceased renal transplantation. We excluded those with pauci-immune vasculitis, systemic lupus erythematosus, drug-induced causes and those with renovascular kidney disease over the age of 50. Patients underwent targeted next generation sequencing using a custom panel of 127 genes known to cause renal disease. All suspected disease-causing variants were classified by American College of Medical Genetics guidelines and discussed by a multidisciplinary team(KB1).

Results: We sequenced 99 patients who presented for renal transplantation. We were able to detect an ACMG-classified pathogenic/likely pathogenic variant in 27 (26%) patients. The most common disease-causing variant identified was in PKDI, which was identified in 14 patients (14%), accounting for 52% of all individuals with a disease-causing gene identified. Four others (16%) had pathogenic variants in COL4A4 or COL4A5 genes. No other disease-causing variant was present in more than one individual.

Conclusions: It is possible to identify monogenic causes of kidney disease in a carefully selected population with ESRD, and this may be useful in stratifying risk in potential living renal donors.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1651

21%-51% of a Single-Center, 15-Year Cohort of All Patients with ESKD Prior to the Age of 50 Have Monogenic Kidney Disease
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Background: Often only CKD patients with high likelihood of genetic disease are offered genetic testing. Early genetic testing could obviate the need for kidney biopsies, allowing for adequate prognostication and treatment. To test the viability of a ‘genetics first’ approach for CKD, we performed genetic testing in a group of renal transplant recipients <50 years, irrespective of cause of transplant.

Methods: From a cohort of 273 transplant patients, we selected 110 that were in the UMC Utrecht, had DNA available and were without clear-cut non-genetic disease. Forty patients had been diagnosed with a genetic disease prior to enrollment, in 70 patients we performed a whole exome sequencing based 379 gene panel analysis.

Results: Genetic analysis yielded a diagnosis in 51%. Extrapoloated to the 273 patients, who did not all fit the inclusion criteria, the diagnostic yield was still 21%. Retrospectively, in 43% of biopsied patients the kidney biopsy would not have had added diagnostic value if genetic testing had been performed as a first tier diagnostic.

Conclusions: The burden of monogenic disease in transplant patients with ESKD of any age prior to the age of 50 is 21-51%. Early genetic testing can provide a non-invasive diagnostic, impacting prognostication and treatment and obviating the need for an invasive biopsy. We conclude that in patients who one expects to develop ESKD prior to the age of 50, genetic testing should be considered as first mode of diagnostics.

PO1652

Genome-Wide Analyses Provide Insights into the Genetic Architecture of Kidney Function and CKD Among Hispanics in the Million Veteran Program
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Background: Hispanics (HAs) have a higher risk of progressing to end-stage renal disease (ESRD) than non-Hispanic Americans. Genetic variants influencing kidney function are known to be identified through genome-wide association studies (GWAS) of CKD and ESRD, as well as estimated glomerular filtration rate (eGFR), however, small sample sizes have stalled discovery in the Hispanic population.

Methods: We performed a GWAS of eGFR in 32,821 Hispanics from the Million Veteran Program (MVP); eGFR was estimated using the CKD-EPI equation with IDMS calibrated creatinine. Patients on dialysis, transplant recipients, or with BMI <18 kg/m² were excluded. eGFR was regressed on to common genetic variants (minor allele frequency > 1%) imputed to the 1000 Genomes reference panel adjusted for age, sex, BMI, and the top ten principal components. Analyses were performed by strata of diabetes, estimates from which were aggregated with fixed-effects meta-analysis.

Results: A total of 397 SNPs representing 8 loci exceeded genome-wide significance. The most significant association was at a previously known locus, SULT1A1 on chromosome 5 (p-value = 3.78E-10). Two novel loci were detected. One in SLC34A4 (rs2643718 p-value = 4.51E-15) a protein-coding gene for zinc transmembrane transporter, and another one on (rs3600563 p-value = 5.49E-7) a protein-coding gene for alpha-enolase. The most significant association was at a previously known locus, APOL1 (rs6029573 p-value = 9.82E-15). Two novel loci were detected. One in LAMA5 (rs1270509 p-value = 2.22E-10) and ALM (rs1271588 p-value = 4.14E-10). Several additional important CKD loci were associated with kidney function at p-values below the genome-wide threshold including: APOA1 (rs3092573 p-value = 2.98E-10), TTR (rs3080563 p-value = 5.49E-10), SHROOM3 (rs10529470 p-value = 1.30E-10). Five of the variants that reached genome-wide significance were non-coding variants.

Conclusions: Our study results emphasize the transethnic nature of genetic variation contributing to kidney function. Overall, this is the largest GWAS of eGFR in Hispanics to date, which replicates previously identified loci in tranethnic analysis and detects two novel loci in Hispanics.

Funding: Veterans Affairs Support

PO1653

Assessing Alport Syndrome and Thin Basement Membrane Nephropathy (TBMN) by Optical Coherence Tomography (OCT)
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Background: Using OCT to identify temporal macular thickening has diagnostic importance in patients with X-linked Alport syndrome (XLAS) but little prior research has been done to evaluate temporal macular thickening in COL4A3 and COL4A4 compound heterozygotes (ARAS) and simple heterozygotes. (TBMN) Individuals with heterozygous COL4A3 or COL4A4 mutations usually have TBMN, which is considered the carrier state of autosomal recessive Alport syndrome (ARAS). The aim of this study is to assess ophthalmologic findings in simple and compound heterozygotes and to compare them to normal control and XLAS.

Methods: Genotyping was done to detect COL4A3 and COL4A4 mutations and to classify family members as ARAS, TBMN or normal. Temporal thinning index (TTI) was calculated from OCT measurements of the more severely affected eye by comparing the ratio of the retinal thickness of the temporal (T) to the nasal (N) subfields with a published normative database. (Figure, y axis) Student’s T-test and ANOVA were used to identify binary and multiple groups’ differences. In addition, multivariate linear regression was performed controlling for age, gender and interaction terms between different variables.

Results: We report results from 12 normal controls, 16 COL4A3 or COL4A4 simple heterozygotes, 7 compound heterozygotes and 18 hemizygous males with XLAS. Mean TTI was 5.75, 7.4, 9.45 and 9.37 in these four groups, respectively, TTI in each group (simple heterozygotes, compound heterozygous, and XLAS) was significantly greater than normal controls (P < 0.01). TTI was not significantly different between simple and compound COL4A3/4 heterozygotes (P = 0.13). Age, gender, and GFR were not associated with significant differences in the regression analysis.

Conclusions: This is the largest study that systematically assessed ophthalmologic findings in XLAS, ARAS and TBMN. OCT may guide our evaluation of family members who are potential donors.

Funding: Private Foundation Support

PO1654

LAMA5 Gene Mutations in Japanese Cases with Infantile Nephrotic Syndrome
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Background: Steroid resistant nephrotic syndrome (SRNS) have high risks to progress to end stage renal disease. Mutations in genes encoding podocyte-associated proteins have been implicated in about 30% of SRNS cases in children. Recently, LAMA5 gene mutation have been identified in patients with nephrotic syndrome. The LAMA5 gene encodes laminin-ε5, an essential component of the glomerular basement membrane. Here, we report the three cases with LAMA5 gene mutations.

Methods: We conducted comprehensive gene screening of Japanese patients with severe proteinuria. Using targeted next-generation sequencing, 60 podocyte-related genes were screened in 326 unrelated patients with proteinuria.

Results: LAMA5 gene variants were detected in two families. The patient 1 and 2 were siblings. They presented with proteinuria at ages three months and four months, respectively. They were subsequently found to have compound heterozygous mutation for LAMA5 gene (NM_005560). One was nonsense mutation (c.9322C>T, p.Arg3077Ter), and the other was splice site mutation (c.1282+1G>A). The patient 3 presented with proteinuria in 6 months old. She had congenital cataract and hypoplastic kidney. Her renal pathology showed remarkable irregular form of glomerular basement membrane. She was subsequently found to have compound heterozygous mutation for LAMA5 gene: c.1282+1G>A (p.Arg3077Ter), c.1282+1G>A. We performed immunofluorescence analysis of laminin ε5 and her renal pathology showed completely negative staining pattern.
PO1655

Variation in Phenoype in Utah Families with Autosomal Recessive Alport Syndrome
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Background: Individuals with heterozygous COL4A3 or COL4A4 mutations usually have thin basement membrane nephropathy (TBMN), which is often considered the carrier state of autosomal recessive Alport syndrome (ARAS). Patients with ARAS usually progress to end-stage renal disease (ESRD) by the fourth decade of life. While ocular abnormalities, hearing loss and renal impairment are classically absent with TBMN, a subset of patients develop focal segmental glomerulosclerosis (FSGS) and 13-25% of patients progress to ESRD. It is unclear why some individuals with heterozygous COL4A3 mutations follow a milder course with isolated microscopic hematuria or low-grade proteinuria while others with the same mutations develop progressive renal dysfunction. It is also unclear why some family members show hematuria while others with the same mutation do not.

Methods: This study was designed to address these clinical questions using unbiased Whole Exome Sequencing (WES) in a population of patients harboring a limited number of pathogenic heterozygous COL4A3 mutations. Our work has focused on detailed examinations of patients carrying the same mutation to assess carefully the inter and intrafamilial variability and assess the impact of mutation on pathology.

Results: Two Utah families (figure) with a unique combination of two pathogenic mutations were identified. These pathogenic mutations have been reported before. However, the compound heterozygous status in each family is unique and has not been reported before. The probands are compound heterozygotes sharing one mutation (c.2085G>A, p.Gly695Arg) but differ in the second mutation (c.4981C>G, p.Arg1661Cy s>c.4421T>C, p.Leu1474Pro).

Conclusions: This study expanded the phenotypic spectrum of COL4A3 mutation carriers. Our findings showed the significant overlap between phenotypes induced by COL4A3 variants and the considerable intra and inter-familial variability and renal disease progression in patients with COL4A3 mutations.

Funding: Private Foundation Support

PO1656

Whole-Exome Sequencing as a Predictive Tool for Severe CAKUT
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Background: Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) represent about 1% of births, with about 20% secondary to genetic causes. The Cincinnati Fetal Center is one of the few centers worldwide offering fetal interventions including amnioinfusion and for infants with oligo/anhydramnios. As these infants are phenotypically severe, we predict they will be genetically enriched. We hypothesize that identification of rare genetic variants in infants with CAKUT will aid in determination of clinical course and improve parental counseling.

Methods: We collected blood from infants whose mothers underwent fetal interventions for oligo/anhydramnios for the purpose of Whole Exome Sequencing as well as blood samples from parents for trio testing.

Results: We collected blood from 2 singletons and 1 maternal sample. Both patients' mothers underwent multiple amnioinfusions, and the patients required initiation of RRT within week 1 of life. In both patients, we identified a nonsynonymous SNV of HSPG2 on chromosome 1. HSPG2 encodes for perlecan, which has a role in renal embryogenesis, specifically the maturation of the epithelial and mesenchymal tissues of the kidney. We identified a rare heterozygous variant found in 0.28% of the population in 1 patient. In the other patient, we identified 2 variants, which form a state of compound heterozygosity. We found a rare heterozygous nonsynonymous SNV mutation in T-box Transcription Factor-18 (TBX18) in 1 sample. TBX18 is imperative for the development of ureteric mesenchyme and is expressed in the renal capsule and glomerular mesangial cells. This patient had bilateral VUR and dysplastic kidneys. The other patient had a rare heterozygous nonsynonymous SNV in the transcriptional repressor GLI3 which is implicated in renal morphogenesis. Variants in GLI3 have been described in renal dysplasia and aplasia. This patient was born with bilateral multicystic dysplastic kidneys.

Conclusions: In our pilot data of WES of 2 singletons and 1 maternal sample, we resequenced candidate genes, HSPG2, TBX18, and GLI3, all of which are necessary for renal and urinary tract development, specifically glomerular and ureteric development and transcriptional regulation. In a small cohort, we demonstrate that WES of a severely affected population provides insight into the molecular mechanisms underlying CAKUT, which can aid in prognosis and parental counseling in the future.

Funding: Other NIH Support - T32 Training Grant

PO1657

Perceived Clinical Utility and Barriers to Genetic Testing in the Adult CKD Population: A Survey of General Nephrologists
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Background: Genetic testing for chronic kidney disease (CKD) can lead to personalized medicine, family planning opportunities, and living kidney donor screening.1 Comprehensive genetic testing in CKD patients with a suspected genetic cause or predisposition is important for accurate diagnosis.2 However, the uptake of genetic testing among nephrologists is still low.3,4 There exists a lack of information on barriers perceived by nephrologists on genetic testing. This survey aims to understand the current barriers and perceptions to performing genetic testing for kidney disease in a general nephrology setting. We describe here in brief the survey design and preliminary results.

Methods: An online, multiple choice survey was sent to 400 general nephrologists in clinical practice to elicit feedback on the use of genetic testing in clinical nephrology care. The questions focused on perceived clinical utility and potential barriers to ordering genetic testing.

Results: Early findings suggest that while clinical utility is acknowledged in many situations, there are opportunities to provide physician education regarding test results and insurance coverage that may increase test adoption. The perceived lack of genetic counseling resources and ethical concerns may inhibit the ordering of genetic testing in patients with CKD. We will present results from the complete dataset of responses to this survey of practicing general nephrologists and provide insights into their concerns about ordering genetic testing.


PO1658

Is There a Contribution of Genes Involved in Hereditary Nephropathies to AKI?
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Background: The diagnosis of hereditary kidney disease has been improving with the use of novel diagnostic tools in the last decades. More than 600 genes have been detected using techniques such as whole exome sequencing. However, it is not clear if those genes causing hereditary nephropathies have any independent contribution in the pathogenesis of acquired nephropathies.

Methods: We analyzed the kidney transcriptomic after 24 hours of acute kidney injury induced by folic acid in a murine model. In this database we evaluated if 625 genes described as responsible for hereditary nephropathies were expressed significantly. Later, using transcriptomic databases of human nephropathies (Nephroseq), we evaluated the correlation between those differentially expressed genes and glomerular filtration. Using the software Gorilla, a functional enrichment analysis was done. Some of those were validated in our laboratory using RT-PCR.

Results: Among 23501 genes, 7443 (29.7%) were found to have a significant modification in their expression in AKI (p<0.05). When analyzing 625 responsible for hereditary nephropathies, we identified 615 in our database. 260 (41.6%) of those genes were differentially expressed in our model. An association between 241 of those 260 differentially expressed genes and glomerular filtration rate in human nephropathies was identified. The most enriched GO process were “complement activation”, “protein activation”, “cellular response to chemical stimulus”, “cellular response to stress” and “RNA processing”. 7 of the 241 mentioned genes, showed changes greater than twofold. On the other hand, 18 of the 241 showed more than a half-fold change. We have validated the expression of 2 of those genes in acute kidney injury (AKI) induced by folic acid in a murine model. In this database we evaluated if 625 genes described as responsible for hereditary nephropathies were expressed significantly. Later, using transcriptomic databases of human nephropathies (Nephroseq), we evaluated the correlation between those differentially expressed genes and glomerular filtration. Using the software Gorilla, a functional enrichment analysis was done. Some of those were validated in our laboratory using RT-PCR.

Conclusions: Several genes responsible for familiar nephropathies are differentially expressed in acquired nephropathies, suggesting that they could play a role in its
pathogenesis, through complement activation, protein activation of immune response and the development of the RCCs. The identification of those genes shows a more significant change will allow us to select candidates for further studies and new possible therapeutic targets in kidney damage.

Funding: Clinical Revenue Support

PO1659

Features of Hereditary Nephropathy with COQ8B Mutation

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Background: Mutations in the genes related to biosynthesis of Coenzyme Q (CoQ8B, ubinuine) cause primary CoQ8B deficiency resulting in various clinical phenotypes. COQ8B referred to as ADCK4 has been first reported in association with nephropathy in 2013, and previously a Korean cohort has reported six patients, notably accompanied by medullary nephrocalcinosis in all the six cases. Because these patients can benefit from COQ8B replacement, early differential diagnosis is essential. This study systematically reviewed clinical features and genotypes of patients with COQ8B-associated nephropathy.

Methods: Electronic databases were searched using related terms (till March 30, 2020) and our report adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.

Results: From 126 articles searched, there were 11 eligible studies with 49 patients with COQ8B-associated nephropathy. Of them, 26 patients were Caucasian and 21 were Asian (rest had no data regarding ethnicity). Female to male ratio was 2:1. Median age at diagnosis was 14.6 years. Proteinuria was reported in 100% of the patients with median serum albumin level of 3.7 g/dL and creatinine level of 1.45 mg/dL. Twenty two patients (43%) had chronic kidney disease and twelve patients had end-stage renal disease (23%). Transplantation was performed in 6 cases out of which 5 had no recurrence. Of 33 patients available for pathology reports, most (32/33, 97%) patients showed histology compatible with focal segmental glomerulosclerosis (FSGS) and seven (14%) patients had abnormal mitochondrial aggregation in the podocyte cytoplasm visualized by electron microscopy.

Conclusion: Seven patients were described with COQ8B associated FSGS and seven (14%) patients presented with medullary nephrocalcinosis who were notably all Koreans. Outcomes related to COQ8B replacement was reported in 14 cases and half of them reported partial or complete remission. Efficacy of calciumin inhibitors were reported in 7 cases which showed partial remission in 4 cases.

PO1660

CKD in Patients with Primary Hyperoxaluria Type 3: A Meta-Analysis from Literature

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Background: Primary hyperoxaluria type 3 (PH3) is considered the most benign phenotype of all forms of primary hyperoxaluria. Being it typical that patients with PH type 1 and 2 develop chronic kidney disease (CKD) or end-stage renal disease (ESRD), it appears to be more or less uncommon that patients with PH3 are on risk of CKD and even do not develop ESRD. We now aimed to determine the number of PH3 patients reported to have any kind of CKD.

Methods: We performed a literature meta-analysis, searching in PubMed and Embase with the following keywords: primary hyperoxaluria, PH, primary hyperoxaluria type III, PH III or PH3.

Results: We found 151 patients in 18 relevant papers published between 2010-2019. Age of diagnosis/disease onset ranged from 1 month to 48 years of life. Most of the patients suffered recurrent urolithiasis, most often during the first years of life, but recurrent kidney stone episodes were also found later in life. The most common mutations found were the c.700+5G>T splice site mutation (37%) and the p.E315del mutation (22%). In 77 patients any information was provided with regard to renal function, in 22 of those kidney function was said to be normal, but no eGFR or CKD stage was mentioned. In 25 patients kidney function was found to be normal based on eGFR levels. CKD stage 1 was reported in 21 patients, CKD stage 2 in 5 patients, CKD-3 in 2 patients and 1 patient each had CKD stage 4 or ESRD, respectively. In 10 patients, follow-up measures were available, as their data were included in two papers. In 2 patients (5 years apart from each other) and, in 1 patient eGFR significantly declined from 134 to 68 ml/min/1.73 m2, while 2 patients remained in CKD-1 and in 5 kidney function remained normal over time. In 1 patient kidney function ameliorated under standard treatment of care from CKD-1 to normal.

Conclusions: There is a massive bias in the data published, as data on kidney function is mostly not completely reported. Kidney function was normal only in 22 of the 54 patients (41%) with complete information. CKD-2 or worse was observed in 16.7% of PH3 patients, and even one patient with ESRD was described. Also, one PH3 patient had died at age 4 months because of respiratory failure and not because of PH. Thus, a long-term follow-up data is still missing, we nevertheless suspect PH3 not being as benign as currently being reported.

Funding: Commercial Support - Dicerma Pharmaceuticals, Inc.

PO1661

Segmental Expression of Nephrin in the Slit Diaphragm of a Patient with a Nonsense Mutation in NPHS1

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Background: Nephrotic syndrome due to nonsense mutations in the NPHS1 gene typically presents with a severe congenital proteinuria. However, patients harboring nonsense mutations close to the carboxyl terminus of the NPHS1 encoded nephrin protein can present with a milder phenotype. In this study, we use high-resolution microscopy to investigate the expression pattern of nephrin p.1160X in a patient with such a mutation.

Methods: We used confocal and stimulated emission depletion (STED) microscopy to visualize the distribution of nephrin p.1160X at the glomerular filtration barrier and to study the correlation between nephrin expression and foot process morphology.

Results: Confocal microscopy revealed a highly heterogeneous expression pattern of nephrin p.1160X. While most glomerular capillaries showed absence of nephrin, there were sharply defined patches with almost normal levels (see figure). To clarify whether this unexpected pattern was due to sporadic re-expression of a wild-type nephrin, we used antibodies raised against the carboxyl terminus of nephrin which is lacking in the mutant protein. These data confirmed expression of nephrin p.1160X. Moreover, qPCR and cell culture experiments indicated normal levels of nephrin mRNA, but a decreased stability of p.1160X nephrin which could partly be rescued by inhibition of proteasomes.

Conclusions: We here show, that mutations in NPHS1 may result in heterogeneous expression patterns of the truncated protein. We also found a directly observable link between insertion of nephrin in the slit diaphragm and normal foot process morphology. Taken together, these data suggest potential therapeutic interventions targeting proteasomal degradation of nephrin as a novel treatment strategy in selected patients with congenital nephrotic syndrome.

Funding: Governmental Support - Non-U.S.
Burden of Alport Syndrome in the United States: A Retrospective Observational Cohort Study Using Optum Humedica Data

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Background: To understand patient characteristics, treatment patterns and natural history of patients diagnosed with Alport syndrome (AS) in the US.

Methods: The study was a retrospective, observational cohort study of electronic health records (EHRs) in the Optum Humedica database. Patients were identified from January 1, 2008 to March 31, 2018, with 1+ outpatient encounters (at least 30 days apart) by ICD-10 code, or by ICD-9 code with at least 2 non-negative mentions of AS in the physician notes within 90 days of diagnosis. Controls were matched to cases on age, sex, and Elixhauser Comorbidity Index (excluding kidney-related comorbidities). All patients had 12 months of activity prior to the AS diagnosis.

Results: A total of 628 patients met the AS criteria; 624 were matched with 2,496 non-AS controls. Median age was 38 years (47.6% were 40 years or older) and 43% were female. At baseline, 27.4% of the AS cohort received ACE inhibitors and 11.7% with ARBs, as compared with 15.8% and 6.8% of the controls, respectively (p<0.0001 for both); 25 (4%) of the AS cohort and 2 (0.1%) of the matched non-AS cohort had a kidney transplant (p<0.0001). Baseline eGFR was significantly lower in the AS cohort (mean [sd] 54.4 [42.5] mL/min/1.73 m²) compared with the matched non-AS cohort (mean [sd] 96.7 [32.8] mL/min/1.73 m²; p<0.001). Median time to ESRD was 504 days, to kidney transplantation 786.5 days, and to death 807 days.

Conclusions: Alport syndrome has a significant unmet medical need due to the burden of kidney disease and short time to onset ESRD.

Funding: Commercial Support - Sanofi Genzyme

A Case with Somatic and Germline Mosaicism in COL4A5 Detected by Multiplex Ligation-Dependent Probe Amplification in X-Linked Alport Syndrome

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Introduction: X-linked Alport syndrome (XLAS) is a progressive hereditary kidney disease caused by mutations in COL4A5 gene encoding the type IV collagen α5 chain. To date, 11 cases with somatic mosaicism in COL4A5 have been reported; however, all of them involved single-nucleotide variations (SNVs). Copy number variations (CNVs) in COL4A5 have also been reported, and pathogenic CNVs are relatively rare. Here, we report a female XLAS patient with somatic mosaicism identified by CNVs in COL4A5.

Case Description: The case was a 35-year-old female, the mother of the proband, whose only clinical symptom was hematuria. The proband was the son of this patient. His hematuria was detected at 3 months of age, and gross hematuria was occasionally exhibited. At the age of 2, proteinuria was persisted, so kidney biopsy was performed. The pathological findings showed diffuse thin basement membrane and partial basket- weave change. Then he was conducted a gene test at the age of 4. He exhibited moderate proteinuria (0.68 g/g creatinine) and hematuria, and his serum albumin was slightly low (3.5 g/dl). He had bilateral hyperopia but no deafness or kidney dysfunction. There was no family history of ESRD. He diagnosed with XLAS by gene testing, which showed a large hemizygous deletion from exon 3 to 51 in COL4A5 detected by next-generation sequencing and then confirmed by multiplex ligation-dependent probe amplification (MLPA). Then, MLPA analysis revealed that the patient had the same deletion with only a 20% copy number reduction compared with a normal female control; she was thus diagnosed with XLAS with somatic mosaicism.

Discussion: Previous XLAS cases with somatic mosaicism in COL4A5 had SNVs, and the changes could be detected by sequencing analysis. In contrast, our case had somatic mosaicism of CNVs in COL4A5. CNVs in COL4A5 are relatively rare (5%) and, CNVs were usually detected by PCR products or MLPA. This case clearly featured a germline variant because the patient’s son exhibited XLAS. In conclusion, this is the first case report with somatic and germline mosaicism caused by CNVs in an XLAS patient detected by MLPA. This information was important for the genetic counseling of this affected family.

Phenotype Characteristics of Patients with Novel and Described COL4A5 Mutations Causing X-Linked Alport Syndrome in Croatian Population

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Background: Alport syndrome (AS) is an inherited renal disorder caused by mutations in collagen IV genes. The most common type is X-linked AS caused by COL4A5 mutations which presents as a progressive nephritis with hematuria, ultrastructural changes of glomerular basement membrane, sensorineural hearing loss and ocular lesions. Males are usually more severely affected.

Methods: We are presenting genotype-phenotype correlation for Croatian patients with X-linked AS. Next generation sequencing for COL4A3, COL4A4 and COL4A5 was performed as part of the nationwide project “Genotype-phenotype correlation in Alport syndrome and thin basement membrane nephropathy (TBMN)”. There were 24 male and 26 female patients from 36 unrelated families. Probands were selected based on the kidney biopsy findings.

Results: We have identified 23 mutations, 13 being novel and 10 previously reported. In two patients additional COL4A4 mutations were found. Male patients, median age 27 years, presented with hematuria (54%), proteinuria (54%), sensorineural hearing loss (27%) and ocular changes (4.5%). Most patients (62%) had normal, 17% mildly and 21% moderately reduced kidney function. No one had severe renal insufficiency or ESRD. Kidney biopsy was performed in 18 male patients and AS was the most common diagnosis (67%) followed by TBMN with FSGS (17%) and isolated TBMN (11%). In one patient (5%) the diagnosis was inconclusive for AS or TBMN. Female patients, median age 16 years, presented with hematuria (89%) and proteinuria (19%). There were no ocular abnormalities and the hearing loss was present in 5% of patients. Most females (73%) had normal kidney function while 8% had mild, 12% moderate, 3.5% severe reduction of renal function and 3.5% had ESRD. The kidney biopsy was performed in 14 female patients. The most common diagnosis was AS (65%) followed by isolated TBMN (21%) and TBMN with FSGS (7%). Only 1 specimen (7%) was signed out as inconclusive for AS or TBMN.
Conclusions: We have presented characteristics of 30 Croatian patients with X-linked mutations where novel combinations of mutations were noted. While renal biopsy provided information about degree and the type of renal parenchyma damage, genetic analysis is crucial for diagnosis.

Funding: Government Support - Non-U.S.

POI666
Clinomics Implementation in the Mayo Clinic Nephrology Practice

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Background: Next generation sequencing has been increasingly used to diagnose monogenic kidney diseases. In 2018, we launched the Nephrology Genetics Clinic (NGC) with a primary focus to identify the etiology of unexplained nephrotic syndrome, chronic kidney disease, or stone disease/ nephrolithiasis. An essential component of the NGC is the Genomic Odyssey Board (GOB) which consists of nephrologists, geneticists, genetic counselors, pathologists, translational ‘omics scientists, and trainees who meet at least monthly to interpret the genomics findings in the context of the patient’s clinical data. Clinical and research follow-up recommendations are made after this careful multidisciplinary review and discussion.

Methods: In 2018 and 2019, the GOB reviewed 118 cases (9 cystic, 79 glomerular, 4 C4KUT, 10 stones, 7 tubulo-interstitial (TI), and 9 other). Table 1. Genetic testing was performed with a targeted analysis of 344 kidney disease-related genes (with MUC1 variant analysis in subset of TI cases).

Results: A definite genetic diagnosis was achieved for 34 families (29%). After a multidisciplinary evaluation of variants of uncertain significance (VUS), another 16 (13.6%) were deemed to have variants likely related to the phenotype. The highest diagnostic yield was achieved in individuals with TI diseases (50%), followed by cysts (33.3%), glomerular (28.7%), C4KUT (25%), stones (20%), and others (11%). Of the unresolved/partially resolved cases, the GOB decided to pursue research activities such as trio whole exome sequencing or transcriptome sequencing for 22 (31%) families.

Conclusions: Implementation of genomic testing and analysis by a multidisciplinary team in a nephrology cohort with clinically suspected monogenic disease has provided a firm diagnosis in 29% of families, often resulting in changes in management/treatment. Ongoing research screening is likely to increase this yield.

Funding: Private Foundation Support

Table 1: Results of Genetic Analysis by Disease Group

POI667
CD11b Activation Suppresses Pro-Inflammatory susPAR in Myeloid Cells and Reduces Lupus Nephritis in Mice

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Background: Lupus nephritis (LN) is a debilitating glomerular disease and a comorbidity of systemic lupus erythematosus (SLE). CD11b, the alpha-chain of integrin (C3/14) plays a critical role in cell signaling. Several mutations in the gene ITGAM, encoding CD11b, are associated with SLE and LN, these mutations are reported to reduce integrin function. susPAR is produced by myeloid cells upon pro-inflammatory activation and is a circulating risk factor for glomerular diseases. susPAR is downstream of TLR-like receptor signaling, where TLR-activation increases susPAR levels. We previously showed that activation of CD11b suppresses TLR-dependent pro-inflammatory signaling. Here, we investigate if this mechanism includes control of susPAR levels, which provide novel therapeutic options for LN.

Methods: To investigate TLR-dependent signaling affected by CD11b activation, we utilized in vitro assays using primary macrophages and genetically engineered K562 cells expressing CD11b and CD14. K562 cells were developed to express either wild type CD11b or CD11b carrying mutations commonly found in LN patients. These cells were treated with TLR agonists or LN patient sera and level of susPAR in cell supernatants was assessed by ELISA. For complementary in vivo studies, we utilized our newly generated mouse model of lupus nephritis in which we incorporated a constitutively active CD11b point mutation (332G2) globally in mice to generate a model for CD11b activation – CD11b knock-in model. C57BL/6 wild type mice, the CD11b knock-out and the CD11b knock-in mice were used in models of SLE and LN to determine the effect of CD11b activation on circulating susPAR levels and disease in the disease.

Results: TLR-stimulation increased susPAR levels in vitro and in vivo. Importantly, CD11b activation resulted in significantly reduced susPAR levels in both systems, suggesting a novel mechanism for controlling glomerular diseases. Additional mechanistic studies are on-going to define the exact molecular mechanism of action.

Conclusions: Using these models, we have identified a possible link between CD11b activation and susPAR levels in myeloid cells. These studies will provide understanding of the influence CD11b has on signaling pathways and inflammation associated with LN.

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POI668
Drug-Induced Thrombotic Microangiopathy as a “Second-Hit” Phenomenon

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Introduction: Thrombotic Microangiopathy (TMA) syndrome is a diverse group of inherited or acquired diseases characterized by microvascular thrombosis and endothelial damage. Etiologies include drugs, thrombotic thrombocytopenic purpura, shiga toxin mediated hemolytic uremic syndrome (HUS), and complement-mediated HUS. Environmental triggers are proposed as a second hit precipitating the disease process in some cases of typical HUS. Here, we present a case of drug induced TMA in a patient with an underlying pathogenic mutation for aHUS.

Case Description: 41-year-old male with presented to an outside hospital with AKI requiring dialysis and uncontrolled hypertension. He had a positive urine toxicology and admitted to marijuana, amphetamine (crystal meth), and heroin use. Labs revealed severe anemia and thrombocytopenia, chronic kidney disease (CKD), low haptoglobin, and low fibrinogen, and schistocytes on blood smear. Shiga toxin assay was negative with normal ADAMS-TS 13 and coagulation factor. C3 was notably low at 63 mg/dL. As such, he was diagnosed with presumed aHUS and treated with steroids, eculizumab, and plasmapheresis. He was then transferred to our facility where a kidney biopsy confirmed TMA. The etiology was presumed to be drug induced, however genetic evaluation showed heterozygosity for a pathogenic variant in the Complement Factor H (CFH) gene region. Notably, his sister also carried the diagnosis of aHUS. The patient was restarted on eculizumab and remained dialysis dependent on discharge. Unfortunately, he was then lost to follow up.

Discussion: Atypical HUS is associated with a myriad of genetic mutations involving the alternate complement pathway. Pathogenic variants of CFH gene have been implicated in autosomal dominant and recessive forms of the disease. While drug use might have triggered the TMA in our patient, it is likely that his underlying mutation was the first hit creating a disease predisposition. It remains unclear how frequently a culprit mutation is present in patients with presumed drug induced TMA. However, in patients with persistent TMA and a suggestive family history, clinical suspicion for aHUS should be maintained. This distinction is important as drug discontinuation alone would be ineffective for aHUS whereas complement-blocking therapies could be potentially curative.

POI669
In Silico Prediction Performance for Type IV Collagen Variants

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Background: Advances in genomics technology and knowledge has led to increased sequencing for diagnosis, including in kidney disease. However, sequencing can reveal rare missense variants for which the relationship to disease is unclear. To address this need, in silico programs have been developed to assign variant categorization. Recently, pathogenic variants in COL4A3/4/5 have been reported to account for a significant majority of chronic kidney disease. Here we evaluate the performance of in silico programs for type IV collagen variants.

Methods: Rare COL4A3/4/5 missense variants were identified in an FSGS cohort, unscreened controls (gnomAD) and disease databases (ClinVAR, ARUP, LOVD). Comparisons between in silico predictions, disease database classifications and functional characterization were performed.

Results: In silico predictions and functional characterization classified all 9 definitely pathogenic COL4A3/4/5 variants in the FSGS cohort correctly. In silico predictions classified the majority (93-97%) of definitely pathogenic COL4A3/4/5 variants in ClinVAR, ARUP and LOVD. However, a significant proportion of benign variants were predicted as pathogenic. Thirty-five percent of COL4A3/4/5 missense variants obtained from gnomAD were also predicted deleterious. In silico predictions tended to overestimate the effects of COL4A variants of uncertain significance (VUS) when compared to functional characterization.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: Our results demonstrate that in silico programs are sensitive but not specific for vascular genetic disease and may classify rare variants. Limitations of our computational work include overestimation of in silico program sensitivity given that they have likely been used in the categorization of variants labelled as pathogenic in disease databases; and the lack of clinical data to correlate rare variants in gnomAD controls.

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PO1670

Genetic Studies of the Etiology and Complications of Nephrotic Syndrome by Large-Scale Exome Sequencing
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Background: Idiopathic nephrotic syndrome (NS) is a major cause of renal failure. NS and its complications, including venous thrombosis, hypercholesterolemia and cancer display strong genetic predisposition. We hypothesize that the utility of exome sequencing (ES) will optimize precision medicine for clinical management of NS and its risk factors.

Methods: ES was performed in 2007 NS patients with variable onset age and steroid responsiveness. ACMG guidelines for clinical variant interpretation were used to classify monogenic causes and risk predisposition for a) NS in curated gene lists (glomerulopathies, N=127; expanded nephropathies, N=670); b) incidental variants in 59 ACMG actionable-genes; c) Genetic risk for NS complications (Coagulation, N=100; lipid metabolism/cardiovascular risk, N=35); d) Germline cancer predisposition (N=77).

Results: We identified a monogenic cause for NS in 13% of cases, with COL4A3 (2.2%), COL4A5 (1.8%) and WT1 (1.3%) representing the lead causes. Monogenic causes were enriched in FSGS and steroid resistant nephrotic syndrome cases. Analysis of the expanded nephropathy gene panel revealed an additional diagnostic rate of ~1%, causes were enriched in FSGS and steroid resistant nephrotic syndrome cases. Analysis of the expanded nephropathy gene panel revealed an additional diagnostic rate of ~1%, corresponding to 1 per 4 cases.

Conclusions: To identify novel monogenic causes of NS, we performed whole exome sequencing (WES) in 232 families with CAKUT. We also screened for mutations in NRIP1 in a cohort of 59 affected individuals with small kidneys and a suspected diagnosis of nephronophthisis (NPHP).

Results: By WES analyses, we discovered three heterozygous mutations (one frameshift and two missense) in three unrelated CAKUT families. In particular, individual B3864 with bilateral hydropoditudenephropsis and right grade 5 vesicoureteral reflux (VUR) carried a heterozygous frameshift variant (c.2028_2031delp: p.Asn676lysf*27). Individual A3460 with left renal agenesis harbored a heterozygous missense variant (c.970C>T; p.His324Tyr). In individual A782 with right renal agenesis, we identified a heterozygous missense variant (c.1343G>A; p.Arg448Gln). Family B3977 with an NPHP diagnosis, showing bilaterally increased echenogchency and corticomediullary cysts, carried a heterozygous missense variant (c.2252T>G; p.Lev751Arg). The four variants occurred 2, 0, 2, and 17 times, respectively as heterozygous in the gnomAD database of 125,000 healthy control individuals. All affected individuals exhibited an isolated CAKUT phenotype.

Conclusions: This study confirms that germline mutations in the transcription co-factor NRIP1 gene are a novel genetic cause of human autosomal dominant CAKUT and strengthens the association between retinoic acid and renal malformations.

PO1671

Additional Mutations in NRIP1 in Families with Congenital Anomalies of the Kidneys and Urinary Tract (CAKUT)
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Background: Congenital anomalies of the kidneys and urinary tract (CAKUT) are the most common cause of chronic kidney disease in the first three decades of life. In a previous study, we identified a dominant mutation in nuclear receptor interacting protein 1 (NRIP1) as causing urinary tract malformations via dysregulation of retinoic acid signaling (JASN 28:2364, 2017), which remains the only family with NRIP1 mutation reported so far.

Methods: To identify additional families with NRIP1 mutations, we performed whole exome sequencing (WES) in 232 families with CAKUT. We also screened for mutations in NRIP1 in a cohort of 59 affected individuals with small kidneys and a suspected diagnosis of nephronophthisis (NPHP).

Results: By WES analyses, we discovered three heterozygous mutations (one frameshift and two missense) in three unrelated CAKUT families. In particular, individual B3864 with bilateral hydropoditudenephropsis and right grade 5 vesicoureteral reflux (VUR) carried a heterozygous frameshift variant (c.2028_2031delp: p.Asn676lysf*27). Individual A3460 with left renal agenesis harbored a heterozygous missense variant (c.970C>T; p.His324Tyr). In individual A782 with right renal agenesis, we identified a heterozygous missense variant (c.1343G>A; p.Arg448Gln). Family B3977 with an NPHP diagnosis, showing bilaterally increased echenogchency and corticomediullary cysts, carried a heterozygous missense variant (c.2252T>G; p.Lev751Arg). The four variants occurred 2, 0, 2, and 17 times, respectively as heterozygous in the gnomAD database of 125,000 healthy control individuals. All affected individuals exhibited an isolated CAKUT phenotype.

Conclusions: This study confirms that germline mutations in the transcription co-factor NRIP1 gene are a novel genetic cause of human autosomal dominant CAKUT and strengthens the association between retinoic acid and renal malformations.
Using Clustering to Facilitate Gene-Based Rare-Variant Collapsing for a Diverse Cohort of FSGS Patients


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Background: Several focal segmental glomerulosclerosis (FSGS) genes have been discovered through family studies. Rare-variant case-control studies, however, have been largely underpowered and/or restricted to a single ancestry.

Methods: We performed exome sequencing of 1,989 cases with FSGS and compared them to 18,835 controls. Using gene-based collapsing, we looked for genes with an excess of rare qualifying variants (QVs) in cases or controls. Standard collapsing was complicated by the diverse ancestry of our cases that not only included African, Asian, and Hispanic samples, but also Caucasian subpopulations not well represented in public databases or our controls. Therefore, we extended our collapsing workflow by a clustering step based on principal components reflecting ancestry. We performed coverage harmonization and frequency filtering within the clusters to capture population-specific differences. We used the Cochran-Mantel-Haenszel test to test for an association between disease status and QV enrichment of QVs in known FSGS genes.

PO1675 Alpha Lipolic Acid Supplementation Prevents the Age-Related Decrease in Nuclear Reduced Glutathione Levels in Kidneys from Old Female Lewis Rats

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Background: The purpose of the present study was to investigate whether supplementation with alpha lipoic acid reverses the decrease in nuclear reduced glutathione (GSH) levels in kidneys from old rats. GSH is the major antioxidant inside cells, and a decrease in GSH levels is associated with increased oxidative damage caused by free radicals.

Methods: There were three groups of female Lewis rats used in the study. The Young Control rats (n=4) were 3 months of age, the Old Control rats (n=4) were 22 months of age, and the Old Experimental rats (n=4) were 22 months of age. Only the Old Experimental rats received alpha lipoic acid (100 mg/Kg body wt) by i.p. injection for one week. The kidneys were harvested from anesthetized rats, and the cortex and medulla were separated and homogenized. The nuclear fractions were isolated using differential centrifugation. The GSH levels were measured with a spectrophotometric assay. Comparisons between groups were done using ANOVA followed by the Fisher’s LSD post hoc test. All data are shown as X ± SEM. Statistical significance was determined at p ≤ 0.05.

Results: Supplementation with alpha lipoic acid reversed the age-related decrease in nuclear GSH levels in the kidney cortex and medulla from old rats. The GSH levels were not different from the levels observed in young rats.

Conclusions: The findings suggest that dietary supplementation is beneficial to cell nuclei in rat kidney by preventing the decrease in GSH levels observed with age.
SIRT3 Confers Protection and Mediates Sex Differences in Aging-Related Kidney Injury
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Background: Fibrosis and mitochondrial dysfunction are hallmarks of most progressive kidney diseases. Studies suggest women have slower progression of CKD and lower ESKD incidence before menopause vs. men. SIRT3, a major mitochondrial acetyltransferase, is critical in maintaining mitochondrial homeostasis and anti-oxidative defense. We observe higher kidney mitochondrial SIRT3 (mtSIRT3) in females vs. males. In this study, we hypothesize that SIRT3 protects from and mediates sex differences in aging-related kidney injury and fibrosis.

Methods: Male and female WT, SIRT3 transgenic (Tg), inducible kidney tubule-specific SIRT3 knockout (KO) or global SIRT3 KO mice were aged under physiologic conditions. Kidney fibrosis was detected by trichrome staining and expression of fibrosis markers (α-SMA, fibronectin). 6-month (mo) old male or female WT mice were treated with S.C. implantation of a 200 mg, 21-day-release testosterone pellet for 3 wks.

Results: In male mice, we observed that lower kidney mtSIRT3 expression vs. age-matched females is associated with higher baseline ROS generation, and development of tubular epithelial cell death and fibrosis in aged 14-mo iKO females; outcomes similar to WT males. Furthermore, young (2-3 mo) male and female global SIRT3 KO mice display matched females is associated with higher baseline ROS generation, and development of tubular epithelial cell death and fibrosis in aged 14-mo WT mice; outcomes similar to WT males. Conversely, 6-mo iKO male mice display higher ROS, tubular injury and fibrosis vs. age-matched control males. In contrast to male mice, WT females display minimal tubular vacuolization or fibrosis at 14-mo. SIRT3 knockout aggravates tubular damage and fibrosis in aged 14-mo iKO females; outcomes similar to WT males. Young (2-3 mo) male and female global SIRT3 KO mice display baseline kidney injury characterized by: increased urinary albumin excretion, ROS and tubular injury vs. WT. Mechanistic studies show that testosterone (T) administration to WT males increased serum T ¬→ 4-fold, decreased kidney mtSIRT3, and caused kidney injury (decreased CCl4 and increased tubular vacuolization). T increased kidney mtSIRT3 and caused no measurable kidney injury in WT females, possibly due to an associated increase in serum estradiol.

Conclusions: 1) SIRT3 is critical for kidney tubular epithelial cell survival under physiologic conditions, and inhibits development of tubular injury and fibrosis in aged kidneys; 2) sex-dependent differences in kidney SIRT3 expression may mediate sexual dimorphism in CKD outcomes.

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Efficient Follow-Up and Its Effects on Questionnaire Responses in the EQUAL Study in the United Kingdom
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Background: Minimising patient contact is more important amidst the COVID-19 pandemic; yet altering follow-up data collection methods may introduce unintentional bias. We describe our findings from the European Quality (EQUAL) study in which UK patients switched from ‘traditional’ clinic follow-up (TFU) to ‘efficient’ postal follow-up (EFU).

Methods: EQUAL is a prospective study on treatment in people aged ≥65 with advanced chronic kidney disease (eGFR ≤20mL/min/1.73m²). UK patients were recruited to EQUAL from 2013-2017. During TFU, patients were invited to complete a questionnaire (SF-36, Dialysis Symptom Index and Renal Treatment Satisfaction Questionnaire) at research clinics every 3-6 months. In 2018, all alive patients were invited to switch to EFU, which used an abbreviated questionnaire administered centrally by post. Questionnaire response and error rates for six-monthly TFU and the first EFU are presented for UK patients who consented to EFU.

Results: In total, 506 UK patients were recruited. In 2018, 236 of these patients were alive and almost half (n=111) consented to the change in follow-up. Of those consenting to EFU, response rates fell from 96.2% (83/86) in TFU to 68.1% (75/111) in the first two-monthly EFU. Of those who were recruited earlier and had completed 3.5 years of TFU, response rates fell again to 20% (3/15). The response rate for the first EFU questionnaire was 59.6% (59/99) of those alive. Errors almost trebled throughout TFU, rising from 0.0% in TFU to 9.7% (5/53) in the first two-monthly EFU. This suggests that even in older people with advanced CKD, returning questionnaires by post is acceptable and may provide more complete data than costly TFU. This is acutely relevant in this period of limited contact in the COVID-19 pandemic.
PO1680

CKD in the Very Elderly: When Is It Only Aging?

Background: Chronic kidney disease (CKD) diagnosis is increasingly common in the elderly and is associated with increased morbidity and mortality. As life expectancy increases, so does the prevalence of risk factors for CKD such as hypertension and diabetes. On the other hand, it is known that in older years, glomerular filtration rates decrease progressively, in a process called renal senescence. This study aims to identify risk factors for progressive CKD versus renal senescence in patients over 80 years.

Methods: We developed a single center retrospective study with 101 patients over 80 years of age, by nephrologist with CKD estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73 m² diagnosed for at least for 5 years. Progressive disease was defined as GFR decline greater than 5 mL/min/1.73 m²/year and in about 66% GFR decline rate was less than 5 mL/min/1.73 m²/year. Regarding CKD complications, 37.6% had anemia and 18.7% needed erythropoiesis-stimulating agents. No patient was under phosphate binders and 4% needed vitamin D analogues. About 20.9% presented metabolic acidosis requiring supplementation. In the progressive CKD group, there was a higher prevalence of obesity (OR 4.1, p = 0.04) and metabolic acidosis (OR 6.1, p = 0.01). Nephrologist follow-up time was also statistically different between the groups (6.1 years in progressive CKD vs 4.1 years in non-progressive CKD, p = 0.04). In the multivariate analysis, only the presence of metabolic acidosis (1.07, 95% CI [1.01-1.73]) was associated with the development of progressive CKD. Nephrology consultation does not seem to have an impact on progressive CKD progression, since the group with progressive disease had the longest follow-up.

PO1682

The Difference in eGFR by Cystatin C vs. Creatinine Is Strongly Associated with Mortality Independent of Measured GFR
O. Alison Potok,1 Dena E. Ritkin,1 Joachim H. Ix,1 Michael Shlipak,2 Alice Schneider,3 Nina Mielke,4 Elke Schaeffner,5 Natalie Ebert.1 University of California San Diego, La Jolla, CA; 2San Francisco VA Medical Center, San Francisco, CA; 3Charité Universitätsmedizin Berlin, Berlin, Germany; 4VA San Diego Healthcare System, San Diego, CA; 5University of California San Diego, San Francisco, CA.

Background: In preliminary work, we have shown that the difference in glomerular filtration rate (eGFR) estimated by cystatin C [eGFR\textsubscript{Cys}] and creatinine [eGFR\textsubscript{Cr}], was associated with risk of frailty, hospitalization, cardiovascular events and mortality. Prior studies lacked directly measured GFR so it remained uncertain if associations were influenced by kidney function.

Methods: 567 participants of the Berlin Initiative Study (BIS) had baseline GFR measured by iohexol clearance (mGFR), as well as serum creatinine and cystatin C levels. eGFR\textsubscript{Cr} and eGFR\textsubscript{Cys} were calculated using CKD-EPI equations, and eGFR\textsubscript{Diff} was defined as eGFR\textsubscript{Cys} - eGFR\textsubscript{Cr}. Mortality was recorded during up to 8 years follow-up. The association between eGFR\textsubscript{Diff} and mortality was assessed using Cox regression.

Results: Average (SD) age was 79 (±6) years, eGFR\textsubscript{Cr} 63 (±21), and eGFR\textsubscript{Cys} 69 (±17) for an eGFR\textsubscript{Diff} of -6 (±12) mL/min/1.73m². Compared to participants with minimal differences in eGFR, those with a substantially positive difference eGFR\textsubscript{Diff} (≥10 mL/min/1.73m²) were younger (76 vs. 78 years), less diabetic (17% vs. 24%) and fewer had hypertension (59% vs. 76%). Those with a substantial negative eGFR\textsubscript{Diff} ≤-10 mL/min/1.73m² were at much higher death risk which was minimally increased with or without adjustment for measured GFR, age, sex, and urine albumin/creatinine ratio (Table). Conclusion: Conclusions: In BIS, an eGFR\textsubscript{Cys} estimate that was substantially less than an eGFR\textsubscript{Cr} estimate was associated with significantly higher risk of death. This association remained after adjusting for mGFR. Important clinical information beyond kidney function is embedded in eGFR\textsubscript{Diff}.

Funding: Private Foundation Support

Table. Association of eGFR\textsubscript{Diff} with Mortality in Older Adults in the Berlin Initiative Study

PO1683

Outcomes of Haemodialysis in Incident Elderly Haemodialysis Patients: Single-Centre Experience
Roukaya Gama, Joaelynn Heinls, David Makanjuola, Subash Somalanka, St Helen Hospital, Carshalton, United Kingdom.

Background: In the UK, elderly patients represent the most rapidly expanding group of the dialysis population. However, there remains little evidence to suggest improved quality of life or increased life expectancy, particularly in those over 80 years old.

Methods: We retrospectively reviewed patients who were initiated on haemodialysis (HD) between January and October 2019 in a tertiary renal centre in the United Kingdom. Data was collected using an electronic database. Baseline characteristics, 3 and 12-month mortality were recorded. Data were presented as counts with percentages and mean ± SD.

Results: There were 263 patients initiated on HD, of which 120 (45.6%) were over 70 years, 67 were aged 70-79 years (group A) and 53 were aged 80-89 years (group B). Mean age was 78.1 ± 5.3 years and 74% were of white ethnicity. Baseline characteristics were summarized in table 1. Sixty patients remained on HD, 14 recovered, 6 moved to other modalities and 40 died. The 90-day mortality was 21% (18% in group A, 25% in group B); 6-month mortality was 41% in group A and 34% in group B; 1-year mortality was 36% in group A and 35% in group B. In those established on HD (>90 days), 1-year mortality was 12% (17% in group A, 4% in group B).

Conclusions: We report a high 1-year mortality of 35% in the elderly population. However, the majority occurred during the 1st 90 days. For those established on HD, mortality is 12%; this is substantially lower than the UK renal registry data for over 75s which was 23% in 2017. Mortality was comparable between age groups, although we were limited by small sample size. A key question is whether there is a difference in quality of life and life expectancy in this cohort.

Table. Baseline characteristics of incident elderly HD patients

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Underline represents presenting author.

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*adjusted for age gender race education BMI serum albumin CRP smoking HTN, antiHTN meds, diabetes CKD category by eGFR\textsubscript{Cr}

** further adjusted for total thigh muscle area & grip strength
Baseline characteristics and mortality in elderly incident haemodialysis patients.

PO1684
Cost Effectiveness Study of Hyperkalemia Management
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Background: Patient (PAT) is a sodium-free, non-absorbed potassium (K+) binder approved for the treatment of hyperkalemia (HK). There is limited real-world evidence on the cost implications associated with PAT treatment of HK. The objective of this study was to assess the cost-effectiveness of treating HK with PAT vs. no K+ binder in a Medicare Advantage population.

Methods: This retrospective, matched cohort study was conducted using the de-identified Optum Clininformatics Data Mart Database from 1/1/16–12/31/18. Two HK cohorts were identified: PAT exposed and unexposed (NoPAT). Patient inclusion criteria included pre-index serum K+ ≥5.0 mEq/L and HK diagnosis (ICD-10 code) and ≥6 months insurance enrollment post-index. Propensity score matching was performed to identify a complete set of matched, unexposed and exposed HK episodes. Follow-up began on index date and ended at the censoring event (insurance disenrollment, death, 12/31/18, sodium polyextereine sulfate or sodium zirconium cyclosilicate initiation, PAT discontinuation [exposed only], PAT initiation [unexposed only]). Cost outcomes measured for 6 months post-index: total, inpatient, emergency department (ED), outpatient services and outpatient pharmacy (mean US$ [CI 95%]).

Results: The study population was 2004 patients (1002 matched pairs). Overall, mean age was 74 years and 66% were male. Patients had a mean of 3 comorbidities. Comorbidities included: DM (73%), CHF (35%), and ESRD (10%). At 6 months post-index, 300 (150 matched pairs) PAT and NoPAT patients remained uncensored. Total PAT mean cost difference (avings) of $7220 ($2211,59584) was observed at 6 months post-index (P<0.01). This cost difference included a pharmacy increase of $3904 ($396.2224) and a decrease in medical costs, specifically, inpatient $4718 ($2222,7215), outpatient $4781 ($2274,7288), and ED $815 ($488,1142).

Conclusions: At 6 months post-index, PAT cohort observed a 27% reduction in cost compared with the unexposed cohort for HK management. Further study is warranted to replicate these findings in a large cohort.

PO1685
Effects of Veverimer on Serum Bicarbonate and Physical Function in Elderly Patients with Metabolic Acidosis in CKD
Donald E. Wesson,1 Vandana S. Mathur,2 Navdeep Tangri,3 Yuri Stasiv,4 Dawn Parsell,5 Elizabeth Li,6 Gerrit Klaerner,7 David A. Bushinsky,8 ‘Bayor Scott & White Health and Wellness Center, Dallas, TX, ‘MathurConsulting, Woodside, CA; ‘University of Manitoba, Winnipeg, MB, Canada; ‘Triada, Inc., South San Francisco, CA; ‘PharmaStat LLC, Fremont, CA; ‘University of Rochester Medical Center, Rochester, NY.

Background: Use of NaHCO3 to treat acidotic pts with CKD increases daily Na load, which may be particularly detrimental to elderly pts who may have hypertension and congestive heart failure. Veverimer is a non-absorbed polymer that treats metabolic acidosis (MA) by binding and removing HCl from the GI tract. It is not an exchange resin and does not introduce unwanted cations such as Na or K. In Phase 3 randomized, blinded, placebo-controlled trials, veverimer significantly increased serum bicarbonate and improved subjective and objective measures of physical function in pts with MA by binding and removing HCl from the GI tract. It is not an exchange resin which may be particularly detrimental to elderly pts who may have hypertension and congestive heart failure.

Methods: Patients were treated for up to 1 yr with veverimer or placebo with frequent determinations of blood bicarbonate. Physical function was assessed at Baseline and improved subjective and objective measures of physical function in pts with MA. In this elderly cohort, more pts receiving veverimer met the primary study endpoint, had a decrease in medical costs, specifically, inpatient $4718 ($2222,7215), outpatient $4781 ($2274,7288), and ED $815 ($488,1142). Cost outcomes measured for 6 months post-index: total, inpatient, emergency department (ED), outpatient services and outpatient pharmacy (mean US$ [CI 95%]).

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Conclusions: At 6 months post-index, PAT cohort observed a 27% reduction in cost compared with the unexposed cohort for HK management. Further study is warranted to replicate these findings in a large cohort.

PO1686
Design of a Consensus-Based Geriatric Assessment Tailored for Older Patients Approaching ESKD
Carolin G. Voorend,1 Noeleen C. Berkhour-Byrne,1 Ady Diepenbroek,2 Caster F. Franzese,2 Winnie W.J. Simon,1,3 Marjolijn Van Buren,4 on behalf of principal investigators of the POLDER study ‘Leids Universitair Medisch Centrum, Leiden, Netherlands; ‘Universitair Medisch Centrum Groningen, Groningen, Netherlands; ‘Sint Antonius Ziekenhuis, Nieuwegein, Netherlands.

Background: Routine geriatric evaluation in older patients approaching end stage kidney disease (ESKD), benefits disclosure of highly prevalent unidentified functional and cognitive impairments. Although recommended in guidelines, a suitable standardized geriatric test set is lacking. We aim to propose a consensus-based test set for geriatric assessment useful in both routine care and research in older (≥ 65 years) patients approaching ESKD.

Methods: A multidisciplinary expert panel of physicians, nurses and supportive disciplines with clinical and/or scientific experience in geriatric nephrology was assembled. Preconditions and selection-criteria for the selection of potential measures resulted from general geriatric principles, critical appraisal of literature, inventory of conventional instruments, and focus group meetings with patients, carers and health professionals. Older patients (aged ≥65 years) approaching end-stage kidney disease (cGFR < 20 ml/min/1.73M2) were selected as the target population. An expert panel meeting and subsequent round of comments by email led to agreement on the best suitable test set.

Results: The final consensus set contains instruments in functional, cognitive, physiologial, and somatic domains, and patient preferences, nutritional status and fall risk. The set comprises a patient questionnaire (six instruments) and a professional-administered test set (including ten instruments). Estimated time for administration in patients was 20 and 40 minutes respectively.

Conclusions: We propose a consensus-based nephrology-tailored geriatric assessment, to benefit clinical care for older (pre-)ESKD patients and enhance research comparability. Future research should investigate effectiveness, feasibility in implementation, patients satisfaction and the value for treatment decision making and outcome improvement.

Funding: Private Foundation Support

PO1687
Correlation Between Patient-Reported Physical Limitation and Objective Physical Performance on the Repeated Chair Stand Test Among Patients with Non-Dialysis Dependent CKD and Metabolic Acidosis

Background: CKD accelerates the loss of physical function, in part due to the development of sarcopenia caused by metabolic acidosis (MA). Decline in the ability to rise from a seated position is consequential as it can lead to loss of independence. However, physical performance is not routinely measured in CKD clinical practice.

Methods: We evaluated the correlation between patient-reported limitation on daily activities on the Kidney Disease and Quality of Life Physical Function Domain (KDQOL-PFD, a 10-item survey in which possible responses are “not limited at all”, “limited a little”, and “limited a lot”) and the standardized 5-times repeat chair stand time (RCS) using data from a 1 year randomized trial of pts (N = 196) with MA in CKD (Wesson et al. Lancet, 2019). Here we report data from pts aged ≥65 yrs from these studies.

Methods: Patients were treated for up to 1 yr with veverimer or placebo with frequent determinations of blood bicarbonate. Physical function was assessed at Baseline and Weeks 12, 40, and 52 using the KDQOL-PFD which quantifies limitations on daily activities and by performance on the repeated chair stand (RCS) test. Results: Of the 217 pts randomized, 113 (52%) were ≥65 yrs (mean 72 yrs). Select comorbidities included HTN (98%), DM (80%), obesity (24%) and CHF (19/2). At Baseline, the mean cGFR was 30.7 mL/min/1.73m2 and the mean serum bicarbonate was 17.2 mEq/L. In this elderly cohort, more pts receiving veverimer met the primary study endpoint, had a significant increase in serum bicarbonate, and improved both KDQOL-PFD scores and RCS time (Table). Effects of veverimer exceeded the minimal clinically important difference for both the KDQOL-PFD (+3 to +5 points) and RCS (1.7 seconds). Safety was similar in both treatment groups.

Conclusion: In older adults with CKD, treatment with veverimer significantly increased serum bicarbonate levels and improved how pts felt and functioned. The safety of veverimer was not different from placebo.

Funding: Commercial Support - Tricida, Inc.

P-values are vs. placebo; An ANCOVA rank-based method was used for physical function endpoint.*Based on evaluable patients enrolled in controlled extension study (placebo, n=38; veverimer, n=58)

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Underline represents presenting author.

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the correlation for all questions). Using a linear model, we found that each category of decline in the SOGCQ was associated with a significant deterioration of RCS time in the range of 3.29 to 3.80 seconds, exceeding the minimally clinically important difference of 1.7 seconds (Jones et al. Thorax, 2013).

Conclusions: Our findings suggest that asking pts if they are limited in their ability to do daily activities such as walking 1 block or climbing or carrying groceries may be a practical way to screen for significant physical performance declines known to have important health, social, and economic consequences. Routine identification of pts with physical functional decline might allow for earlier implementation of interventions to forestall impairment.

Funding: Commercial Support - Tricida, Inc.

PO1688

Mobility in Older Hemodialysis Patients: A Mixed Methods Study

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Background: Mobility, or the ability to move reliably and safely, impacts quality of life and predicts future disability and mortality. This is especially relevant for older adults, who comprise a large part of the hemodialysis (HD) population. For older hemodialysis patients, factors that limit mobility and which specific components of mobility are involved are not well-defined. Using a mixed methods approach, we investigated these factors and components in older HD patients.

Methods: Eligibility criteria were age ≥60 years and receipt of maintenance HD. Participants had a single mobility assessment that occurred in their home when feasible. We administered the Short Physical Performance Battery (SPPB) to assess balance, walking speed, and lower leg strength (range 0-12 for full SPPB, range 0-4 for individual domains). We conducted semi-structured key informant interviews, using an interview guide based on the literature. Interview transcripts were descriptive coded and major themes were extracted using both deductive and inductive approaches.

Results: A total of 31 persons enrolled, with a mean age of 72.5±8.1(S.D.) years and mean vintage of 4.6±3.5 years; 42% were female and 68% African-American. Mean overall SPPB was 4.6±2.3 points; mean scores for balance, walking and lower leg strength were 2.3±1.1, 1.8±1.1, and 1.3±0.7 points, respectively. Mean gait speed was 0.46±0.22 meters/second. Coder inter-rater reliability > 0.8. Three major themes emerged: 1) losses in balance and walking are the most debilitating; 2) fluctuations in mobility are frequent, and 3) post-HD procedure fatigue and the presence of amputations limit mobility (Table). Conclusions: In a diverse sample of older HD patients, mobility is significantly limited with multiple domains affected. Patients identified balance and walking as the most problematic, and cope with frequent changes in mobility. Future studies should focus on improving balance and walking, and include strategies to mitigate fluctuations in mobility.

Funding: Other NIH Support - K23AG057813, Government Support - Non-U.S.

Key themes regarding mobility in older hemodialysis patients

<table>
<thead>
<tr>
<th>Themes</th>
<th>Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic domains that are limited by balance and walking</td>
<td>&quot;Oh, you've lost so much balance and walking that this makes me nervous.&quot;</td>
</tr>
</tbody>
</table>
| Frequent changes in mobility | "I get off the machine, cross the room to the car. "I have my good leg on one side and my bad leg on the other. Sometimes I can't walk and I sit down in the chair (when I'm only right through the center)."
| Causes of mobility limitations | "I can't walk far."
| Impact of poor mobility on caregiver burden | "I'm only walking 60 yards at a time."

PO1689

Rehabilitation in CKD

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Background: Older patients with impaired renal function (renal patients: RP) often show the criteria of a geriatric patient with increasing stages of CKD. Geriatric phenomena such as frailty are considered a predictor of poor outcomes particularly during acute illness in these patients. These consequences can be alleviated in patients without phenomena such as frailty are considered a predictor of poor outcomes particularly during acute illness in these patients. These consequences can be alleviated in patients without frailty, sarcopenia and co-morbidities. We studied the prognostic value of clinical and laboratory parameters for functional status change in older patients with CKD.

Methods: We studied 37 patients (F:M 1.8:1; mean age 84.5±10.2 yrs). 10 received long-term dialysis, whilst non-dialysis CKD patients had a mean eGFR 33±15 mL/min/1.73m2. Mean age difference between Hip# is 1.4 yrs (p=0.032). Mean KPS difference between Hip# is 1 ±0.6 (p=0.028). AUC values from ROC analyses are shown in Table 1.

Conclusions: There was a significant decline in functional status between Hip# 1 and 2. Frailty assessment tools (CFS, HFS, and CKD-Frailty-LAB) had the best predictive performance for functional status change. Frailty measures may be utilized as risk prediction tools of functional status change and should be used in older patients with CKD. Further research is needed to determine if frailty interventions that aim to maintain functional status and reduce subsequent frailty risk.

Funding: Government Support - Non-U.S.

Table 1

<table>
<thead>
<tr>
<th>Predictors</th>
<th>AUROC Value (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Frailty Scale</td>
<td>0.56 (0.39-0.73)</td>
</tr>
<tr>
<td>Hopkins Frailty Score</td>
<td>0.51 (0.34-0.67)</td>
</tr>
<tr>
<td>CKD Frailty-LAB</td>
<td>0.85 (0.64-0.98)</td>
</tr>
<tr>
<td>Karnofsky Performance Status</td>
<td>0.73 (0.55-0.87)</td>
</tr>
<tr>
<td>Charlson's Co-morbidity Index</td>
<td>0.74 (0.55-0.92)</td>
</tr>
<tr>
<td>Barthel ADL</td>
<td>0.57 (0.38-0.77)</td>
</tr>
<tr>
<td>ASA Score</td>
<td>0.56 (0.38-0.74)</td>
</tr>
<tr>
<td>Abbreviated Mental Test Score</td>
<td>0.67 (0.47-0.86)</td>
</tr>
</tbody>
</table>

PO1691

Which Parameters Best Predict Mortality After Hip Fracture for Patients with CKD? Insights from a 6-Year Prospective Study

Henry Wu,1,2 Rene Van Mierlo,1 Ajay P. Dhaygude,1,2 Sandip Mitra,3,4 Andrew C. Nixon,1,2 Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom; 3The University of Manchester, Manchester, United Kingdom; 4Manchester University NHS Foundation Trust, Manchester, United Kingdom.

Background: Hip fracture is more prevalent in patients with CKD and has associated worse clinical outcomes than those without CKD. Uncertainties remain on which clinical and laboratory parameters best predict mortality outcomes following hip fracture for patients with CKD.

Methods: Patients with CKD G3b-5 admitted to a tertiary hospital in North West UK with hip fracture between June 2013 and Dec 2019 were included. Mortality outcomes
Fractures in a Tertiary London Renal Centre 
Mortality Outcomes of Dialysis Patients Who Sustained Neck of Femur Fracture

Eleanor I. Reave, Diya Kapila, Nivi Singh, Bhrigu Raj Sood. St Helier Hospital, Carshalton, United Kingdom.

Background: Patients with end stage renal disease have an increased risk of fractures, including neck of femur (NOF) fractures, partly due to bone mineral disorders. Studies show higher post-operative mortality rates in this group, attributed to abnormal vitamin D metabolism, challenges with fluid status, and pain management issues impeding physical therapy rehabilitation. St Helier hospital has an onsite tertiary renal centre and the Hip Fracture Unit has been ranked as one of the best performing in the country. We sought to establish if this on-site standardised local practice translated to reduced mortality outcomes in dialysis patients who sustained NOF fractures.

Methods: We performed a retrospective analysis of the 30 day mortality of dialysis patients sustaining NOF fractures between April 2011 and July 2018. Patients with NOF fractures were identified from the National Hip Fracture Database and dialysis patients from the renal unit database. We reviewed demographics, pre and post-surgical parameters and 30-day unadjusted mortality.

Results: We identified 3164 NOF patients and 46 of these patients were on dialysis (n=46). 43 were on haemodialysis and 3 were on peritoneal dialysis. The dialysis cohort included 20 females and 26 males and average age was 77 years (53-95). ASA grades were 3 in 23 patients, 4 in 22 patients, and 5 in 1 patient. 29 operations were conducted under general anaesthesia, 16 under spinal anaesthesia and 1 patient had non-operative treatment. One patient was discharged home, 2 patients were transferred to another hospital and 27 patients died. The mortality rate was 6.5% (n=27). The median length of stay was 26 days (IQR 5-87). The average length of stay for the dialysis cohort was 801 days following admission.

Conclusions: Previous studies have demonstrated 2 to 4 fold increased mortality in dialysis patients with NOF fractures. Our data shows that patients on renal replacement therapy did not have higher 30-day mortality compared to the general cohort. A multidisciplinary service with close collaboration between specialties can lead to good outcomes in this high risk population.

Intensive Blood Pressure Control and Fall Injuries in Older Adults: A Systematic Review and Meta-Analysis

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Background: Hypertension is the leading preventable risk factor for cardiovascular disease (CVD), and its prevalence increases with age. While prior studies suggested that intensive blood pressure (BP) control achieved a reduction in CVD, antihypertensive treatment may cause adverse events such as falls. Falls are one of the leading causes of hip fractures and traumatic brain injuries. However, it remains unclear if intensive BP control could lead to an increased risk of falls.

Methods: We performed a systematic literature search up to April 2020. We selected randomized control trials (RCTs) and cohort studies which compared the risk of falls in the intensive BP control group with that in the less intensive control group the elderly. Risk ratios (RRs) with corresponding 95% confidence interval (CI) were synthesized.

Results: Five studies (three RCTs and two cohort studies) were included, with 11,245 patients. The characteristics were shown in Table. Intensive BP control was associated with significantly increased risk of falls, but the results showed high heterogeneity. (RR [95% CI]; 1.10 [0.87-1.39], 12- 73%)

Conclusions: In older patients, intensive BP control was not associated with an increased risk of falls, but with high heterogeneity. The proportion of frail patients might be a source of heterogeneity. Further studies that stratify patients with risk of frail are needed.

Potentially Inappropriate Antihypertensive Medications and Mortality in Older Adults on Hemodialysis

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Background: Older patients on hemodialysis often have difficult to control hypertension, but also suffer from orthostatic or post-dialysis hypotension. Some orthostasis-causing antihypertensives (i.e., central alpha agonists (CAA) and alpha blockers (AB)), are considered potentially inappropriate medications (PIMs) for older adults because they carry more risk than benefit. We sought to determine if these PIMs are associated with mortality risk among older adults on hemodialysis.

Methods: Using USRDS analytic files, we studied adults aged ≥66 years initiating in-center hemodialysis (ICHFD) from 2013-2014 with a Medicare Part D prescription for CAA or AB at initiation. All had Medicare Parts A, B, and D a year prior to initiation, no hospice care within prior 6 months, and continued ICHFD for ≥120 days. We classified patients as continuing or discontinuing CAA/AB at 120 days and examined risk of death associated with mortality risk among older adults on hemodialysis. If this on-site standardised local practice translated to reduced mortality outcomes in dialysis patients who sustained NOF fractures.

Results: Of 5,981 patients, mean age 75.6±9.4 years, 51.4% women, and 24.6% black. Most (65.5% [n=3,920]) continued CAA/AB prescription at 120 days. Compared to those who discontinued, those who continued were more likely to be black (26.3% vs. 21.3%), dual eligible (31.5% vs. 27.3%), and have no functional limitations (84.1% vs. 79.8%). A smaller proportion of deaths compared to discontinuers (17.3% vs. 20.9%), continuation if this on-site standardised local practice translated to reduced mortality outcomes in dialysis patients who sustained NOF fractures. Five studies (three RCTs and two cohort studies) were included, with 11,245 patients. The characteristics were shown in Table. Intensive BP control was associated with significantly increased risk of falls, but the results showed high heterogeneity. (RR [95% CI]; 1.10 [0.87-1.39], 12- 73%)

Conclusions: In older patients, intensive BP control was not associated with an increased risk of falls, but with high heterogeneity. The proportion of frail patients might be a source of heterogeneity. Further studies that stratify patients with risk of frail are needed.

Characteristics of the studies included in the Meta-analysis
Tailoring the Beers Criteria for Mortality Risk Stratification Among Older Adults Initiating Hemodialysis

Rasheeda K. Hall, 1,2 Abinereki Muzawale, 1 Dorry L. Segev, 1 Mara McAdams-DeMarco, 1,2 Durham VA Medical Center, Durham, NC; 3Duke University School of Medicine, Durham, NC; 4Johns Hopkins University, Baltimore, MD.

Background: American Geriatrics Society’s Beers Criteria lists potentially inappropriate medications (PIMs) that carry more risk of harm than benefit in older adults, but PIM risks may differ in kidney failure. To tailor the Beers Criteria, we developed a novel mortality risk score for older patients initiating hemodialysis.

Methods: We assembled a USRDS cohort of 39,098 adults aged ≥65 initiating hemodialysis (2013-2014) and enrolled in Medicare Part D by 90 days post-initiation. We used Part D claims data to quantify prescription length of Beers Criteria PIMs. In a training cohort (60% sample), we identified which of 38 PIM classes were associated with mortality using Cox modeling; censoring for loss of Medicare coverage, mortality change, or 9/1/2015. Models were adjusted for demographics, initiation year, comorbidities, drug dependence, smoking status, inability to ambulate, and institutionalization. PIMs classes that were associated with mortality were summed to create a PIM count risk score. We used Cox models to estimate the association of PIM count risk score (time-varying) with mortality in training and validation cohorts.

Results: The training cohort (n=23,521) had mean age 75 years, 43% women, 21% black, and 75% (n=17,706) had ≥2 PIM fills/month. We identified 15 PIMs (HR ≥1) to include in the risk score (Figure). Patients with ≥2 fills/month (vs. no fills) were more likely institutionalized (13.8% vs. 10.1%), non-ambulatory (20.8% vs. 17.2%), and have cardiovascular disease (62.4% vs. 50.7%). Compared to those with no fills, there was increased mortality risk among those with 1 fill (ahR=1.32,1.25-1.39) and ≥2 fills (ahR=1.66;1.56-1.75).

Conclusions: We identified 15 of 38 PIM classes associated with mortality to yield a novel PIM count risk score. This score facilitates tailoring the Beers Criteria to promote age-appropriate prescribing in older adults initiating hemodialysis.

Funding: NIDDK Support, Other NIH Support - NIA, Private Foundation Support

PO1696

Symptoms and Suffering at the End of Life in ICU Patients Receiving Dialysis

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Background: Patients with end-stage kidney disease (ESKD) on dialysis suffer from a significant burden of physical symptoms. Little is known, however, about the symptoms that intensive care unit (ICU) patients receiving dialysis experience at the end of life.

Methods: This is a cohort study conducted at NewYork-Presbyterian Hospital / Weill Cornell Medical Center and Brigham and Women’s Hospital from September 2015 to March 2017. Nurses who cared for deceased ICU patients were interviewed within 3-5 weeks of the deaths about patients’ physical and psychological symptoms in their last week of life. On a 1-10 scale, nurses rated 16 different symptoms on how much they contributed to a patient’s suffering and rated the patient’s overall suffering in the last week of life. Study staff abstracted demographic and clinical data from patient charts.

Results: One-hundred nurses completed interviews on 200 deceased patients, 67 of whom underwent dialysis in the last week of life (for ESKD or acute kidney injury). Mean dialysis patient age was 63 years; 39% were female; 32% were non-white; 12% were Hispanic. The nurses rated patients who underwent dialysis in the last week of life as having significantly more suffering from painful, broken skin than non-dialysis patients (mean 4.6 vs. 3.5 out of 10, P=0.045) but significantly less suffering from hunger (mean 2.4 vs. 3.6 out of 10, P=0.012) or thirst (mean 3.2 vs. 4.8 out of 10, P=0.005). There was a trend towards more suffering from swelling in the dialysis patients (mean 6.2 vs. 5.3 out of 10, P=0.083). An unadjusted linear regression model revealed that receipt of dialysis in the last week of life was significantly associated with perceived overall suffering (β=1.35, P=0.006); however, after adjustment for painful, broken skin (β=0.19, P=0.02); non-hunger (β=0.20, P=0.007) and swelling (β=0.22, P=0.074) in the model, the relationship between dialysis and overall suffering was attenuated (β=0.04, P=0.074).

Conclusions: Nurses rated ICU patients who received dialysis in the last week of life as suffering from more painful, broken skin but less hunger or thirst than non-dialysis patients. The relationship between dialysis and perceived overall suffering was attenuated by painful, broken skin and swelling, suggesting that attention to these problems might reduce suffering at the end of life in ICU dialysis patients.

Funding: Other NIH Support - National Cancer Institute CA197730 to HGP

PO1697

Want to Reduce Regret with Dialysis Initiation? Implement Shared Decision-Making

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Background: The American Society of Nephrology’s “Choosing Wisely Campaign” recommends that nephrologists should not initiate chronic dialysis without implementing a shared decision-making (SDM) process. The current literature lacks details on the relationship of SDM with outcomes such as quality of life and decisional regret.

Methods: We surveyed 223/380 (response rate 59%) hospitalized patients receiving maintenance dialysis in the Upstate, NY, and asked them about their experience with dialysis decision-making using the SDM-9 Questionnaire. Quality of life and decisional regret were assessed by KDQOL-36 and Decisional Regret Scale, respectively. Candidate predictors in the final linear regression model included age, sex, time on dialysis, race, marital status, income level, education level, quality of life, fear of death, and decisional regret.

Results: Nearly 41% of patients were <65 years old, 47% were women, and 41% were White. The mean scores for SDM were 25.9 ± 12.2. In the bivariate analyses, patients who were married or in a relationship had greater mean SDM scores (p<0.01) than those who were single. Patients with higher scores on SDM had less anxiety over death and less decisional regret (R² = 0.17 and -0.29, respectively). The candidate predictors in the final model together explained 21.4% of the variance in SDM (p = 0.02). SDM decreased for every 0.15 unit increase in decisional regret score (CI: -0.25, -0.07) when controlling for all other predictors in the model.

Conclusions: We found that patients with higher scores on the SDM-9 Questionnaire had less decisional regret regarding their decision to initiate dialysis. Future interventions to implement SDM in clinical settings are a top research priority.

Funding: Private Foundation Support

PO1698

Attitudes Towards Physician-Assisted Death in Patients Receiving Maintenance Dialysis

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Background: During recent years, the debate about the legalization of physician-assisted death (PAD) has intensified at both public and policy levels. Surveys and polls on this issue have included seriously ill patients such as those with cancer; however, voices of patients receiving maintenance dialysis are not represented in the current literature.

Methods: We surveyed 223/380 (response rate 59%) hospitalized patients receiving chronic dialysis in Upstate, NY. We asked patients about their views on PAD using the following two questions: (1) Which of the following best describes your views about whether a physician should ever be allowed to take the final action in response to a patient’s request for assisted death? (2) In case you had a great degree of pain and suffering and if physician-assisted death were legally available, do you think you might request it for yourself? Response options for the first and second questions included: (a) support/yes (b) oppose/no (c) uncertain. Candidate predictors in the final logistic regression model included age, time on dialysis, race, marital status, income level, education level, spirituality, social support, symptom burden, sense of burdensomeness, fear of death, and fear of the dying process.

Results: Nearly 41% of patients were <65 years old, 47% were women, and 41% were White. Fifty-five percent supported PAD, 20% expressed uncertainty, and 22% were against. Patients who supported PAD were more likely to be older, male, White, and married or in a relationship (p<0.05). In the bivariate analyses, those who supported PAD had higher spirituality, higher anxiety about the dying process, and had spent more time on dialysis compared to those who opposed or were uncertain (p<0.05) about it. In the final model, none of the candidate predictors were significant for support/oppose/uncertainty about PAD.

Conclusions: More than half of hospitalized dialysis patients supported PAD, while fewer would actually use this option in case of pain and suffering. In the absence of the legalization of PAD in the NY state, the promotion of palliative care and hospice services and high-quality end-of-life care for dialysis patients are high priority policy issues.

Funding: Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

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PO1699
Perspectives on Conservative Management of Advanced Kidney Disease: A Qualitative Study of US Patients and Family Members
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Background: Growing recognition of the limits of maintenance dialysis for some groups of patients has led to the emergence of conservative care models for advanced kidney disease in several countries outside the US. There is strong interest in replicating similar models in the US, however little is known about how these models are perceived by US patients and family members.

Methods: We conducted a qualitative study using cognitive interviews with 14 patients aged ≥75 years with advanced kidney disease and 6 of their family members about their perception of conservative care approaches in other countries as described in available patient decision aids on treatment of advanced kidney disease. We performed an inductive thematic analysis of interviews to identify themes reflecting participants’ understanding and receptivity to conservative care.

Results: Subjects were mostly white (n=15) and had at least some college education (n=16). 4 prominent themes emerged from analysis of interviews: 1) Core elements of conservative care: aspects of conservative care that were appealing to participants included a whole-person, multidisciplinary approach to care that focused on symptom management, maintaining current lifestyle and managing health setbacks; 2) Importance of how conservative care is framed: participants were more receptive to conservative care when this was framed as an active rather than passive treatment approach and were less receptive to uncertainty in disease prognosis; 3) An explicit approach to shared decision-making: participants believed decisions about conservative care or dialysis address considerations about risk and benefits of treatment options, family and clinician perspectives and personal goals, values and preferences; and, 4) Relationship between conservative care and dialysis: although conservative care models outside the US are generally intended to serve as an alternative to dialysis, participants’ comments implied that they did not view conservative care and dialysis as mutually exclusive.

Conclusions: Although participants in this study found many aspects of conservative care models developed in other countries to be appealing, models will likely require adaptation to meet the needs and preferences of US patients and their families.

Funding: Private Foundation Support

PO1700
Feasibility and Acceptability of Telepalliative Care in Rural Dialysis Units
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Background: Limited access to palliative care is a key barrier to its integration in routine dialysis care. We evaluated the feasibility and acceptability of telepalliative care while patients received dialysis in rural units.

Methods: The target population included any patients with end-stage kidney disease receiving dialysis. Palliative care physicians and APPs conducted consultations as per their usual practice and used a large wall mounted screen with centrally positioned camera to establish a connection with an iPad attached to an IV pole positioned next to the dialysis chair. Patients were provided the option of having family present, receiving the consult on dialysis or off dialysis in a private room. Feasibility was measured by 1-month completion rate. Acceptability was measured using an adapted telemedicine questionnaire.

Results: We recruited 40 patients to undergo a telepalliative care consultation while receiving dialysis. Four specialty palliative care clinicians (3 physicians and 1 nurse practitioner) conducted the visits. The recruitment rate was 35% (40/113), scheduling rate was 97.5% (39/40) and completion rate was 85% (33/39). Thirty-six patient participants (15 women, 21 men) completed the baseline survey. One patient requested family to be present during the conversation. No patients requested to have the conversation off dialysis in a private room. Audiovisual aspects of the conversation were rated highly. More than 3/4 reported the visit being at least as good as an in-person visit and 40% felt it was better. Patients felt the appointment changed the way they think about dialysis. More than 3/4 reported the visit being at least as good as an in-person visit and 40% felt it was better. No patients requested to have the conversation off dialysis in a private room. Audiovisual aspects of the conversation were rated highly. More than 3/4 reported the visit being at least as good as an in-person visit and 40% felt it was better. Patients felt the appointment changed the way they think about dialysis.

Conclusions: Telepalliative care is acceptable to patients receiving dialysis and is a feasible approach to integrating palliative care in rural dialysis units.

Funding: Private Foundation Support

POI701
Abstract Withdrawn

POI702
Modestly Low eGFR Is Not Associated with Cognitive Decline in the Elderly

Background: Although participants in this study found many aspects of conservative care models developed in other countries to be appealing, models will likely require adaptation to meet the needs and preferences of US patients and their families.

Methods: We used a single center cohort of 912 adult KT recipients with delirium assessments abstracted from medical records and global (3MS) and domain-specific (executive function: time to complete TMT-B minus TMT-A) cognitive performance measured at KT, 1-month, 3-months, 6-months, 1-year, and annually thereafter post-KT. We used mixed effects models to describe repeated measures of cognitive performance and compare trajectories by post-operative delirium.

Results: Among 912 KT recipients, 44 (4.8%) had post-operative delirium. Delirium was associated with higher levels of cognitive impairment at KT (18.2% vs 8.0%), and was associated with lower 3MS component scores including memory, identification/association, and orientation. After adjustment, those with delirium had 3MS scores that were on average 3.6 points lower than those without delirium (95%CI: -6.9, 0.3) at time of KT; delirium was not associated with differing global cognitive trajectories post-KT (difference = 0.04 points/month, 95%CI: -0.01, 0.21) (Figure A). However, delirium was associated with lower executive function at KT (difference = 44.0s, 95%CI: 17.4, 70.6) and steeper decline in executive function post-KT (difference = -1.1s/month, 95%CI: -2.1, -0.05) (Figure B).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

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Conclusions: KT recipients with delirium experience greater decline in executive function, indicating greater cognitive vulnerability with potential vascular etiologies. Nephrologists and transplant centers should be aware of cognitive risks associated with post-KT delirium and implement available preventative interventions to reduce risk of delirium.

Funding: NIDDK Support, Other NIH Support - National Institute on Aging (NIA) (Figure). Transformed cognition trajectories for post-operative delirium in kidney transplantation (KT) recipients (n=122). (A) Global cognitive function (IQCODE scores); (B) motor function (Fugl-Meyer fine motor score); (C) verbal function (Fogelberg AFT score); (D) visuoperceptual function (Sensory Motor Test AFT score). The details are in Table S1.}

Conclusions: DNA damage accumulation after DSBs is the common histological end-point of various kidney diseases. In vitro study of MMc-induced DNA damage, COL6 excretion decreased by the decrease of COL6 positive cells was suppressed in the ATR-inhibited group (p <0.01 for 2 h, p<0.001 for 24 h). Moreover, CPT treated cells induced the COL6 excretion as well as MMc treated cells (p <0.001 for MMc, p=0.002 for CPT).

Conclusions: This study showed that DNA damage-sensing kinase of ATR was activated in response to DSBS and induced COL6 secretion of human glomerular endothelial cells. Furthermore, DNA damage may induce the nodular glomerulosclerosis in various kidney diseases.

Funding: Government Support - Non-U.S.

PO1705
DNA Double-Strand Breaks of Human Glomerular Endothelial Cell-Induced Collagen Type IV Excretion and Nodular Lesions in Various Kidney Diseases
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The prevalence of frailty varies using different measurement tools and there are differences in perceived (CFS) versus measured (FP/FI) frailty among patients referred for transplantation. Determining which tool is most associated with outcomes for waitlisted patients is a future objective of this study.

Methods: Kidney transplant waitlist candidates were prospectively enrolled from six centers from June 2016-Feb 2020. Frailty was primarily defined using the FP as five or more of the following: weakness, weight loss, low activity or exhaustion (the latter three using questionnaires). Secondary tools included a Frailty Index (FI) consisting of 37 variables across the domains of social function/cognition, function, mobility and comorbidity, and the Clinical Frailty Scale (CFS), a frailty screen based on clinician gestalt that ranges from 1 (very fit) to 8 (very severely frail). We used adjusted logistic regression to identify factors associated with frailty measured by the FP. Area under the receiver-operator characteristics (ROC) curves were calculated to compare the FP to the FI and CFS.

Results: Of 542 enrolled patients, 64% were male, 80% were white, and the mean age was 54±14. The prevalence of frailty by the FP was 16%; it was 27% for those >65 years old. Of the FP components, low grip strength (41%), and exhaustion (36%) were the most prevalent. Using an established cut point of 0.25 yielded a prevalence of 38% by the FI (46% for those >65). Using a cut-off of 5 on the CFS (mildly frail), frailty prevalence was 4% (7% for those >65). The mean FI score was 0.23±0.14 (max 0.70) and median CFS score was 3 (IQR 2.9) or “managing well”. Diabetes (adjusted odds ratio; aOR 2.0, 95% CI 1.0, 3.8), and cerebrovascular disease (aOR 3.3 95% CI 1.3, 8.5) were associated with frailty measured by the FP. Area under the ROC curve for the FP and FI/CFS were 0.86 (good) and 0.69 (poor) respectively.

Conclusions: The prevalence of frailty varies using different measurement tools and there are differences in perceived (CFS) versus measured (FP/FI) frailty among patients referred for transplantation. Determining which tool is most associated with outcomes for waitlisted patients is a future objective of this study.

Conclusions:

PO1706
Clinical Course of a Patient with FSGS and a Basement Membrane Defect
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Introduction: We present a case of a patient with a familial basement membrane abnormality who developed nephrotic syndrome and worsening CKD due to FSGS and outline her response to immunosuppressive therapy over 15 months. Our case suggests that immunosuppressive therapy may benefit such patients and delay progression to ESRD.

Case Description: A 38-year-old woman with microscopic hematuria was found to have a urine Pr/Cr ratio of 2.4 during pregnancy. Her s.Cr was 1.4-1.6 mg/dL and she had over 13g of proteinuria during pregnancy. After delivery, the serum creatinine stabilized between 1.1-1.3 mg/dL and her urine Pr/Cr ratio was 5.0 with an unrevealing serologic workup. She has no family history of renal insufficiency, but her father and 14-year-old daughter have microscopic hematuria. A renal biopsy revealed FSGS with ultrastructural GBM alterations including thinning and lamellation as well as nearly complete foot process effacement. Collagen IV staining demonstrated a normal IF pattern for α2 and α5 chains. She was started on prednisone, however, her glycemic control deteriorated and therapy was stopped after 1 week. She was then treated with Losartan and Cyclosporine and her Pr/Cr ratio improved to 1.3-1.5 mg/dL but her serum creatinine gradually rose to 2.0 mg/dL. Losartan was changed to Diltiazem and CsA was changed to MMF. Her s.Cr has trended down to 1.4 mg/dL with a urine Pr/Cr of 1.9 fifteen months after diagnosis. She was referred for genetic testing and was found to be heterozygous for a mutation of COL4A4 (Exon 39, c.3679G> A, p.Gly1227Arg).

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PO1709
Protection of the Remnant Rat Glomeruli from Mechanical Stress Through Structural Adaptation and Pharmacological Intervention After 5/6-Nephrectomy: A Modeling Study
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Background: 5/6-nephrectomy leads to increased blood flow and pressure in the remaining glomeruli, ultimately resulting in sclerosis. It is hypothesized that these hemodynamic alterations increase mechanical stresses, including shear stress on the glomerular endothelial cells and circumferential hoop stress on podocytes, however these mechanical stresses have not been rigorously quantified. In renoproliferative conditions glomerular capillary diameters increase, and it is unclear how these structural adaptations affect the mechanical stress magnitudes.

Methods: A mathematical microvascular hemodynamic model was developed to simulate blood flow and plasma filtration on each capillary segment of an anatomically-accurate rat glomerular capillary network. Model parameters were adjusted to match glomerular hemodynamic data for control and 5/6-nephrectomized conditions with and without the presence of the ACE inhibitor, enalapril (Meyer TW et al. Kidney Int. 1987;31(3):752-759). Glomerular capillary diameters were increased according to experimental imaging data (Ferrell, Nicholas, et al. Am J Kidney Dis. 30(6) (2015): F388-F393) to simulate glomerular structural adaptations post-5/6-nephrectomy.

Results: Post-5/6-nephrectomy, glomerular capillary structural adaptations reduced mean network shear stress from 156.5 to 92.8 dyne/cm2. Without structural adaptations enalapril reduced mean shear stress to 136.1 dyne/cm2. The increase in glomerular capillary diameter reduced shear stress while the increased diameters combined with glomerular hypertension increased mean hoop stress from 9.09 to 104.3 kPa. The combination of enalapril and structural adaptations resulted in a mean network shear stress of 81.1 dyne/cm2 and hoop stress of 69.7 kPa.

Conclusions: Our results indicate that glomerular structural adaptations protect the glomerular endothelial cells from increased levels of shear stress, thus preserving kidney function. However, these structural adaptations in turn lead to increased hoop stresses. The combination of enalapril with structural adaptations reduces mechanical stress, providing protection and maintaining function for longer periods.

Funding: NIDDK Support

PO1710
Major Vault Protein Contributes to Increased Interstitial Fibrosis in a Murine Model of CKD
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Background: Chronic kidney disease (CKD) is a global health issue characterized by interstitial fibrosis and tubular atrophy, and progressive CKD results in kidney failure. There is currently no effective intervention for interstitial fibrosis. We previously showed that major vault protein (MVP), a key component of the vault complex, contributed to increased matrix protein deposition in murine unilateral ureteral obstruction (UUO) animal model. We extended our investigations to a murine model of CKD.

Methods: CKD was induced in MVP wild-type (WT) and knockout (KO) mice by feeding a standard diet containing 0.2% adenine for 8 weeks, after which time mice were sacrificed and kidneys were harvested and examined. Spot urine albumin-to-creatinine ratio was also measured. MVP WT and KO mice fed with standard chow served as controls.

Results: MVP WT mice with CKD showed increased MVP expression, predominantly in proximal tubular epithelial cells, compared to MVP WT control mice, and this was accompanied by development of proteinuria, tubular atrophy, tubulointerstitial macrophage infiltration, and increased interstitial extracellular matrix, fibronectin and collagen III expression. MVP KO mice with CKD showed less proteinuria (P<0.05) and less severe kidney histopathological features with reduced immune cell infiltration, and also reduced expression of fibrosis mediators compared to WT CKD mice. Exogenous TNF-α, IL-6, or MCP-1 increased MVP expression in cultured renal proximal tubular epithelial cells.

Conclusions: The data suggest that progressive CKD in this murine model is accompanied by increased renal tubular epithelial MVP expression, and MVP may contribute to the pathogenesis of tubulo-interstitial injury and damage.

Funding: Government Support - Non-U.S.

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537
**PO1171**

**Signaling at the Mesangial Cell (MC) Membrane in Light Chain Deposition Disease (LCDD) and AL-Amyloidosis (AL-Am) Involves Sortilin-Related Receptor (SORL1), Caveolins, and C-Fos**

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**Background:** AL-Am and LCDD are two diametrically opposed glomerulopathies in terms of mesangial alterations produced by glomerulopathic light chains (GLCs). Their pathogenesis involves surface MC interactions resulting in cytoskeletal changes, c-fos translocation, phenotypic transformations, lysosomal activation (AL-Am), rough endoplasmic reticulum expansion (LCDD), and ultimately, mesangial matrix alterations.

The present study addressed signaling pathways involved.

**Methods:** Human (H) MCs (both caveolin 1- wild type / knock-out) were incubated with monoclonal LCs purified from the urine of renal biopsy-proven AL-Am, LCDD, myeloma cast nephropathy (MCN) patients or albumin for up to 96 hours at different time frames. The samples were analyzed using light, immunofluorescence and electron microscopy, including immunolabeling for c-fos, kappa / lambda light LCs, caveolin-1 and SORL1.

**Results:** Co-localizations in cup-shaped MC membrane indentations (caveolae) of GLCs with caveolin-1, and SORL1 were documented using double immunofluorescence and immunogold labeling ultrastructural techniques. Upon interactions with GLC (but not MCNLCs or albumin) caveolae on the surface of MCs increased dramatically, SORL1 was activated and c-fos translocated from cytoplasm to nuclei.

**Conclusions:** SORL1 is a key component of GLCs signal transduction in MCs. Co-localization supported the notion that Interactions of GLCs with MCs occurred in caveolae activating SORL1. Caveolin-1 knock out HMCs abolished c-fos translocation from cytoplasm to nuclei and the downstream mesangial alterations (i.e. mesangial expansions / increased protein production) in LCDD group. In ALLC group, c-fos translocation and amyloid production were decreased but not totally abolished, suggesting that other mechanism may be involved in amyloidogenesis. C-fos plays a crucial role following SORL1 activation to promote mesangial cell phenotypic transformation essential for amyloidogenesis and extracellular matrix over production, in AL-amyloidosis and LCDD, respectively.

**Funding:** Private Foundation Support

**PO1172**

**Compartmental Differences Within the COL3A1 Network in Proteinuric Kidney Disease: Informing Drug Activity Using the Jaccard-Tanimoto Index**


**Background:** In proteinuric kidney disease, type III collagen (COL III) participates in mesangial expansion, cell proliferation, and glomerulosclerosis. Matrix deposition within the tubulointerstitium is associated with worse prognosis. A semi-quantitative analysis was conducted to understand compartmental differences within the COL3A1 transcriptomic network, and to inform therapeutic potential of drugs that mitigate COL III deposition.

**Methods:** Proteins and renal COL3A1 (day 21) mRNA were measured in adult male Wistar rats administered PAN (~100 mg/kg, intraperitoneal). HumanBase was used to build glomerular (G) and tubular (T) COL3A1 transcriptomic networks. Network analysis was restricted to 51 elements each, inclusive of COL3A1, with a minimum interaction confidence of 0.01. The Jaccard-Tanimoto similarity index was used to calculate common elements within the two compartments.

**Results:** The rat PAN model was associated with increased proteinuria, which correlated directly and significantly with renal COL3A1 mRNA expression level. Network analysis revealed a strong positive jaccard COL3A1 interactome with an average strength of 0.40±0.08 and a relatively weaker tubular COL3A1 interactome with an average strength of 0.53±0.01. The Jaccard-Tanimoto similarity index between the glomerular and tubular COL3A1 signaling elements was 5.1%.

**Conclusions:** Glomerulosclerosis in proteinuric kidney disease may result from a relatively strong COL3A1 transcriptomic network within that compartment. Tubulointerstitial matrix deposition is rare in proteinuric kidney disease, possibly due to a weaker COL3A1 transcriptomic network in that compartment. Drugs designed to specifically mitigate COL III deposition might be most effective against glomerulosclerosis.

**Funding:** Other U.S. Government Support

**PO1173**

**The Correlation Between Urinary MicroRNA-21 and Renal Parameters in Patients with IgA Nephropathy**

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**Background:** The expression of microRNA-21 (miR-21) in renal tissue is reported to be related to tubulointerstitial fibrosis and renal outcome in IgA nephropathy. In this study, we examined whether the urinary concentration of miR-21 is related to clinicopathological parameters and short-term changes in renal function in patients with IgA nephropathy.

**Methods:** We extracted and quantified miRNAs in morning spot urine in 88 patients with IgA nephropathy at biopsy and five control subjects, and examined the relationship between clinical and histological parameters, one-year changes in eGFR and urinary miR-21. The concentrations of microRNAs and proteins were corrected to the concentration of urinary creatinine and were log-transformed for simple correlation analysis.

**Results:** The urinary excretion of miR-21 was detected in all subjects, and the urinary concentration of miR-21 in patients with IgA nephropathy was significantly higher than those in controls. Among 88 patients with IgA nephropathy, urinary miR-21 levels showed a significantly positive correlation with the urinary concentration of total microRNA (r=0.65), total protein (r=0.40), beta2-microglobulin (r=0.62), and N-acetyl-beta-D-glucosaminidase (NAG) (r=0.37), but not with baseline GFR, and urinary red blood cells. In contrast, the urinary miR-21 levels did not show a significant correlation with histological changes, including glomerular proliferation/sclerosis and tubulointerstitial fibrosis. The one-year changes in eGFR after biopsy showed a significant inverse correlation with the urinary concentration of miR-21 (r=0.31) and total protein (r=0.37), but not total microRNA, beta2-microglobulin, and NAG. The correlation between urinary miR-21 and one-year change in eGFR was similar in the subjects with and without steroid treatment.

**Conclusions:** In this study, the urinary excretion of miR-21 was associated with clinical parameters and one-year changes in renal function in patients with IgA nephropathy, suggesting that urinary miR-21 might be used as a biomarker of IgA nephropathy.

**Funding:** Government Support - Non-U.S.

**PO1174**

**Diagnostic Delay and the Clinical Prodrome in US Adults with Systemic Light Chain (AL) Amyloidosis with Renal Involvement**

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**Background:** Early therapy for AL can reverse renal impairment, but AL diagnosis (dx) is often delayed. We report the first population-level study of the diagnostic delay in AL nephropathy in systemic AL patients (pts) with prior signs/symptoms (S/Sx) of renal impairment.

The present study addressed signaling pathways involved.

**Methods:** Pts with renal S/Sx at AL dx were identified in the US Optum Clininformatics® claims data since June 2001. AL was defined as ≥1 impatient or ≥2 outpatient AL codes, followed by ≥1 anti-plasma cell therapy in 2 yrs. Renal S/Sx were defined as ≥1 prior dx code for stage 1-3 chronic kidney disease (CKD), renal failure/ESRD, nephrotic syndrome, acute kidney injury, or proteinuria. We described prevalence and overlap of S/Sx and time from first S/Sx to AL dx in renal AL pts. Kaplan-Meier estimates and log-rank tests compared time to AL diagnosis by prior monoclonal gammopathy (MG).

**Results:** Of 870 renal AL pts (67% of AL pts), 70% had CKD, 46% had renal failure, 58% had acute renal failure, 29% had nephrotic syndrome, and 61% had proteinuria by AL dx. Median time since first renal S/Sx and AL dx was 196 days, with a median of 205 days since CKD dx and 23 days from first nephrotic syndrome dx (Figure). Among renal AL pts, 89% had cardiac S/Sx, 67% had neurologic S/Sx, and 57% had ≥3 systems involved. Median time from first nephropathy visit for renal S/Sx and AL dx was 67 days (6 visits). AL dx was earlier for pts with prior MG than without (median 83 vs 210 days, P=0.002).

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.


Conclusions: The median time to AL dx after the first renal Sx/was 196 days and 67 days after the first nephrology visit. The presence of a prior MG shortened the time to AL dx.

Funding: Commercial Support - Janssen Research & Development LLC

PO1715
Case of Leukocyte Cell-Derived Chemotaxin 2-Associated Renal Amyloidosis
Anita Kamarzarian, Masood Mahmood, Golriz Jafari. Olive View Medical Center, Sylmar, CA.

Introduction: Amyloidosis is a disorder characterized by the abnormal deposition of insoluble protein fibrils in tissues. The most recently described form of amyloidosis is derived from leukocyte cell-derived chemotaxin 2 (LECT2).

Case Description: 60 yo with history of HTN and COPD referred for evaluation of proteinuria. Urinalysis showed 1+ protein and 1 RBC. 24 hour urine protein showed 190 mg of protein. Renal Ultrasound was normal and all other serologic labs were normal. She had a Renal Biopsy that showed Congo red positive amyloid deposits and Mass Spectrometry based proteomics analysis showed peptide profile consistent with ALECT-2 type Amyloid deposition.

Discussion: Ever since the first case of ALECT2 was discovered in 2008, several cases have been reported. ALECT2 affects patients mainly of Hispanic origin, especially Mexican Americans. It is less common in African Americans and Caucasians. The pathogenesis of this disease is related to accumulation of a protein called LECT2 which was first isolated in 1998. LECT2 protein is a multifunctional factor involved in chemotaxis, inflammation, immunomodulation, and the damage/repair process. Most patients with ALECT2 present with minimal proteinuria, bland urine sediment and impaired renal function, and the diagnosis of ALECT2 is usually incidental following biopsies for unrelated conditions or uncertain diagnoses. ALECT2 is a slowly progressive disease likely due to the selective involvement of the interstitium. A full nephrotic syndrome is uncommon in renal ALECT2. Neither the renal function nor the proteinuria correlates with the amyloid load in the renal biopsy. There is no specific therapy for ALECT2. Transplantation remains the only effective treatment. But there is a high risk of recurrence in view of ongoing synthesis of the abnormal protein by the liver. In addition to the renal biopsy findings, confirmation of ALECT2 diagnosis requires immunohistochemistry or chemical analysis by tandem mass spectrometry.

POI1716
Idiopathic Fibrillary Glomerulonephritis: A Report of Two Cases
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Introduction: Fibrillary glomerulonephritis(FGN) is a rare glomerular disease characterized by the presence of fibrillar deposits in glomeruli and is associated with poor prognosis, often leading to end stage renal disease(ESRD). Previously considered to be idiopathic, new data suggests there is a secondary association in 30-50% of cases with underlying hepatitis C infection, malignancy, dysproteinemia and autoimmune disease. Immunohistochemical staining for DNA-J heat shock protein B9(DNAJB9) is emerging as a marker for rapid diagnosis of FGN.

Case Description: We report two patients with FGN who initially presented with monoclonal gammopathy(MG), but varied clinical courses. First patient, 60 year-old female presented with MG(IgG4 subclass), acanthocyturia and nephrotic syndrome. Renal biopsy showed PAS positive deposits in capillary loops and mesangium; Immunofluorescence microscopy showed IgG, C3, κ and λ light chains. Electron microscopy showed 20nm non-branching randomly arranged fibrils. Five years later, she is still in remission after treatment with bortezomib, cyclophosphamide and dexamethasone. Another 63 years old female presented with renal failure, positive PANCA and MG. Biopsy showed DNAJB9-positive sclerosing and proliferative FGN with 10% cellular crescents and severe interstitial fibrosis and tubular atrophy. She was treated with corticosteroids and rituximab for idiopathic FGN mimicking type III RPGN. However, she became dialysis dependent.

Discussion: FGN has broad presentation and course despite aggressive therapy. A study determined the strongest predictor of outcome to be initial serum creatinine. Other predictors were age, degree of glomerulosclerosis and proteinuria. Knowledge on pathogenesis along with renal pathology can help differentiate this from other fibril deposition diseases like amyloidosis and immunotactoid glomerulopathy. It is imperative to promptly identify FGN as it often progresses to ESRD and has limited data on optimal therapy.

POI1717
A Case of Secondary Focal Segmental Glomerulosclerosis and Thrombotic Microangiopathy in a Heart Transplant Patient
Neha Deval, Hay Me Me, Jennifer Griffiths, Arromma Kapoor, Savneek S. Chugh. Westchester Medical Center, Valhalla, NY.

Introduction: A few case reports have shown that focal segmental glomerulosclerosis (FSGS) can lead to thrombotic microangiopathy (TMA) in chronic kidney disease patients with severe hypertension. One case report presented the development of FSGS and TMA in liver transplant patient on Thyroxine kinase inhibitor. We present a case of FSGS without vascular injury despite clinically diagnosed TMA in heart transplant patient.

Case Description: A 42-year old female with history of postpartum cardiomyopathy with implantable cardioverter defibrillator since 2005 was admitted for heart transplant evaluation. Patient developed rapid progressive worsening of renal failure requiring hemodialysis after the heart transplant. Urinalysis showed proteinuria, hematuria; blood work showed hemolytic anemia, thrombocytopenia and schistocytes. TMA was diagnosed and eculizumab was started while continuing with hemodialysis. Heart biopsy showed no rejection, but kidney biopsy revealed the pathological diagnosis of secondary FSGS of not otherwise specified type without vasculitis under both light and electron microscopy. No significant glomerular staining seen on immunofluorescence microscopy as well. Patient was maintained on immunosuppressive regime with mycophenolate, tacrolimus and prednisone, receiving eculizumab weekly for 3 months, and subsequently recovered from hemodialysis.

Discussion: It is very rare to have FSGS without microangiopathy in hematologically confirmed TMA. Calcineurin induced inhibitors (CIN) are known to cause various forms of acute kidney injury including FSGS. In our case, presumed calcineurin induced nephrotoxicity presented as secondary FSGS without angiopathy. This case reflects the unpredictability of the etiology of kidney disease based solely on clinical features and blood tests. No improvement in kidney function necessitated the renal biopsy. It also raises the challenging points in treatment regime in transplant patient populations.
years on compound heterogenous Wilson’s disease diagnosed by liver biopsy, Western blotting and gene sequence on ATP7B. Serum creatinine(Cr) was around 4.5 mg/dl, antimonylperoxidasem(MPO)-ANCA 350 U/ml, antinuclear factors titer 1/640. Both anti-proteinase(PR3) antibody and anti-glomelular basement membrane(GBM) antibody were negative. Renal biopsy specimen show pauci-immune crescentic glomerulonephritis with 7/9 fibrods or fibrocellular crescents, and 2/9 global collapsing sclerosis. Also, mild diffuse interstitial fibrosis was found with lymphoid and other chronic inflammatory cells. No pathological finding was detected on vasculitis. Diagnosed as ANCA-associated proteinase(PR3) antibody and anti-glomelular basement membrane(GBM) antibody were antimyeloperoxidase(MPO)-ANCA 350 U/ml, antinuclear factors titer 1/640. Both anti-


PO1719
In Silico Prediction of Potential New Biomarkers of IgA Nephropathy
Intestinal Lesion
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Background: IgA nephropathy remains one of the major causes of end stage renal diseases globally. Interstitial lesion in IgA nephropathy is correlated with unfavorable prognosis. This study aims to find new potential biomarkers in IgA nephropathy patients with interstitial lesion based on an in silico method.

Methods: Proteomics matrix data from IgA nephropathy patients are obtained from a local renal biopsy patient cohort. Discovery is determined using the Two-stage linear step-up procedure of Benjamini, Krieger and Yekutieli, with Q = 1%. Transcriptomic data from peripheral mononuclear blood cell of IgA nephropathy patients are obtained from GEO (GSE73953). Detection of transcriptomic difference genes are made with limma method in GEO2R.

Results: Multiple t test indicates 887 differentially expressed genes between IgA nephropathy interstitial lesion (T1 or T2) and control renal tissue. KEGG pathway annotation reveals that cytochrome p450 related drug metabolism pathway and oxidative phosphorylation pathway are significantly clustered in IgA nephropathy patients with interstitial lesion. No herbal medicine or drug use (apart from ACEI or ARB) were recorded. Differential gene analysis reveals a total of 250 genes with positive discoveries in peripheral mononuclear blood cell of IgA nephropathy compared with membranous nephropathy (GSE73953). Further screening of overlapping genes demonstrates that ABCD3, CLPTM1, FMHO, RARS2, SFNX2 are the most significantly enriched proteins in IgA patients with interstitial lesion.

Conclusions: Preliminary results from this in silico study of proteomics and transcriptomics data in IgA nephropathy patients using a T score specific and overlapping screening approach provide a new possibility of noninvasive detection of interstitial lesion in IgA nephropathy patients.

PO1720
Pacemaker Macula Densa Cells Form a Nephron-Level Autonomous Somatosensory Neuronal Network
Georgina Gvaramati, Anne Riquier-brison, Urvi Nikhil Shroff, Janos Peti-Peterdi. University of Southern California, Los Angeles, CA.

Background: The autonomous nervous system in several organs performs local control of organ functions. Macula densa (MD) cells that are specialized renal epithelial cells capable of sensing the local tissue environment and releasing various chemical messengers to control nearby cells have well-known neuronal features. This study addressed the hypothesis that MD cells perform neuron-like functions that play important roles in maintaining key organ functions.

Methods: MD-GT mice with MD-specific inducible expression of the Ca2+ sensitive fluorescence reporter GCaMP5 and the calcium insensitive tdTomato were developed to visualize the Ca2+ homeostasis of MD cells with multiphoton microscopy (MPM). Whole transcriptome RNA seq was performed to establish the gene profile of MD cells providing molecular detail of their function.

Results: MD cell imaging in vivo revealed regularly oscillating, propagating Ca2+- firing pacemaker activity with peaks showing ~4-fold elevations and average frequency of 0.03/s. This phenomenon was preserved in freshly isolated MD-GT cells in vitro indicating autonomous pacemaker function. Several divergent stimuli altered steady-state Ca2+ and/or firing frequency, including mechanical (tubule flow), altered tubular fluid composition (low salt diet), local autacoids (angiotensin II), systemic hormones (AVP, CaSR mimetic), and metabolic states (diabetic hyperglycemia). Bolus injection of the β-agonist Isoproterenol caused the most robust changes in firing frequency as compared to control (frequency fold change 3.4±0.6 and 0.9±0.1, respectively). Diabetic hyperglycemia was associated with the greatest increase in firing frequency as compared to control (frequency fold change 3.4±0.6 and 0.9±0.1, respectively). MPM

PO1721
A New View of Macula Densa Cell Protein Synthesis
Urvi Nikhil Shroff, Georgina Gvaramati, Anne Riquier-brison, Audrey Izuhara, Janos Peti-Peterdi. University of Southern California, Los Angeles, CA.

Background: Macula densa (MD) cells, a chief regulatory cell type in the kidney, have prominent protein synthetic organelles. mRNA translation and protein synthesis are tightly regulated processes and the mTOR and Wnt signaling pathways play a central role in regulating this activity. The present study aimed to examine the role of Wnt/mTOR in regulating MD protein synthesis.

Methods: Changes in bulk protein synthesis activity were quantitatively visualized using an OPP-incorporation based fluorescence assay in a new mouse MD cell line (mMD) treated with low salt medium or the GSK3β inhibitor lithium to activate MD cells. For studies in vivo, MD-Wnt and MD-mTOR mice were developed using a nNOS-Cre inducible system with Wnt and mTOR gain-of-function, respectively, to

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upregulate signaling specifically in MD cells. MD gene profiling validated by data from Human Protein Atlas (HPA) was used to confirm expression of various pathways and regulators of protein synthesis and vesicular exocytosis. 

Results: OPP experiments in mMDrd cells in vitro showed that low salt (5.9 ± 1.15) and lithium (5.67 ± 0.24) treated cells had significantly higher protein synthetic activity as compared to control (3.13 ± 0.15). Similarly, MD cells in vivo in wildtype mice on a low salt (2.59 ± 0.26) or lithium diet (2.00 ± 0.26) had significantly higher OPP fluorescence as compared to control diet (1.16 ± 0.18). Upregulation of MD-Wnt signaling in MD-Wnt45 mice (1.36 ± 0.04) also resulted in a significant increase in MD protein synthesis as compared to control (1.06 ± 0.06). The expression profiles of MD-specific activated proteins (Ccn1, Pappa2, Nov, Cxcl14) was enhanced in activated MD cells. Finally, results from MD gene profile analysis with HPA validation showed high MD-specific expression of several pathways involved in mRNA translation (706SK6, eIF3C, eEF2), chaperones (HSPA1B) along with key components of protein synthesis and vesicular exocytosis.

Conclusions: In conclusion, the unique MD microanatomy and cell-specific protein synthetic machinery support the robust synthesis and secretion of a diverse array of tissue remodeling and angiogenic proteins which are regulated by mTOR and Wnt signaling in these cells. The regulatory pathways MD protein synthesis and secretion may be targeted to enhance endogenous glomerular and vascular tissue remodeling and repair.

Funding: NIDDK Support, Private Foundation Support

PO1722
Kidney Transcriptome-Wide Association Study Analysis Identifies Dach1 as a Kidney Disease Risk Gene
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Background: Genome-wide association studies (GWAS) has identified more than 300 loci where genetic variants are associated with kidney function, however, the causal variants, genes, cell types and the disease mechanism remain mostly unknown. Transcriptome-wide association studies (TWAS) is a method to prioritize GWAS-identified variants by linking gene expression data to phenotypic and genetic variation. Methods: We obtained genotype and gene expression data for 121 microdissected human kidney tubule and glomerular samples. We applied a variety of TWAS models, such as Mendelian Randomization, TWAS Fusion, Metaxan. Bulk kidney epithogen maps and single cell ATAC-Seq data were used for fine-mapping. We generated tubule specific Dach1 knock-out (KspCre/Dach1flox/flox) and transgenic (Pax8-TREDach1) mice to define the functional role of Dach1 in kidney disease development. Murine cultured tubule and single cell RNA sequencing were used for functional studies. Results: Integration of the 3 TWAS methods with CKD GWAS datasets highlighted only 5 genes those levels were consistently influenced by the GWAS variants. The strongest prediction of DACH1; a transcription factor, was lower in tubules of patients with CKD risk variant. Immunofluorescence analysis indicated that DACH1 was mainly expressed in podocytes and in distal convoluted tubule (DCT) in the kidney. Bulk and single cell ATAC-TWAS showed that DACH1 risk variants knocked up (KapC/T) Dach1 (Dox/box) and transgenic (Pax8TREDach1) mice to define the functional role of Dach1 in kidney disease development. Murine cultured tubule and single cell RNA sequencing were used for functional studies.

Conclusions: Integration of GWAS, TWAS, single cell expression, epigenome analysis, mouse models and cultured cell systems identified Dach1 as a causal gene for CKD.

Funding: NIDDK Support

PO1723
Role of Plin5 Deficiency in Podocyte Lipotoxicity and the Progression of Alport Syndrome
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Background: Alport Syndrome (AS) is a hereditary disease caused by mutations in collagen type IV. We and others have demonstrated pathogenic renal lipid accumulation in experimental AS (Col4a3KO mice). Excess lipids stored in lipid droplets (LD) as cholesteryl ester and triglyceride (TG) are known to cause lipotoxicity. Excessive FFA catabolism resulting from excessive lipolysis of TG is a major contributor to cell lipotoxicity in obesity and diabetes. Perilipin 5 (PLIN5) is a LD-related protein that plays a critical role in the regulation of triglyceride lipase activity and in the interactions between LD and mitochondria, where it protects mitochondria from excessive exportation of FFA. Here we test the hypothesis that PLIN5 is express in podocytes and that excessive TG breakdown occur in AS podocytes as a consequence of PLIN5 deficiency.

Methods: Immunolabeled AS podocytes (AS podocyte) and WT podocytes were established from mice with clinical nephropathy by our laboratory by breeder colony at Immortal mouse (Charles River). PLIN5 expression was determined by RT-PCR and western blot analysis in podocytes from Col4a3KO mice when compared to controls. TG lipolysis and FFA quantification were determined and normalized to protein content. Experiments were performed by using cells from multiple donors. Results: We demonstrate that PLIN5 is expressed in podocytes and the expression of PLIN5 was significantly decreased in AS podocytes when compared to WT podocytes (p<0.01). AS podocytes also showed significantly increased rates of TG lipolysis (p<0.05), intracellular free fatty acids (p<0.05) and apoptosis (p<0.01) when compared to WT podocytes. As podocytes had increased protein leak, implying that the FFA may uncouple the mito-organellar dysfunction and apoptosis. Moreover, exosome, which in vivo improved kidney function was found to in vitro restorePLIN5 expression in a dose-dependent manner.

Conclusions: Our study suggests that podocyte PLIN5 deficiency may cause podocyte injury in AS through excessive TG lipolysis and mitochondrial dysfunction.

Funding: Private Foundation Support

PO1724
The Mesenchymal Stem Cell Marker Meflin Defines a Novel Subset of Renal Fibroblasts and Counteracts the Action of TGF-β
Shun Minatoguchi, Shoji Saito, Shoichi Maruyama, Nagoya university graduate school of Medicine, Department of Nephrology, Nagoya, Japan.

Background: Fibroblasts proliferation is the hallmark of renal fibrosis and is important for the progression of CKD. Recently developed single-cell sequencing technology has revealed the substantial heterogeneity of cells that constitute the kidney in health and disease. The heterogeneity of renal fibroblasts, however, has not been completely understood. We recently reported that a fibroblast subset marked by Meflin, and a group of undifferentiated mesenchymal stem cells, has a role to suppress fibrosis in cardiac disease conditions and pancreatic cancer. In the present study, we examined the role of Meflin and the distribution of Meflin-positive fibroblasts in kidney by using cultured fibroblasts and mouse models.

Methods: We evaluated the expression of Meflin in normal and fibrotic kidney by in situ hybridization (ISH). To assess the expression of Meflin at a cellular level, we used the rat renal fibroblast cell line NRK49f. Results: ISH revealed that Meflin was expressed by some rare stromal cells found in the interstitial and peri-glomerular areas in the normal kidney. Meflin-positive cells were detected in the wall of middle-sized vessels in the medulla of the kidney. Induction of renal fibrosis by obstructive nephropathy(UUO model) led to a significant proliferation of Meflin-positive cells, which seemed to be distinct from αSMA positive myofibroblasts.

Conclusions: Our present study identified a new subset of renal fibroblasts, which is positive for Meflin but negative or weakly positive for αSMA. Consistent with our previous studies, Meflin has a role to counteract the action of TGF-β, implying that Meflin-positive fibroblasts have a role to suppress or alleviate renal fibrosis.

Funding: Private Foundation Support

PO1725
CD14 Contributes to Increased Inflammation and Fibrogenesis in Lupus Nephritis
Jing Yu,1 Chi pang Tai, Susan Yung, Tak Mao D. Chan. University of Hong Kong, Hong Kong, Hong Kong.

Background: CD14 is a G-protein-coupled membrane protein that serves as a pattern recognition receptor in the clinical setting of sepsis. CD14 transfers lipopolysaccharide (LPS) from the acute phase protein LPS-binding protein (LBP) to TLR-4-MD-2 complex, to initiate signal transduction and cytokines release. Serum CD14 level is increased in SLE patients, but little is known about its clinical significance or pathogenic role in lupus nephritis (LN).

Methods: Serum LPS and CD14 levels were determined in LN patients and healthy subjects using commercially available assays. CD14 expression in LN kidney biopsies was examined by cytochemical staining. CD14-overexpressing HK-2 cells were generated and the role of CD14 in inflammatory and fibrotic processes investigated.

Results: Serum LPS and CD14 levels were determined in LN patients and healthy subjects using commercially available assays. CD14 expression in LN kidney biopsies was examined by cytochemical staining. CD14-overexpressing HK-2 cells were generated and the role of CD14 in inflammatory and fibrotic processes investigated.

Conclusions: Our present study identified a new subset of renal fibroblasts, which is positive for Meflin but negative or weakly positive for αSMA. Consistent with our previous studies, Meflin has a role to counteract the action of TGF-β, implying that Meflin-positive fibroblasts have a role to suppress or alleviate renal fibrosis.

Funding: Private Foundation Support
PO1726
CircZNF609 Participates in the Pathogenesis of Focal Segmental Glomerulosclerosis by Sponging miR-615-5p
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Background: Focal segmental glomerulosclerosis (FGS) is the most common cause of adult nephrotic syndrome, but its mechanism remains unclear. We recently identified and validated that circZNF609 increased in renal biopsies of lupus nephritis patients. We aim to explore whether circZNF609 participates in the pathogenesis of FGS and the underlying mechanisms.

Methods: FGS was induced by adriamycin (ADR) injection to mice. Proteinuria and serum albumin were examined six weeks after ADR administration. Glomerulocrescence and tubulointerstitial fibrosis were verified on PAS and Masson staining. Podocyte injury indicated with Wilms tumor 1(WT1) and Podocin, pro-fibrotic proteins including collagen 1 (COL1) and transforming growth factor-beta1 (TGF-β1) were analyzed by western blotting. Further, renal circZNF609 and miR-615 were measured by qPCR and fluorescence in situ hybridization (FISH). The correlation between renal circZNF609 and above indices were analyzed. In vitro study, circZNF609 in bovine serum albumin (BSA) stimulated HK2 cells for 24 h, which mimic the toxicity of proteinuria from FGS to tubules. CircZNF609, miR-615, COL1 and TGF-β1 were analyzed by qPCR. Lastly, The renal localization of circZNF609 in FGS patients was stained by FISH.

Results: In vivo study, proteinuria and hypoalbuminemia were found six weeks after FGS onset by ADR injection. Glomerulocrescence and tubulointerstitial fibrosis showed on PAS and Masson staining. CircZNF609 was upregulated while miR-615-5p was downregulated in FGS mice analyzed by qPCR and FISH. Podocyte proteins WT1 and Podocin were decreased; pro-fibrotic proteins COL1 and TGF-β1 were increased on western blotting. Renal circZNF609 positively correlated and miR-615-5p negatively correlated with podocyte injury and renal fibrosis. Importantly, circZNF609 and miR-615-5p co-localized on glomeruli and tubules on FISH. Perfect match seeds were found between circZNF609 and miR-615-5p and COL-1. In vitro study, circZNF609 increased and miR-615-5p decreased after BSA stimulation and negatively correlated between each other. COL-1 and TGF-β1 were upregulated and negatively correlated with miR-615-5p. Lastly, circZNF609 was confirmed to increase in glomeruli and tubules in renal biopsies from FGS patients.

Conclusions: We conclude that circZNF609 may play an important role in FGS by sponging miR-615-5p and may be a novel therapeutic target.

Funding: Government Support - Non-U.S.

PO1727
The Role of Proteoglycans in Glomerular Physiological and Pathophysiology

Background: Diabetic kidney disease (DKD) is the leading cause of renal failure in the world. Diabetes is associated with damage to the endothelial glycocalyx (eGCX), the layer of negatively charge molecules, such as proteoglycans (PGs) that cover the cells. The negatively charge restrain the flow of charged molecules, as albumin, over the filtration barrier. Loss of the glomerular eGCX leads to proteinuria without other visible damage to the barrier, but the composition of this structure is still largely unknown. The aim of this study was to gain new knowledge about the composition and role of the eGCX in health and DKD.

Methods: The negatively charged PGs in the eGCX was eluted from rats using 1 M NaCl solution (high salt), 1 M mannitol was used as osmotic control (HO) and 0.15 M NaCl as physiological salt (NS). Solutions were introduced intra-arterially to rat kidneys under anesthesia in vivo. Venous effluent was analyzed using mass spectrometry. Fractional clearance of albumin and GFR was measured. Electron microscopy (EM) was used to investigate morphology. Expression of PGs and PG related genes in glomeruli from patients with DKD was investigated using deep sequencing data from the Swedish DKD cohort (DKD n=19, controls n=20).

Results: We identified 17 PGs in the eluates from rats. PGs were found in the highest yields in the HS samples. EM demonstrated that the eGCX thickness was significantly reduced in the HS rats compared to NS. Rats perfused with HS had significantly increased fractional clearance of albumin and reduced GFR, compared to NS and HO, 10 minutes after perfusion. In glomeruli from patients with DKD 12 PGs were found to be significantly regulated, and 4 of these PGs were also identified in the eGCX eluates from rats. There was an overall decrease in expression of enzymes responsible for PG side chain synthesis and an increase in proteins involved in PG degradation.

Conclusions: In our study, we identified several PGs novel to the glomerular eGCX. We show that the systemic fed mice GFR, stronglysuggesting that the eGCX is important for preventing proteinuria. In glomeruli from patients with DKD we found significant changes in the gene expression of PGs, indicating a changed composition of the matrices in the glomeruli. Further investigation is needed to clarify how these changes are involved in development of DKD, and especially the eGCX.

Funding: Private Foundation Support, Government Support - Non-U.S.

PO1728
Low- vs. Standard-Dose Rituximab for Induction and Maintenance Treatment of ANCA-Associated Vasculitis in Elderly Patients: A Single-Centre Observational Study
Shams Ur Rehman, Ethakum Metraia, Dana Kidder. Aberdeen Royal Infirmary, Aberdeen, United Kingdom.

Background: ANCA associated vasculitis (AAV) affects more than 20 per million population per year, with a peak age of 65-74 years. Elderly patients (Age > 65 years) with AAV tend to have higher rates of mortality and treatment-related adverse events. However, outcomes are better for those treated with immunosuppressive regimens. Rituximab is now widely used in the treatment of AAV based on the results of randomized controlled trials. Elderly patients were relatively under-represented in these trials. We aimed to examine the outcome of elderly patients who received either low dose Rituximab (LDR) or standard-dose (SDR) for remission induction and maintenance.

Methods: We investigated the outcome of three treatment strategies in the elderly patients who presented with AAV to our Vasculitis clinic from July 1, 2007 to July 9, 2017. These strategies included: LDR (17 patients), SDR (14 patients) and Cyclophosphamide/ Azathioprine (Cyc/A) 26 patients. LDR patients received two doses of 500mg Rituximab fortnightly followed by six monthly 500mg doses for 2 years. SDR patients received 1g Rituximab fortnightly followed by six monthly 1g doses for 2 years. Cyc/A patients received 1.5mg/kg oral Cyclophosphamide for 3 months followed by 18 months of Azathioprine.

Results: Among 57 AAV patients, 17 received LDR, 14 received SDR and 26 were treated with Cyc/A. 56% were females, mean age of 76 +/- 6.6 (LDR), 72.4 +/- 7.2 (SDR), and 71.1 +/- 7.5 (Cyc/A) (p=0.001). The distribution of MPA and GPA was 11.6 in LDR, 7.7 in SDR and 18.8 in Cyc/A, respectively. Relapsing AAV was significantly higher in SDR 12 of 14 compared to LDR 3 of 17, and Cyc/A none (p<0.0001). There were no significant differences in serum creatinine, BVAS scores or CRP between groups. Patients survival at 2 years was 88% (LDR), 92% (SDR), and 77% (Cyc/A), p=0.3. The mean corticosteroids dose at 3 months from onset of treatment was significantly lower in the LDR (7.6 +/- 1.7) and SDR (8.6 +/- 3.1) compared with Cyc/A (12.5 +/- 3.6), p<0.0001. One patient relapsed in the SDR group and 4 in the Cyc/A group. Hospitalization for infections were seen 5 times higher in the LDR compared to Cyc/A (17 episodes), p=0.001.

Conclusions: Low dose Rituximab for remission induction and maintenance was associated with similar patient outcome compared to SDR.

Funding: Government Support - Non-U.S.
Methods: All patients in the MAINTANCAVAS trial were included. Patients were enrolled after a 2 years of continuous B cell depletion. B cells were measured at 3-month intervals with a a 2 week window. Days to B cell return were calculated as the time from the last rituximab dose (1000 mg) to date of first detectable CD20 B cells by flow cytometry. Kaplan Meier curves were produced for each round of B cell depletion.

Results: We analyzed data from 109 patients. Median (IQR) duration of B cell depletion was 280.0 (272.0 – 363.0) days until first episode of recovery (Table 1). >80% of subjects had B cell return by 1 year and <10% had B cell return prior to 6 months (Figure 1). Median (IQR) duration of B cell depletion was 265.0 (247.0 – 354.5) days for patients who received a second round of rituximab (Table 1).

Conclusions: This data suggests that after 2 years, maintenance RTX dosing can be extended beyond 6 months for many patients. Further analysis is needed to determine optimal dosing based on B cell return vs ANCA titer and the associated adverse event profiles and RTX utilization.

Table 1. Demographics and B cell depletion duration (median (IQR)).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naotake</td>
<td>280.0 (272.0 – 363.0)</td>
</tr>
<tr>
<td>Japan</td>
<td>265.0 (247.0 – 354.5)</td>
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</table>

Figure 1. Kaplan-Meier for B cell depletion.

PO1731

Predictive Significance of Urinary CD11b and CD163 for the Renal Outcomes in ANCA-Associated Glomerulonephritis

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Background: We hypothesized that the detection of leukocyte-derived CD11b (a subunit of integrin Mac-1) and CD163 (scavenger receptor) in urine may reflect renal inflammation and predict the renal outcomes in anti-neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-GN). The aim of this study was to evaluate the clinical significance of urinary CD11b (U-CD11b) and CD163 (U-CD163) as alternative noninvasive tests for ANCA-GN.

Methods: U-CD11b and U-CD163 levels were examined using ELISA in ANCA-GN urine samples from institutional cohort (n = 88) and a nationwide cohort (n = 138), and their association with renal histology were analyzed. Logistic regression analyses were performed on a nationwide ANCA cohort to determine the associations of the two urinary molecules with renal remission failure at 6 months or with yearly eGFR slope over a 24-month observation period.

Results: The significant elevations of U-CD11b and U-CD163 were observed in ANCA-GN patients histologically classified to the crescentic category. Histological analyses focusing on the distributions of CD11b+ or CD163+ leukocyte subsets in diseased glomeruli demonstrated dominant distribution of CD11b+ cells in undisturbed area than in glomerular crescent as contrasted with global distribution of CD163+ cells in diseased glomeruli. In addition, levels of U-CD11b and U-CD163 significantly correlated with crescent formation rate, respectively with CD11b+ cell and CD163+ cell number in glomerular crescents. Association analyses of both urinary molecules with post-treatment renal outcomes at 6 months after the treatment demonstrated that U-CD163 levels were significantly reduced and those at the time of diagnosis were already increased in patients who failed to remission or progressed renal insufficiency. Although these associations were not found in U-CD11b, analyses to determine the associations of the two urinary molecules and other clinical parameters with yearly impairment of renal function over a 24-month observation period demonstrated U-CD11b, but not U-CD163, at diagnosis as an independent factor predicting renal recovery.

Conclusions: Although both U-CD11b and U-CD163 reflect renal leukocyte accumulation, U-CD11b at diagnosis predicts the recovery rate after the treatment of ANCA-GN.

Funding: Government Support - Non-U.S.

PO1732

Urinary Biomarkers as a Tool for Monitoring Remissions and Predicting Relapses in Autoimmune Glomerulonephritis

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Background: Complement-mediated injury, inflammation and fibrosis play central roles in the pathogenesis of autoimmune glomerulonephritis. The use of urinary biomarkers as a surrogate of these pathways of injury could assist clinicians during the clinical follow-up. We investigated the value of urinary biomarkers of complement activation, inflammation and fibrosis during periods of sustained remission among patients with autoimmune glomerulonephritis.

Methods: We prospectively examined 100 patients with ANCA-associated vasculitis, focal segmental glomerulosclerosis, IgA nephropathy, lupus nephritis, membranoproliferative glomerulonephritis and membranous nephropathy. Proteinuria, urinary sC5b-9, monocyte chemoattractant protein-1 (MCP-1) and transforming growth factor-β1 (TGF-β1), expressed as creatinine ratios, were measured at presentation and during follow-up visits. We used standard definitions of remission and relapse for each type of glomerulonephritis. Wilcoxon signed-rank test was used to compare changes in urinary biomarkers during remissions and relapses.

Results: We identified 95 periods of active disease and 82 episodes of sustained remission. Inactive periods lasted a median of 22 (11-32) months. Eighty percent (n=66) of these were not followed by a relapse. During these episodes of remission, urinary biomarkers continued to steadily decrease, achieving a reduction of 40% for proteinuria, 38% for urinary sC5b-9, 38% for MCP-1 and 40% for TGF-β1 (all p < 0.05). Twenty percent (n=16) of inactive periods reflected remissions with subsequent relapses. Biomarker levels during the inactive period preceding relapses did not significantly change for proteinuria (+8%), urinary sC5b-9 (+15%) and MCP-1 (+4%) while they decreased for TGF-β1 (-30%, p<0.02). During relapses, we observed a 3.2-fold (1.98-3.3) increase in proteinuria and a significantly greater 8.5-fold (4.2-56.9) increase in urinary sC5b-9 (p=0.001). By contrast, urinary MCP-1 and TGF-β1 increased significantly less than proteinuria.

Conclusions: Failure to achieve a sustained reduction in urinary biomarkers during remission was associated with a subsequent risk of relapse of autoimmune glomerulonephritis. Urinary sC5b-9 appears to be a more discerning marker of immunological relapse.

Funding: Private Foundation Support

PO1733

Clinical Impact of PRTN3 Polymorphism in Antineutrophil Cytoplasmic Antibody (ANCA) and Similar Vasculitides


Background: Genetic variants associated with ANCA vasculitis include a single-nucleotide polymorphism (SNP) at the proteasine 3 (PRTN3) locus, however the impact of this risk variant on demographics and disease characteristics has not been fully described.

Methods: 401 patients with ANCA and similar vasculitides from the Glomerular Disease Collaborative Network were genotyped for the PRTN3 SNP (rs62132293): myeloperoxidase (MPO) (n=197), proteinase 3 (PR3) (n=170), dual positive (n=9), and seronegative (n=25). SNP homoygous (“GG”) were compared to heterozygotes (“CG”) and homoygous (“CC”). PRTN3 expression was measured by quantitative polymerase
chain reaction amplification of cDNA from patient peripheral blood polymorphonuclear leucocytes during active disease. Comparisons were done using Fisher exact and Wilcoxon tests or ANOVA. Bonferroni correction and Tukey test used for multiple comparisons Cox regression was used for multivariable time to relapse and end stage kidney disease (ESKD), with hazards ratios (HR), 95% confidence intervals (CI) reported.

Results: 179 CC, 181 CG and 41 GG patients with median follow-up of 4.8 years were studied. GG patients were significantly younger at disease-onset than others (FIGURE, A). There were no statistical differences in race/sex categories, ANCA seropositivity, organ involvement, or estimated glomerular filtration rate between groups. In a subset of the cohort (n=298) GG had significantly higher peak expression of PRTN3 (FIGURE, B). In the entire group, renal disease was predominant (CC 78%, CG 83%, GG 76%, p = 0.34) and the majority of the treated patients reached remission (91% CC, 88% CG and 90% GG, p=0.79). Upon remission there was no difference in time to first relapse in GG vs. others (HR 1.02, CI 0.62,1.68, p=0.94) and time to ESKD (HR 0.62, CI 0.15, 2.67, p=0.52) adjusted for age and seropositivity.

Conclusions: Disease starts at an earlier age among GG patients, with no clear impact on outcomes. Higher PRTN3expression may explain earlier disease onset.

Funding: NIDDK Support

Figure 1. Altered gut microbiota in CreGN. a)PCoA. b)LEfSe. c)Spearman correlation. A1:CreGN, A2:Control.

POI1734

Role of Repeated Renal Biopsy in ANCA Vasculitis


Background: Pauci-immune necrotizing crescentic glomerulonephritis is a severe renal complication of AAV. Despite immunosuppressive therapy, relapses are frequent during the course of the disease. Kidney biopsy is routinely used to diagnose AAV at initial presentation. Although the activity of renal AAV is not easily evaluated by plasma or urine biomarkers, kidney biopsy is rarely performed when relapse is suspected. We herein analyze the clinical, laboratory and renal pathology data from patients who underwent repeated kidney biopsies during the course of AAV.

Methods: We retrospectively reviewed data from 37 patients who underwent at least 2 kidney biopsies in our centre, between 2002 and 2018. The first renal biopsy (B1) was constantly performed at diagnosis. A follow-up biopsy (B2) was performed for purpose, either for suspicion of refractory disease or confirmation of renal relapse. Modifications of renal pathology between B1 and B2 were studied, by comparing presence of active and chronic lesions.

Results: The median delay between B1 and B2 was 3,3 [0,9-5,8] years. B2 was done for suspicion of refractory disease (n=8) or of renal relapse (n=29). Causes of B2 were : persistence or reappearance of haematuria in 78% of cases, increase of creatinine in 43%, increase of ANCA titer in 67%. Systemic AAV activity was more important at B1 vs B2 (median BVAS 18 vs 9), as well as renal dysfunction (median sCreat 200 vs 156 μmol/l). Active glomerulonephritis was constantly found at B1 but was present in only 35% of B2. Presence of cellular crescents decreased from 71,4 to 29,7% (p = 0,002), whereas fibrinoid necrosis decreased from 80,6 to 35,1% (p = 0.0003). Five factors were significantly associated with the presence of active lesions : presence of at least one extra-renal AAV manifestations (p = 0.0006), increase of ANCA titer (p = 0.002), CRP>30mg/l (p = 0.001), absence of IF/TA (p=0.02) and high percentage of normal glomeruli (p=0.014) at B1. Interestingly, level of proteinuria and persistence of hematuria were not associated with histological activity at B2 (p =0.64 and 0.22 respectively). In contrast, chronic lesions were more severe at B2 compared to B1 (p <0.0001 and 0.014 respectively).

Conclusions: Despite several clinical and laboratory signs suggesting active renal AAV, B2 revealed no relapse in 2/3 of cases, allowing avoidance of a new immunosuppressive induction treatment.

Funding: NIDDK Support

POI1735

Single-Center Experience of Antineutrophil Cytoplasmic Autoantibody-Associated Vasculitis in a Region of Central Appalachia

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Background: Antineutrophil cytoplasmic autoantibody-associated vasculitis (AAV) is a rare disease with significant morbidity and mortality. Suspicions that our caseload of AAV might exceed the estimated 3 in 100,000 incidence estimates prompted us to investigate the characteristics of our patients with AAV.

Methods: A retrospective study of all patients diagnosed with AAV at our center prior to December 31, 2019 was performed. Patients were identified based on ICD10 (349),
ICD 9 (1846) codes or diagnosis of a positive ANCA lab test (589). Charts were reviewed for demographic and clinical information. Incidence was estimated for the 10-year period being January 1, 2009 using population estimate.

Results: A total of 225 patients had a confirmed diagnosis of AAV of whom 114 were males (50.6%) and 111 females (49.4%). 94.7% were Caucasian, 2.2% African American and 2.2% Hispanics, reflective of our population. Most were older (50.2% >60 years). The kidneys (67.6%), lungs (42.2%) and ENT organs (30.2%) were most commonly involved. The predominant ANCA subtype was p-ANCA (52.3%), followed by c-ANCA (43%) and ANCA-negative (4.7%). p-ANCA was most common in patients with renal involvement (58.8%) and c-ANCA was most common in patients with ENT involvement (60%); p <0.01. Of those with renal involvement, 51 needed dialysis (33.6%), 47 of whom became dialysis-dependent (30.9%). Mortality was high in patients with kidney (32.2%) and lung involvement (30.2%) compared to those with ENT involvement (16.2%); p=0.04. Preliminary estimates suggest a regional incidence that may exceed that of other states.

Conclusions: In our population, p-ANCA was the predominant subtype and incidence estimates did not mirror those of other areas. These findings suggest that AAV may differ in subtype predominance and incidence by geographic setting.

Organ Involvement

PO1737
Exploring the Role of Type I Interferons in ANCA-Associated Vasculitis
Isabella Batton,1 Mark W. Robinson,2 Arthur White,3 Barbara Fazekas,3 Cathal D. Walsh,3 Jason Wye,3 Suzanne D’Arcy,1 Antonia Buettner,1 Mark A. Little,1 Nollaig M. Bourke,1 Trinity Health Kidney Centre, Trinity Translational Medicine Institute, Trinity College Dublin, Ireland, Dublin, Ireland; 2School of Computer Science and Statistics, Trinity College Dublin, Dublin, Ireland; 3Department of Mathematics and Statistics, University of Limerick, Limerick, Ireland. 

Background: ANCA-associated vasculitis (AAV) is a group of autoimmune diseases characterised by inflammation of small blood vessels. Type I interferons (IFNs) are cytokine mediators of the innate immune response, most known for their anti-viral properties. Dysregulation of type I IFNs is a major factor in the development of several autoimmune diseases, now termed type I interferonopathies, and thought to be the pathogenic link with chronic inflammation in these conditions. Despite evidence of type I IFNs driving autoimmunity, they have not been comprehensively studied in AAV. We hypothesised that type I IFN responses are systemically dysregulated in AAV, indicative of a type I interferonopathy.

Methods: Matched whole blood and serum samples collected from healthy individuals (n=67), disease control patients (n=32) and AAV patients (n=71) were obtained from the Rare Kidney Disease Biobank of Ireland. qPCR was used to measure gene expression of the type I IFN gene (ISG) regulated genes, and thought to be the pathogenic link with chronic inflammation in these conditions. Despite evidence of type I IFNs driving autoimmunity, they have not been comprehensively studied in AAV. We hypothesised that type I IFN responses are systemically dysregulated in AAV, indicative of a type I interferonopathy.

Conclusions: Systemic type I IFN responses are not dysregulated in AAV and are unlikely to contribute towards AAV pathogenesis; therefore AAV should not be considered as a type I interferonopathy.

Funding: Private Foundation Support

PO1738
Angiotensin Converting Enzyme-Overexpressing Neutrophils Suppress Glomerular Injury in Crescentic Glomerulonephritis
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Background: Angiotensin Converting Enzyme (ACE) is well known as the responsible enzyme to regulate blood pressure by producing angiotensin II in renin-angiotensin system, yet recent studies have revealed that ACE has a novel function in immune cells. We previously found that ACE overexpressed myeloid lineage cells promoted an inflammatory response resulting in increasing resistance to bacterial infection and tumor growth. These results prompt us to investigate the effect of overexpressed ACE in myeloid lineage cells on immune complex (IC)-mediated crescentic glomerulonephritis (GN).

Methods: We induced the nephrotoxic serum nephritis (N TN) in C57Bl6/WT, and NeoACE mice that overexpressing ACE in neutrophils. In addition, IC uptake and IC-mediated responses were investigated in both WT and NeoACE neutrophils by ex vivo experiments.

Results: Seven days after induction of NTN, NeoACE mice showed less severe proteinuria, histological glomerular injury, and less number of macrophages infiltration into the glomeruli than those in WT mice. While production and serum level of autologous antibody titer were comparable, IC deposits in glomeruli were reduced in NeoACE mice compared to WT mice. In ex vivo experiments, IC uptake was significantly promoted in NeoACE neutrophils as compared to WT cells. As an underlying mechanism of the promoted IC uptake in neutrophils, we found that serum level of complement C3b and expression of complement receptor CR1/2 on neutrophils were significantly elevated in NeoACE mice compared to WT mice in both normal and ACE overexpressing neutrophils. These results suggest that ACE in neutrophils directly or indirectly pre-activate C3, and that both the elevated CR1/2 expression and the increased serum C3b play the pivotal role in IC uptake by neutrophils. Despite the increase in IC uptake, neutrophils from NeoACE mice showed better cell survival after IC stimulation compared to those from WT mice.

Conclusions: Overexpressed ACE in neutrophils contributes to the effective elimination and suppression of IC deposits in glomeruli via C3b-CR1/2 axis, ameliorating glomerular injury in crescentic GN. These results indicate a novel immunological aspect of ACE in GN.

Funding: Other NIH Support - NIHAND, Private Foundation Support

PO1739
Recurrence of Anti-GBM Disease: An Epiphenomenon?
Sri Vihavari Guntupalli,2 Robert Mark Black. Saint Vincent Hospital, Worcester, MA.

Introduction: The simultaneous presentation of anti-GBM antibodies with ANCA-associated glomerulonephritis occurs in about 40% of patients with anti-GBM disease. However, recurrence of anti-GBM disease is rare. We report a case of relapsing disease where the recurrent anti-GBM may have been caused by the ANCA-induced glomerular injury.

Case Description: A 62-year-old woman presented with generalized weakness and arthralgia. Creatinine was elevated to 1.7 mg/dL from 0.8 mg/dL, urinalysis showed 3+ blood and 1+ protein with dysmorphic RBCs. Her serologies showed an elevated anti-MPO and a moderately high anti-GBM titre. Her renal biopsy revealed crescentic glomerulonephritis with segmental linear IgG staining of the glomerular basement membrane on immunofluorescence. In 2015, at the time of her presentation, she was treated with plasmapheresis, cyclophosphamide and maintained on tapering doses of azathioprine and prednisone. In 2017, as her immunosuppression was tapered, her Pcr rose, her urine showed RBCs and her anti-GBM titer, which had been undetectable each month, again became positive. She was retreated with a similar regimen. In 2019, she had another relapse with a higher ANCA titer, a mild rise in creatinine and hematruia. Her anti-GBM, by comparison, remained negative. Her repeat renal biopsy was consistent with vasculitis, but the immunofluorescence at this time was negative. She was treated with an escalated steroid dose and with rituximab. She appears to be in clinical and laboratory remission at this time with a persistently negative anti-GBM, but with continued anti-MPO positivity. A re-review of her initial biopsy showed that there was linear staining, but it was discontinuous and segmental.

Discussion: On initial presentation, this patient appeared to have anti-GBM disease with concomitant ANCA positivity, a not uncommon combination. Both titers rose with each relapse. However, during her second recurrence she was noted to have an elevated ANCA with necrotizing vasculitis and was promptly treated. At that time, her anti-GBM remained negative. We suggest that this patient has an ANCA-positive vasculitis and that the anti-GBM may have been a secondary or epiphenomenon due to release of GBM antigens as a result of glomerular damage by anti-MPO antibodies [1]. We believe that this might explain the unusual recurrence of anti-GBM serology in this patient.
**PO1740**
Activation of the cGAS-STING Signaling Pathway Is Associated with Glomerular Diseases

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**Background:** Podocytes express elements of the innate immune system which may participate in the local immune response and contribute to chronic inflammation and glomerular damage. The cGAS-STING pathway is activated as part of the innate immune response to pathogens or host cytosolic DNA and has been shown to regulate inflammation and energy homeostasis under obesity conditions, kidney fibrosis and acute kidney injury. Whether cGAS-STING pathway contributes to development and progression of glomerular diseases remains largely unknown. This study aimed at filling this gap.

**Methods:** Immortalized human podocytes were cultured in RPMI medium and differentiated for 14 days. c-diAMP treatment (10 μM) was performed for 24h. Real-time PCR and Western blot analysis were used to evaluate mRNA and protein expression. Male and female, 8-week-old C57BL/6J mice were randomly divided into two groups: control (n=7) and I.P. injected with a single dose of c-diAMP, 25 mg/kg (n=9). The animals were sacrificed 72 h after injection, blood and kidneys were harvested and processed for in-depth phenotypical analysis, including urinary albumin-to-creatinine ratio, histological analysis, transmission electron microscopy analysis (foot process effacement quantification), immunohistochemistry, glomeruli isolation and serum analysis.

**Results:** In vitro, podocytes showed expression all of the cGAS-STING components at the mRNA and protein level under physiological conditions and treatment with c-diAMP, an antagonist of STING, lead to activation of the cGAS-STING pathway. In vivo, treatment of mice with c-diAMP resulted in an increased expression of all components along the cGAS-STING pathway at both the mRNA and protein levels. Histology data show that c-diAMP-treated mice have a lower number of podocytes per glomerulus and a lower podocyte density, showing an increase in foot process effacement. This is further confirmed by increase in blood urine nitrogen and serum creatinine levels and in the urine albumin-to-creatinine ratio.

**Conclusions:** Genes of the cGAS-STING pathway are expressed in human podocytes and the pathway can be activated both in vitro and in vivo. Activation of the cGAS-STING pathway in mouse models in vivo is associated with increased podocyte injury and contributes to the glomerular diseases.

**Funding:** NIDDK Support

**PO1741**
C5a Enhanced the Recruitment of CD16+ Monocytes by CX3CL1-CX3CR1 Axis in ANCA-Associated Vasculitis

**Jigle Tang, Zhonghua Liao, Xiao Zhao Li. Xiangya Hospital Central South University, Changsha, China.**

**Background:** Monocytes play a major role in ANCA-associated glomerulonephritis. The mechanism is not well understood. Additionally, it is a consensus that C5a participates ANCA-associated vasculitis (AVV) pathogenesis. The relevance of C5a in terms of monocytes recruitment, as well as the nature and function of monocytes has not been well studied in AVV.

**Methods:** Monocytes in blood was counted and its phenotypic characteristics were analyzed by Flow cytometry. C5a and monocyte - related cytokines and chemokines was detected in AA. The phenotype of monocytes in Kidney tissues from MPO-AVVs patients was studied by immunohistochemistry and immunofluorescence. The chemoattractant activity of chemokines produced by human renal glomerular endothelial cells(HRGEC) for monocytes was observed.

**Results:** Monocytes were higher in activated MPO-AAV patients. The proportion of CD16+ monocytes in the peripheral blood of the patients was significantly reduced and CX3CL1 was only expressed in CD16+ monocytes. C5a, IL-6, TNF-α, and chemokine CX3CL1 were significantly increased in serum of activated MPO-AAV patients. CD16+ monocytes were clearly seen in the glomeruli of MPO- AVV patients. Chemokine CX3CL1 was expressed in glomerular endothelial cells. Consistently, we demonstrated C5a increased recruitment of CD16+ monocyte via CX3CL1 produced by TNF-κ-induced HRGEC in vitro.

**Conclusions:** We report an altered distribution of monocyte subsets in MPO-AAV patients; CD16+ monocytes may be recruited to kidney through CX3CL1-CX3CR1 axis to aggravate ANCA-associated GN.

**PO1742**
Melanocortin 5 Receptor (MC5R) Deficiency Aggravates Glomerular Injury and Proteinuria in the Autologous Phase of Nephrotoxic Serum (NTS) Nephritis

**Juale Chen, Lance D. Dworkin, Rujun Gong. University of Toledo Medical Center, Toledo, OH.**

**Background:** The successful use of corticotropin in steroid-resistant nephrotic syndrome suggests a unique proteinuria-reducing activity of adrenocorticotropic hormone that is steroidogenic-independent and may be attributable to its melanocortinergic activity. It remains uncertain which melanocortin receptor conveys this beneficial effect. Emerging evidence implicates MC3R signaling in the regulation of immune response. However, the role of MC5R in glomerular disease is unknown.

**Methods:** NTS nephritis was induced in MC5R knockout (MC5R−/−) and wild-type (WT) mice. Kidney function, proteinuria and renal pathology were evaluated in the autologous phase.

**Results:** On 14 days after NTS injection in the autologous phase, MC5R−/− as compared with WT mice exhibited an exacerbated kidney dysfunction and injury, as evidenced by higher serum creatinine levels, heavier proteinuria and aggravated renal pathology, featured by crescent formation, glomerular hypercellularity, mesangial expansion, protein casts in renal tubules, inflammatory infiltration in both glomeruli and tubulointerstitium and renal fibrosis. Consistent with the worsened proteinuria, MC5R+ mice displayed more severe podocyte injury and loss, as evidenced by diminished WT-1 staining and loss of homeostatic podocyte markers, like synaptopodin and podocin, as determined by immunohistochemistry staining and immunoblot analysis of isolated glomeruli. Mechanistically, although glomerular basement membrane-reactive rabbit IgG was found to deposit in glomeruli in both MC5R−/− and WT mice to a comparable magnitude, MC5R+ mice demonstrated much more glomerular deposition of autologous anti-rabbit IgG together with enhanced fixation of the terminal complement complex C5b-9 along glomerular capillary loops in the autologous phase, suggesting that a potentiated humoral immune response to NTS antigen resulting from MC5R deficiency may contribute to the aggravated NTS nephritis.

**Conclusions:** MC5R signaling is essential for protection against glomerular injury and proteinuria in murine NTS nephritis via, at least in part, a regulatory effect on humoral immunity.

**Funding:** NIDDK Support

**PO1743**
Glomerular Complement Proteins in Thrombotic Microangiopathy

**Lilian M. Palma,1 Meera Sridharan,2 Kenneth L. Johnson,3 Benjamin J. Madden,2 Cristina Charlesworth,2 Sanjeev Sethi.1 Universidade Estadual de Campinas, Campinas, Brazil; 2 Mayo Clinic, Rochester, MN.**

**Background:** Thrombotic Microangiopathy (TMA) is a clinicopathological entity resulting from complement abnormalities (atypical hemolytic uraemic syndrome, aHUS) and a number of secondary causes including malignant hypertension, autoimmune diseases and drugs. Distinguishing aHUS from secondary TMA is a challenge. A comprehensive evaluation of complement burden in TMA has not been done.

**Methods:** Glomeruli were laser microdissected and mass spectrometry (MS) was performed. The glomerular complement protein profile was analyzed in aHUS (n=12) and secondary TMA (n=12). The spectral counts obtained from MS are semiquantitative with regards to abundance of the protein.

**Results:** C3 was the most abundant complement protein in all cases (Figure). The remaining complement proteins were grouped into classical (C1/C4A/C4B), terminal pathway (C5/6/7/8/9) and complement regulatory proteins (CRP=CFH/CFHR1-2-3-5/CFB/CFD). MS studies show accumulation of C3, and complement proteins of classical and terminal pathways in all cases. Overall, there was greater accumulation of complement proteins in secondary TMA compared to aHUS (248.3 vs. 192.5). Importantly, even though C3 was higher in aHUS, both classical pathway and terminal pathway protein accumulation were higher in secondary TMA compared to aHUS. Among the secondary TMA, drug-induced TMA showed the highest accumulation of complement proteins compared to autoimmune and hypertension-induced TMA (306.9 vs. 217 vs. 219.9, respectively). CRP were present in all TMA, of which CFH was the most abundant protein.

**Conclusions:** Complement proteins of all pathways were identified in TMA. C3 followed by C4A/C4B and C9 were most abundant proteins. Higher counts of C3 in aHUS versus higher counts of C4A/C4B in secondary TMA, suggests a greater role of alternative pathway in aHUS and a greater role of classical pathway in secondary TMA.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
POI1744

Complement 3 Glomerulonephritis in a Patient with Microscopic Polyangiitis
Hammad Siddiqui, Ayasha Ahmed, Bushra Z. Saleem. Robert Wood Johnson University Hospital, New Brunswick, NJ.

Introduction: C3GN is a rare disorder of excessive alternative complement pathway activation, with renal biopsy characteristic of C3 deposits. We present a unique case, where patient has I/O MPA, admitted for AKI and hematuria, found to have C3GN on renal biopsy.

Case Description: 69 yo M with I/O CKD stage 4 due to microscopic polyangiitis (baseline Cr 2.6 - 2.9), spinal stenosis, HTN and BPH presented with complaint of painless hematuria, epistaxis, decrease UOP and weight gain x 4 days. He was diagnosed with MPA in 2005 after a renal biopsy, received treatment with steroids, Cyclophosphamide for 18 months, switched to MMF for 2 years and then to Azathioprine which was discontinued due to intolerance (off all immunosuppressant’s since 2012.). On admission labs; BUN/Cr 90/6.5, K 5.6, ESR 39, C- RP 1.24, P-ANCA and MPPO positive. UA +3 protein, +3 blood, > 180 RBC’s and 16 WBC’s. Random urine protein > 600 mg per dl. C3 was low (44.1), C4 normal. AH50 was low (36.1%). Hepatitis panel, C-ANCA, CR-3 and anti-GBM were negative. Pt was admitted with preliminary diagnosis of AKI on CKD 2/2 MPA flare and was started on pulse dose of steroid. He was also started on HD and plasmapheresis. Renal biopsy showed active crescents with strong C3 global glomerular staining in the mesangium and the capillary wall and trace to no staining of IgG, IgA, IgM, C1q, kappa, lambda. S. EM showed mesangial and sub endothelial deposit suggestive of active crescentic C3 GN.

Discussion: C3 GN is rare in clinical practice. Incidence is estimated to be 2-3 cases per 1,000,000 in the United States. MPA, like other ANCA-associated vasculitis, is typically associated with a pauci-immune GN. We presented a case with signs, symptoms, labs and histopathology consistent with both C3GN and MPA. It is unclear whether this patient truly had both diseases, which are typically caused by different immunologic pathways. Depressed C3 levels and normal C4 levels, diffuse glomerular C3 deposits on immunohistochemistry, and subendothelial deposits on electron microscopy strongly supports the diagnosis of C3GN in our patient with MPA.

POI1746

Thrombotic Microangiopathy and AKI Induced After Intravitreal Injection of Vascular Endothelial Growth Factor Inhibitors
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Introduction: Vascular Endothelial Growth Factor (VEGF) inhibition can cause worsening hypertension, proteinuria, acute and chronic kidney injury, as well as glomerular disease from Thrombotic Microangiopathy (TMA) and other nephrotic disorders when given systemically. These same agents are given intravitreally for age related macular degeneration (AMD) and Diabetic Retinopathy (DR) among other ophthalmologic conditions, albeit at lower doses than those given for systemic indications. Systemic absorption of anti-VEGF agents when given intravitreally has been shown consistently to have evidence of significant intravascular VEGF inhibition. While worsening hypertension has only been seen in some large-scale studies, case reports show worsening proteinuria and diverse glomerular diseases. These include TMA-associated lesions like Focal and Segmental Glomerulosclerosis with Collapsing Features (fSGS).

Case Description: In this paper, we report 3 cases of TMA likely associated with use of intravitreal anti VEGF therapy. These patients developed the signature lesion of VEGF blockade in a 6 month – 11 month time frame after starting intravitreal VEGF inhibitors.

Discussion: The literature is reviewed showing similar cases. Intravitreal VEGF blockade may cause these adverse events in a hitherto unidentified subgroup of patients. Further studies are needed to determine the event rate and identify which patients are at increased risk for hypertension, proteinuria worsening, renal injury, and glomerular diseases from intravitreal VEGF blockade.

Table 1 TMA and fSGS observed with Intravitreal VEGF blockade

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Age</th>
<th>Gender</th>
<th>Agent Pathology on Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neubauer et al. (2)</td>
<td>109</td>
<td>45</td>
<td>Female</td>
<td>CFE Glomerular Thrombotic Microangiopathy</td>
</tr>
<tr>
<td>Ghoneim et al. (1)</td>
<td>67</td>
<td>M</td>
<td>Male</td>
<td>TMA</td>
</tr>
<tr>
<td>Robert et al. (4)</td>
<td>52</td>
<td>M</td>
<td>Male</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Tousari et al. (3)</td>
<td>72</td>
<td>M</td>
<td>Male</td>
<td>TMA</td>
</tr>
<tr>
<td>von Goeldner et al. (9)</td>
<td>59</td>
<td>M</td>
<td>Male</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>OC (Hanna et al.)</td>
<td>18</td>
<td>60</td>
<td>M</td>
<td>CFE</td>
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</tbody>
</table>

All, antiepoetin; ANCA, anti-neutrophil cytoplasmic antibody; CFE, collapsing focal and segmental glomerulosclerosis; fSGS, focal and segmental glomerulosclerosis; M, male; N, number; TMA, thrombotic microangiopathy

POI1747

Bintrafung α-Associated Thrombotic Microangiopathy
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Introduction: Immune check point inhibitors (ICPIs) have been reported to cause acute kidney injury. Acute tubulointerstitial nephritis is the most common finding on renal biopsy. This has resulted in recommendations for forgoing renal biopsy in some patients and therapy with empiric steroids. Here we present a different renal pathology related to use of Bintrafung-α, a novel therapy targeting TGF-beta and PD-L1.

Case Description: A 41 year old man with metastatic cholangiocarcinoma was admitted for hypertension urgency and acute kidney injury following 2 cycles of Bintrafung-α 204/101 mg every 14 days for 4 cycles. Presents was remarkable for labs 109/62 mm, muscle wasting and anasarca. His labs revealed hemoglobin 8.9 g/dL, platelets 109 x 10^9/L, occasional schistocytes, lactate dehydrogenase 626 U/L, undetectable haptoglobin, serum creatinine 2.8 mg/dL, microscopic hematuria and protein with creatinine ratio 2.79 g/l, ADAMS/S1 activity 72% (37%), and anti-cardiolipin antibody was negative, complement levels normal. The renal biopsy demonstrated acute and subacute thrombotic microangiopathy(TMA). The patient received a dose of Soliris empirically, pending workup for atypical HUS. Further doses of Soliris were held as there was no current renal pathology related to use of Bintrafung-α.

Discussion: TMA is characterized by microangiopathic hemolytic anemia and thrombocytopenia. The most studied secondary cause of TMA is drugs. The pathogenesis of drug-mediated TMA is either the generation of an immunologic reaction or its direct complement activation. Presence of autoantibodies against vascular receptor (against angiotensin II type 1 receptor and endothelin-1 type A receptor) have been associated with pulmonary hypertension, pulmonary fibrosis and digital ulcers but no association with TMA and Bintrafung has been reported yet. On the other hand, hemodynamic shear stress itself has been shown to activate the classical pathway, and trigger secondary TMA. In addition, an increased Fb/FB ratio has been reported in a SRC with TMA, suggestive of subsequent recruitment of the alternative pathway through the C3b feedback cycle leading to further endothelial injury. These data support the potential role of complement blockade for the treatment of SRA with TMA.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
patients with steroids. We believe renal biopsy is essential, if safe, to rule out causes of AKI that are not remediable with steroids. Renal biopsy would expand our knowledge on the pathiology of AKI post-ICP treatment. We report the first case of TMA associated with the new bifunctional immunotherapy for solid cancers.

PO1748

Atypical Hemolytic Uremic Syndrome Associated to Complement Dysregulation in Setting of Metastatic Prostate Cancer Patient Matthew Van Norman,1,2 Omar Mamlouk,1 Biruh Workenhe,2 1University of Texas Health Science Center at Houston, Houston, TX; 2University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction: Thrombotic microangiopathy (TMA) is a collection of syndromes, with the most frequent types encountered being hereditary hemolytic uremia syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), and atypical HUS. Atypical HUS (aHUS) may be attributed to inherited or acquired complement abnormalities, or secondary causes such as pregnancy, malignancy, transplantation, drugs. Malignancy-associated aHUS is caused by a two-hit event with complement activation playing minor role while in primary aHUS, the primary hit is complement dysregulation. We describe an unusual case of aHUS in a metastatic cancer patient attributed primarily to complement dysregulation.

Case Description: A 64-year old male with history of metastatic prostate adenocarcinoma with spinal involvement presented with a chief complaint of new onset hypertension. He reported dark "coke-colored" urine for one day with intermittent episodes of hematuria. Patient last received chemotherapy with cabazitaxel five months prior. Rest of history and physical exam was unremarkable. Laboratory findings were significant for thrombocytopenia, anemia, and peripheral smear demonstrating schistocytes. Ct peaked at 6.58 mg/dL, ADAMTS13 activity was 100%, and stool PCR was negative for shigella. Complements C3 and C4 were within normal limits. Patient became oliguric with worsening acidosis and was initiated on renal replacement therapy. He underwent a bone marrow biopsy showing no evidence of infiltration of malignancy into the bone marrow. He then had a renal biopsy with pathology showing acute TMA with fibrin thrombi in approximately 50% of the glomerular. C5b9 levels were 7990 ng/mL. He was initiated on Eculizumab 900mg once weekly and began to show signs of renal recovery. Within two weeks, he was transitioned off renal replacement therapy.

Discussion: Primary aHUS as a result of complement dysregulation can occur in patients with malignancy. This patient had elevated C5b9 complex levels with increased alternative pathway activation. He responded to eculizumab, monoclonal antibody inhibiting activation of C5, with full recovery of his renal function. In cases of aHUS presenting in patients with malignancy, physicians should be aware that aHUS may still occur secondary to the primary hit of complement dysregulation and should consider treatments targeting this complement pathway.

PO1749

An Unusual Case of Complement-Mediated Thrombotic Microangiopathy Sobia N. Khan, Wilfred Lieberthal, Stony Brook University, Stony Brook, NY.

Introduction: Thrombotic microangiopathy is a specific pathologic lesion in which abnormalities in the vessel wall of arterioles and capillaries lead to microvascular thrombosis. Diagnosis is made by tissue biopsy. Complement mediated TMA is hereditary deficiency of regulatory proteins that restrict activation of alternative pathway or hereditary abnormality of proteins that accelerate activation of this pathway. Deficiency of complement factor H or I can also be acquired.

Case Description: 19-year-old female with ulcerative colitis presented with bloody diarrhea and decreased oral intake for one week. She endorsed not taking mesalamine and use of naproxen daily for two weeks. Laboratory data, leukocytosis 22k with 84% neutrophils, 5% bands and schistocytes, hemoglobin 6.1g/dL, thrombocytopenia, BUN 77 mg/dL, creatinine 7.16 mg/dL, Lactate dehydrogenase 1042U/L and haptoglobin undetectable. Coombs’ test negative. The patient was admitted for presumed Colitis flare given methylprednisolone. Renal biopsy obtained for acute kidney injury showed glomerular basement membrane duplication, multi layered and arterioles showed focal obliterative changes and onion skinning. 50% global sclerosis and 18% of glomeruli showed segmental sclerosis. Electron microscopy showed active endothelial injury, including subendothelial expansion. Microangiopathic anemia, thrombocytopenia and acute kidney injury occurred from a herpes simplex type 2 reactivation. She was treated with methylprednisolone and ADAMTS13 activity ~ 72%. Complement factors and autoantibodies to H, I, and B and membrane cofactor were sent out. Patient started treatment for TTP, presumably aHUS. She received soludemol 500mg/ day IV x 3 and then prednisone 60mg/day. Plasma exchange was initiated. She was noted to have persistent high LDH and undetectable haptoglobin indicating ongoing MAHA. After 2 weeks of miconazole venous cath, she was started on Eculizumab. Prednisone, Eculizumab and PEG were continued. In the interim, labs showed CFH level ~ 105 mcg/ mL (normal range 160-142). A genetic renal panel, which tested for CFH, CFI, C1, MCP, and several other genes showed she had a heterozygous deletion of a CFH related gene, CFIHR1-CFIHR3, as well as autoantibodies to CFH.

Discussion: In our case, aHUS was likely predisposed by her heterozygous deletion of CFH-related genes CFIHR1-CFIHR3 genes. This makes this case unusual as she did not have a homzygous deletion, but developed autoantibodies to CFH, to our knowledge has not been previously reported.
PO1752
A Case of Granulomatosis with Polyangiitis Complicated by Renal Mass-Like Lesion
Naichi Kaikoi, Koichi Sato, Hisayuki Ogura, Taro Miyagawa, Tadashi Toyama, Shinji Kitajima, Akinori Haru, Yasunori Iwata, Norihiko Sakai, Mih0 Shimizu, Takashi Wada. Department of Nephrology and Laboratory Medicine, Kanazawa University, Kanazawa, Japan.

Introduction: Granulomatosis with polyangiitis (GPA) is a multiorgan systemic disease. Some cases of GPA may mimic IgG4-related disease (IgG4-RD) on histologic examination. Here we report a case of GPA complicated by renal mass-like lesion with infiltration of IgG4-positive plasma cells.

Case Description: A 76-year-old woman was diagnosed with otitis media with effusion 6 years before admission, and scleritis 3 years before admission. She developed nasal leaks and nasal bleeding a year before admission, and high fever and general malaise a month before admission. She visited nearby hospital and was detected a mass-like lesion in the right nasal cavity. Contrast-enhanced computed tomography (CT) of the head revealed an enhanced soft-tissue from the right middle meatus to the nasal septum and cervical lymphadenopathy. Serum proteinase 3-antineutrophil cytoplasmic antibody (PR3-ANCA) was positive (271.7 U/mL) with high C-reactive protein (CRP) level (29.7 mg/dL). Urinalysis findings showed minor proteinuria (0.1 g/gCr), but elevated tubular injury markers such as urinary beta 2-microglobulin. So, she admitted to our department.

Contrast-enhanced CT of the abdomen revealed a 47-mm large mass-like lesion in the right kidney, and CT-guided renal biopsy was performed. Cellular to fibro-cellular crescent and fibrinous necrosis were observed in the glomeruli. In the interstitium, granulomas with multinucleated giant cells and infiltration of IgG4-positive (IgG4+) plasma cells were observed. In addition, cell infiltration into the arterial wall and the rupture of lamina elastica were observed. From these findings with small vessel vasculitis, we diagnosed her as GPA with infiltration of IgG4+ plasma cells. After two courses of methylprednisolone pulse therapy, we added two courses of cyclophosphamide pulse therapy. With improved symptoms and serum data (PR3-ANCA level reduced from 266.8 to 39.0 U/mL), mass-like lesions in nasal turbinates and right kidney diminished.

Discussion: We experienced a case of GPA complicated by renal mass-like lesion. Renal biopsy revealed a coexistence of microvasculitis and infiltration of IgG4+ plasma cells. Further investigation will be required to clarify the role of IgG4+ cells in the pathogenesis of GPA.

PO1753
Granulomatosis with Polyangiitis and Acute Tubulointerstitial Nephritis in the Absence of Glomerulonephritis
Weiven Guo, Cynthia C. Lim, Jason Choo Chon Jun, Singapore General Hospital, Singapore, Singapore.

Introduction: Isolated TIN in the absence of glomerular involvement is uncommon in ANCA-associated vasculitis(AAV).

Case Description: 77 year old female with normal renal function presented with acute kidney injury (AKI) with peak Scr 482 μmol/L and required dialysis. She received antibiotics for sinusitis and pneumonia 2 weeks prior. Urinalysis noted iso-morphic RBCs and proteinuria of 2g/24Hrs. Anti-proteinase3(PR3) antibody was positive at 114U/ml. Anti-nuclear, anti-dsDNA and anti-GBM antibodies were negative. Bronchoalveolar lavage was negative for alveolar hemorrhage. Kidney biopsy revealed minor glomerular abnormalities and acute TIN with interstitial non-necrotising granuloma and multinucleated giant cells. Ziehl-Neelsen stain was negative. Immunofluorescence, electron microscopy were non-contributory. She was treated for possible drug-induced interstitial nephritis with oral prednisone 0.6mg/kg and therapy was rapidly tapered due to cytomegalovirus infection. She was on prednisolone 5mg daily by 3 months. SCr improved to 174μmol/L and anti-PR3 was 4.4U/ml. A year later, she presented with episcoritis, fever, weight loss and AKI. Scr was 399μmol/L with glomerular hematuria and proteinuria. Patient refused a repeat biopsy but in view of AKI with concurrent rise in AKI, and proteinuria. Patient refused a repeat biopsy but in view of AKI with concurrent rise in SCR. Although serum creatinine subsequently improved to 1.6mg/dL, the peripheral platelet count was low blood platelet count. Secondary ITP is defined as an ITP induced by other diseases.

Discussion: Rapidly progressive glomerulonephritis (RPGN) is a clinical syndrome that develops within weeks and is manifested by glomerular disease that is histologically delineated by crescent formation and progressively worsening renal dysfunction. The most common causes of RPGN include anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, immune complex-mediated injury, and anti-glomerular basement membrane disease. We report a case of proteinase-3 (PR-3) ANCA associated crescentic glomerulonephritis with concurrent immunoglobulin A (IgA) nephropathy and lambda light chain. The co-existence of ANCA associated crescentic GN, IgA nephropathy and lambda light chain is rare.

Case Description: A previously healthy 53-year-old Caucasian woman with newly diagnosed Granulomatosis with Polyangiitis (PR-3 ANCA positive) presented with dyspnea, cough and non-necrotising granuloma. The definitive diagnosis of MPA was notable for sinus tachycardia and tenderness to palpation over maxillary sinuses. Urinalysis revealed active sediment with dysmorphic red blood cells. Initial workup was significant for serum creatinine of 1.35 mg/dl (baseline of 0.7 mg/dl), positive C-ANCA (1:160), anti-Proteinase-3 antibody 28.4 (normal <1) and 24-hour urine protein of 576 mg. Preliminary native kidney biopsy light microscopy showed active and organizing crescentic glomerulonephritis involving 15 of 34 (44%) non-globally sclerotic glomeruli. Immunofluorescence and electron microscopy were significant for granular mesangial staining for IgA and lambda light chain and presence of few mesangial electron-dense deposits. The patient was empirically pooled in intravenous steroids for three days. She was given one dose of Rituximab with a planned second dose two weeks after discharge.

Discussion: Rapidly progressive ANCA associated crescentic GN along with mesangial staining for IgA and lambda light chain is extremely uncommon with limited literature. By presenting this case, we highlight the significance of a renal biopsy as an essential tool for diagnostic purposes and the need to have a low threshold to biopsy in otherwise clinically straightforward cases given unexpected histologic and immunologic findings that could affect therapy and consequently patient’s morbidity and mortality.

PO1754
Coexisting Proteinase 3 Antineutrophil Cytoplasmic Antibody-Associated Crescentic Glomerulonephritis, Immunoglobulin A Nephropathy, and Lambda Light Chains
Arian L. Kalaria, Amoghavarsha Puli, Sheldon Bastacky, UPMC, University of Pittsburgh Medical Center, Pittsburgh, PA.

Introduction: Rapidly progressive glomerulonephritis (RPGN) is a clinical syndrome that develops within weeks and is manifested by glomerular disease that is histologically delineated by crescent formation and progressively worsening renal dysfunction. The most common causes of RPGN include anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, immune complex-mediated injury, and anti-glomerular basement membrane disease. We report a case of proteinase-3 (PR-3) ANCA associated crescentic glomerulonephritis with concurrent immunoglobulin A (IgA) nephropathy and lambda light chain. The co-existence of ANCA associated crescentic GN, IgA nephropathy and lambda light chain is rare.

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PO1755
A Case of Microscopic Polyangiitis Accompanied by Refractory Immune Thrombocytopenic Purpura
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Introduction: Microscopic polyangiitis (MPA) is an idiopathic autoimmune disease characterized by systemic vasculitis that predominantly affects the small blood vessels and is mediated by the presence of antineutrophil cytoplasmic autoantibodies (ANCA). Immune thrombocytopenic purpura (ITP) is also an autoimmune disease characterized by autoantibody induced platelet destruction and reduced platelet production, leading to low blood platelet count. Secondary ITP is defined as an ITP induced by other diseases including autoimmune disorders. Here we present a rare case of a patient who developed ITP just after treatment with steroids for MPA with rapidly progressive glomerulonephritis (RPGN)

Case Description: 66-year-old female was hospitalized due to microscopic hematuria, proteinuria, elevated serum creatinine (2.8mg/dL) and high Myeloperoxidase-ANCA (MPO-ANCA) titres (94.1U/ml). We performed a renal biopsy that revealed pauci immune necrotizing glomerulonephritis involving 15 of 34 (44%) non-globally sclerotic glomeruli. The patient was treated with intravenous corticosteroids and oral prednisone (0.8mg/kg). Although serum creatinine subsequently improved to 1.6mg/dL, the peripheral platelet count was...
rapidly reduced from 20×10^9/L to 2×10^9/L after a week treatment with steroids. She was frequently treated with platelet transfusion. Bone marrow examination revealed normal morphology of all the cell lines, with increased megakaryocytes. Based on the clinical findings, we diagnosed as ITP. Then, the patient received rituximab followed by thrombopoietin-receptor agonists eltrombopag. After a week of treatment with oral eltrombopag at 25mg daily, the platelet count increased from 0.5×10^9/L to 4×10^9/L. After six weeks from initiation of eltrombopag, her platelet count remains >3×10^9/L, and she has not shown any signs of bleeding or hemorrhage. MPO-ANCA titres reduced to 1.3U/ml.

**Discussion:** It is a novel case of MPA with RPGN accompanied by ITP. It was recently recognized that diversity existed in both pathogenesis and clinical characteristics in patients with MPA and ITP. Present case showed the possibility for an association of pathological mediator for both diseases. Although further studies are needed to confirm this idea, present findings provide clues for our understanding of this association for a better management of these diseases.

**PO1756**

**Rituximab Rescue in Anti-GBM Nephritis**

Shikha Shailly, Lorin Berman, Sofia Rubinstein. Nassau University Medical Center, East Meadow, NY.

**Introduction:** Anti-GBM nephritis is a rare, severe autoimmune disease. If left untreated or in patients requiring dialysis at presentation, it has a renal survival of 8% at 1 year. Conventional therapy includes corticosteroids, cyclophosphamide and plasmapheresis. An anti-B cell agent, rituximab is more recently being used in refractory cases (defined as no response after 4 weeks of standard therapy).

**Case Description:** 59-year-old female with hypertension presented with 1 month of fever, generalized malaise, and cough following recent travel to Iraq. Laboratory evaluation showed serum creatinine 1.3 mg/dl with hematuria and proteinuria (0.6g/day). ANA, ANCA, RF, Hepatitis B/C, HIV, RPR, and streptozyme panel were negative. Renal and pulmonary imaging were unremarkable. With creatinine rising rapidly, renal biopsy was performed revealing acute focal segmental necrotizing and crescentic glomerulonephritis involving 50% of glomeruli. Anti-GBM antibody level was 8U. Plasmapheresis daily, cyclophosphamide and steroids were initiated. She remained non-oliguric, but developed edema requiring intermittent diuresis. On day 15, plasmapheresis was reduced to every 48 hours. Anti-GBM antibody failed to decline, therefore 1 gr of rituximab infusion was initiated 3 weeks later. Standard therapy was continued until the second dose of 1gr of rituximab 2 weeks later. Patient was discharged with creatinine stable at 4 mg/dL, anti-GBM antibody level at 1.4U and on prednisone taper. On follow up day 75, antibody levels were undetectable and on day 147 she remained dialysis free.

**Discussion:** Our patient presented with favorable prognostic markers including non-oliguria, low creatinine and anti-GBM antibody levels, negative ANCA, involvement of 50% of glomeruli, and no dialysis requirement. Despite these factors, she did not respond to standard therapy alone. Our patient was initiated on rituximab earlier than reported with favorable outcome of remaining dialysis free. We suggest early use of rituximab with overlapping of the standard regimen is safe and effective in older age group.

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

**Underline represents presenting author.**
Peripheral neuropathy is rare. Our case illustrates an unusual presentation of IgG4-RKD with peripheral neuropathy, which has never been reported before.

Case Description: A 55-year-old Southeast Asian woman with allergic rhinitis presented to her PCP with burning and tingling from the knees down and difficulty with gait for about 6 months. Neurological examination was notable for weakness of ankle dorsiflexion and plantarflexion and loss of pinprick and vibration sense distal to ankles.

This was attributed to iron deficiency anemia and a compressed nerve. However, her symptoms worsened on iron supplements and gabapentin and were accompanied by weight loss. CT scan of abdomen showed heterogeneous masses of the kidneys with few enlarged retroperitoneal lymph nodes. Kidney biopsy was performed and showed stromal fibrosis and pancreatic cell rich interstitial infiltration (~30 IgG4+ plasma cells/HPF) suggesting IgG4-RKD. Further work up was significant for serum IgE 1309 IU/ml (1.5-165), IgG4 177 mg/dl (2.4-121), positive MPO-ANCA, RF 38 IU/ml (<14), ESR 77 mm/hr, CRP, complement levels and kidney function were normal.

Prior to initiating therapy for IgG4-RKD she was referred for sural nerve biopsy for concern of associated vasculitis. Nerve biopsy showed severe myelinated and unmyelinated fiber loss in all fascicles, a recanalized epineural blood vessel, and dense perineuronal mononuclear cell infiltrates consistent with vasculitic neuropathy. Additionally, immunostaining showed IgG4 plasma cells up to 10/HPF. Her symptoms resolved with steroids, IVIG and rituximab. Serum IgG4 level improved to 26 mg/dl.

Discussion: IgG4-RD can have varied systemic manifestations. Although neurologic disease is less commonly seen in IgG4-RD, we report for the first time an associated vasculitic neuropathy that should be considered and worked up in symptomatic patients.

PO1760
Differential Expression of Interferon-Stimulated Genes in ANCA-Associated Vasculitis
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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a multi-systemic, necrotising vasculitis, causing severe morbidity and mortality. It is characterised by the presence of auto-reactive antibodies against neutrophil granule components, myeloperoxidase (MPO) and proteinase 3 (PR3). The disease course remains variable, and patients suffer substantial morbidity and mortality. Therapeutic advances are hampered by a lack of understanding of the mechanisms driving both initial disease susceptibility and long-term clinical outcome. To increase our understanding of disease mechanism and to uncover untargeted pathways for treatment, we studied the transcriptionomes and serum proteomes of patients with active AAV.

Methods: The transcriptional profiles and protein expression of patients with AAV (31 PR3-AAV, 15 MPO-AAV, 1 dual ANCA positivity, 4 ANCA-negative) were studied at the time of diagnosis or during an active flare, whilst on minimal immunosuppression, along with healthy controls. AAV patients were profiled longitudinally at 3 and 12 months. Separated leucocyte transcriptomes were profiled, using Affymetrix HuGene ST1.1 gene expression microarrays. Transcriptional profiles were available on peripheral blood mononuclear cells (PBMC's), neutrophils, monocytes and CD4 and CD8 T cells. Protein expression was assessed on the SOMAcalc platform. Analytical techniques included differential gene-expression, weighted gene co-expression network, gene set enrichment and multi-omics factor analyses.

Results: Here we identify, a module of interferon stimulated genes (ISG) that distinguishes the serological subtypes of AAV, MPO- and PR3-ANCA. This module of ISG was upregulated in MPO- compared with PR3-AAV during the time of active disease, and at 3 months post treatment. The signature was present in the neutrophil, monocyte and PBMC transcriptome but was absent in T cells. Multi-omic factor analysis revealed a parallel upregulation of interferon like proteins in serum, coinciding with the increase in gene expression.

Conclusions: AAV causes severe morbidity and mortality. The differential expression of ISG in MPO compared with PR3-AAV highlights potential differences in pathogenesis. The presence of an interferon response in MPO-AAV opens new avenues for targeted treatment with agents such as Jak inhibitors and monoclonal anti-JFN-α antibodies.

PO1761
IL-233-Induced Remission from Lupus Glomerulonephritis Involves Regulation of Mitochondrial Function and Canonical WNT Signaling
Rakulukshmi Venkatadri, Vikram Sabapathy, Murat Dogan, Saleh Mohammad, Shu man Fu, Rahul Sharma. University of Virginia, Charlottesville, VA.

Background: We recently showed the efficacy of a hybrid cytokine IL233 to protect mice from lupus glomerulonephritis (GN). We now investigated the status of mitochondrial function, canonical Wnt signaling and metabolic fitness of regulatory T cells (Tregs), risk factors known to be associated with lupus GN to further delineate the mechanisms of protection offered by IL-233.

Methods: We used a constitutively active hybrid cytokine (IL-233) bearing activities of IL-2 and IL-33 and tested its efficacy to prevent glomerular nephritis in the adenovirus (Ad)IFNA3 treated lupus model NZM232 model. Kidney lysates were screened for transcripts of mitochondrial and Wnt inhibitor genes by real time PCR and Western blotting, and kidney metabolic fitness in IL-233 treated and Ig M state renal tissues. Pathological changes were assessed by immunostaining glomerular endothelial cells (MGECS) was investigated by flow cytometry and Seahorse assay. Metabolic fitness of Tregs with and without IL-233 treatments were investigated by Seahorse assay by employing ex vivo and in vivo approaches.

Results: Analysis of transcript levels of mitochondrial function and biogenesis related genes (Pgc1α, Nrf1, Nrf2, Tbk1, Drp1 and Mitf) confirmed that IL-233 treated kidneys displayed an elevated status. In vitro, changes in Pgc1α and its downstream target Nrf2 were recapitated in treated MGECS cells. IL233 treated Tregs (ex vivo and in vivo) and MGECS (in vitro) also exhibited better mitochondrial metabolic fitness and displayed elevated levels of basal respiration, maximal respiration and ATP production investigated by the Seahorse assay. Wnt activators LRPPR, Dvl3 and Wnt mediators - Axin1, GSK3α and GSK3β were significantly reduced in IL-233 protected kidney. Levels of Axin2 was significantly upregulated with IL-233 treatment indicating activation of a negative feedback loop for Wnt inhibition.

Conclusions: We present in depth mechanistic evidence of the observed remission from lupus GN with IL-233 treatment. IL-233 treated kidneys exhibit better mitochondrial dynamics and function. We show in vitro, in vivo and ex vivo evidence of IL-233 treatment leading to betterment of mitochondrial function and metabolic fitness. Canonical Wnt signaling was attenuated. The data presented confirms the therapeutic efficacy of IL-233 as a promising therapeutic agent for lupus nephritis and kidney injury.

Funding: Other NIH Support - National Institute of Diabetes and Kidney Diseases

PO1762
Prediction of Histologic Class Using Deep Learning on Renal Biopsies from a Trial of Obinutuzumab for Proliferative Lupus Nephritis
Bryan D. He,1 Matthew Cassino,2 Thomas Schindler,3 Cary D. Austin,2 Wei Tew,3 Jay P. Garg,2 James Zou,1 Marco Prunotto,1,2 Stanford University, Palo Alto, CA; 1Genentech Inc, South San Francisco, CA; 2H Hoffmann-La Roche AG, Basel, Switzerland; 3University of Geneva, Geneva, Switzerland.

Background: Glomerular lesions in lupus nephritis (LN) are classified according to the International Society of Nephrology and the Renal Pathology Society classification system and significant disagreement between pathologists can occur on histopathologic lesions. The aim of this study was to assess if deep learning on renal biopsy whole-slide images could be used to predict class III vs. IV status among patients enrolled in a randomized trial of obinutuzumab for the treatment of proliferative LN (NCT02550552).

Methods: Baseline biopsies from 84 of the 126 patients randomized were available for analysis. From each hematoxylin and eosin (H&E) slide, patches of 512x512 pixels were extracted resulting in an average of 500 patches per slide. An Inception v3 neural network (NN) with weights pretrained on the ImageNet dataset was used to make a prediction for each patch, which were then combined to make a prediction for the patient (Fig A). From the initial weights, all slide’s layers were further fine-tuned using the cross-entropy loss between the model’s prediction and the patient’s true class. To evaluate the trained model, 25% of patients were held-out as a test set.

Results: The NN was able to classify the held-out patients with an area under the receiver operating characteristic of 0.82 (95% CI 0.60 - 1.00). Patches associated with class III vs. IV prediction could be extracted from each patient to provide interpretation (Fig B).

Conclusions: These preliminary results showed that deep learning on renal biopsies can predict LN histologic class. The predictive patches provided additional interpretation. Such objective classification method has potential value to help minimize reading variability between pathologists.
PO1763
A Prospective Randomized Study on Pre-emptive Immunosuppressive Therapy in Lupus Nephritis Patients with Asymptomatic Serological Reactivation
Desmond Y. Yap, Paul Lee, Irene Yam, Tak Mao D. Chan. University of Hong Kong, Hong Kong, Hong Kong.

Background: The optimal management for asymptomatic serological reactivation (ASR) in lupus nephritis (LN) patients remains undefined. Our previous retrospective study suggested that pre-emptive moderate increase in immunosuppression may prevent subsequent clinical relapses.

Methods: We prospectively randomized LN patients with ASR (defined as ≥2-fold increase of anti-dsDNA to >100 IU/mL, with or without change in complement level, and absence of clinical lupus exacerbation) to receive pre-emptive treatment or unchanged management (‘Control’ group). Pre-emptive treatment included increasing prednisolone to 0.5 mg/kg/D, and the dose of mycophenolate to 1g/D or azathioprine to 75 mg/D, then tapered over 12-16 weeks back to the original dosages.

Results: Eighteen patients pre-emptive group and 17 in control group respectively. Pre-emptive group showed lower anti-dsDNA and higher C3 levels after 12 weeks compared with Controls (p<0.001, for both) (Figure 1). Pre-emptive group showed significantly lower incidence rates of all clinical relapses and renal relapse during subsequent 9 months follow-up compared with Controls (11.1% vs 41.2%, p=0.02, and 0% vs 17.6%, p=0.03, respectively). The pre-emptive group showed lower serum mir-148a compared with baseline value and also the Controls (p=0.001, for both). There was no clinically significant adverse event.

Conclusions: Our results suggest that pre-emptive moderate increase of immunosuppressive treatment reduces the risk of disease flare in LN patients with ASR and is well tolerated.

Funding: Government Support - Non-U.S.

PO1764
Kidney Thrombotic Microangiopathy Associated to Lupus Nephritis Is Mediated by the Activation of the Alternative Complement Pathway
Juan M. Mejía, Ismael A. Gómez Ruiz, Rossa A. Méndez, Cristino Cruz, Luis E. Morales-Buenrostro, Ricardo Correa-Rotter. Department of Nephrology and Mineral Metabolism, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico.

Background: Thrombotic microangiopathy (TMA) in the context of lupus nephritis is a rare disease whose pathogenesis has been linked to complement activation. This study aimed to evaluate complement pathway activation products in plasma and urine from patients with LN associated TMA (LN-TMA) and to compare its levels to patients with active LN (aLN), patients with inactive lupus (iSLE) and kidney donors (KD). Methods: Plasma and urine samples were obtained from 19 patients with active LN-TMA and 19 patients with biopsy-proven aLN matched by histologic activity index. Patients with iSLE (n=16) and kidney donors (n=10) were included as controls. Complement activation fragments C3a, C4a, C5a, Ba, C5b-9, and factor H were assessed by ELISA. Kidney C4d deposition was detected by immunohistochemistry. After 12 months, complement activation products were re-assessed after treatment.

Results: Both, the acute LN-TMA and aLN patients had increased plasma Ba and C5b-9 along with decreased plasma C3, C4, C4a, and factor H. Urine C5a, Ba, and C5b-9 were higher in patients with active LN-TMA than in aLN. The levels of the urine complement fragment correlated with the degree of interstitial inflammation, interstitial fibrosis, and tubular atrophy in the kidney biopsy. After treatment, the levels of circulating C3, C4, and factor H increased, and the levels of urine C5b-9 decreased. In two patients with repeated LN-TMA episodes, factor H and urine C5a levels decreased, while urine Ba and C5b-9 increased after treatment in each episode. There was no difference in C4d fragment deposition in glomerular capillaries, tubular basement membrane, peritubular capillaries, and arterioles, between patients with aLN and those with acute LN-TMA.

Conclusions: The levels of plasma and urine complement activation products suggest that the pathogenesis of acute LN-TMA is mediated through activation of the complement alternative pathway.

Funding: Government Support - Non-U.S.

Levels of plasma factor H (A), urine complement fragment Ba (B) and urine complement fragment C5a (C) in the studied groups.

PO1765
Glycol Chitosan-Based Tacrolimus-Loaded Nanomicelle Therapy Ameliorates Lupus Nephritis
Chang Seong Kim, Tae ryom Oh, Hong sang Choi, Eun Hui Bae, Seong Kwon Ma, Soo Wan Kim. Chonnam National University, Gwangju, Jeollanam-do, Republic of Korea.

Background: Hydrophobically modified glycol chitosan (HGC) nanomicelles loaded with tacrolimus (HGC-TAC) enhance the renal delivery of tacrolimus. Here, we determined whether the administration of HGC-TAC nanomicelles decreases kidney injury in a model of lupus nephritis.

Methods: Lupus-prone female MRL/lpr mice were randomly divided into 2 groups and given either intravenous vehicle or HGC-TAC (0.5 mg/kg tacrolimus) weekly for 8 weeks. Age-matched MRL/MpJ mice without Faslpr mutation were treated with a vehicle and used as healthy controls.

Results: Weekly treatment with intravenous HGC-TAC remarkably reduced genetically attributable lupus activity, blood urea nitrogen, and proteinuria in lupus nephritis-positive mice. In addition, HGC-TAC treatment mitigated renal dysfunction and histological injury, including glomerular proliferative lesions and tubulointerstitial infiltration. Furthermore, HGC-TAC treatment reduced renal inflammation and inflammatory gene expression, as well as ameliorated the increased glomerular fibrosis. Moreover, the administration of HGC-TAC appeared to regulate renal injury via the TGF-β/Smad3/1/5/9, MAPK/NF-κB signaling pathway.

Conclusions: Our study clearly indicates that weekly treatment with HGC-TAC nanomicelles reduces kidney injury resulting from lupus nephritis by preventing inflammation and fibrosis. This advantage of HGC-TAC nanocarriers may improve drug adherence and treatment efficacy in lupus nephritis patients.

Funding: Government Support - Non-U.S.
PO1766

Renal Activity Index for Lupus Nephritis Distinguishes Active Renal Disease Among Lupus Patients

Naija F. Albajeri,1 Arjun Mathur,1 Steffy Jose,1,2 Theresa Hennard,3 Angela Merritt,4 Qiang Ma,1 James Rose,3 Rashmi Sahay,2 Chanyuan Liu,5 Hermine Brunner,1 Scott E. Wenderfer,2 Baylor College of Medicine, Houston, TX; 3Texas Children's Hospital, Houston, TX; 4Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Background: Conventional tools to identify active nephritis in SLE (LN) fail to supersede invasive kidney biopsy. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity (Brummer, et al., 2016). Our objective was to test RAIL for identifying active LN in childhood-onset SLE.

Methods: Urine samples obtained from cross-sectional sampling of 2 eSLE cohorts, classified as active LN, inactive LN or non-LN SLE. RAIL scores were calculated from ELISA or nephelometry data for six urine markers (NGAL-1, ceruloplasmin, MCP-1, adiponectin, hemopexin, kidney injury molecule-1). Data collected included ISN/RPS histologic classification and extra-renal component of SLE disease activity index (SLEDAI) score.

Results: Among 117 cSLE patients, 37 had active LN; 30, inactive LN; 50, no-LN. RAIL scores of inactive LN and no-LN group largely overlapped, so they were combined (Group 2) and compared to active LN (Group 1, Table). Group 1 had higher RAIL score (0.7 vs. -1.1). After adjusting for age and extra-renal SLEDAI score, RAIL score odds ratio was 2.16 (95%CI 1.43-3.3, p<0.001) for active LN. A receiver operating curve (ROC) for an adjusted RAIL cut-off score of 0.35 produced an AUC=0.9 (sensitivity 88%, specificity 84%) for active LN. Adjustment for urinal protein and creatinine did not influence results.

Conclusions: The RAIL score is highly accurate in distinguishing active from inactive LN and non-LN SLE. Scores >0.35 identify cSLE patients who very likely have active LN.

Clinical characteristics and distribution of RAIL scores among Group 1 (active LN) and Group 2 (inactive LN + active non-LN SLE) patients

<table>
<thead>
<tr>
<th>Group 1 (active LN)</th>
<th>Group 2 (inactive LN + active non-LN SLE)</th>
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<tbody>
<tr>
<td><strong>Age</strong> (years)</td>
<td><strong>mRNA</strong> (log 2)</td>
</tr>
<tr>
<td>15 (13-17)</td>
<td>15 (13-17)</td>
</tr>
<tr>
<td>16 (14-17)</td>
<td>16 (14-17)</td>
</tr>
<tr>
<td><strong>mRNA</strong> (log 2)</td>
<td><strong>mRNA</strong> (log 2)</td>
</tr>
<tr>
<td>0.66 (0.38)</td>
<td>0.66 (0.38)</td>
</tr>
</tbody>
</table>

Conclusions: In this study, we identified a novel population of IFN-IC not previously described for LN. During LN flares, IFN-IC are present in abundance in the interstitium. Their presence next to T cells suggests IFN-IC dictates the nature of the T cell response during LN flare. Targeting IFN-IC or their associated T cell phenotype may attenuate renal inflammation and improve outcomes in LN.

Funding: Other NIH Support - NIAIMS

PO1768

Burden of Illness of Lupus Nephritis in Patients with Systemic Lupus Erythematosus

Christopher F. Bell,1 Benjamin Wu,2 Bin Xie,3 Shirley Huang,1 Benjamin Chasteck,2 Bernice Rubin,4 Joan Von Feldt,3,4 Gary Bryant,3 GlaxoSmithKline, Research Triangle, NC; 2Optum, Eden Prairie, MN; 3GlaxoSmithKline, Philadelphia, PA; 4University of Pennsylvania, Philadelphia, PA.

Background: Approximately 35% of adults with systemic lupus erythematosus (SLE) develop lupus nephritis (LN). LN is associated with an increased risk of renal failure, cardiovascular disease, and death. Little is known about healthcare resource utilization (HRU) or cost of care for patients with LN versus those without SLE.

Methods: This retrospective cohort study used Optum Research Database administrative claims data (GSK Study 213062). Patients with LN had a2 renal diagnosis codes during 08/01/2016–7/31/2018 and a1 inpatient or outpatient SLE diagnosis code >30 days apart in the 12 months prior to index; index date was the date of first renal diagnosis code. The control cohort had plan members with no diagnosis codes for SLE or LN during 08/01/2016–7/31/2018. Control patients were matched 1:1 to patients with LN based on baseline demographics. Inclusion criteria: ≥18 years at age at index, and continuous medical and pharmacy coverage in the 12 months pre and post index. HRU in the LN and non-LN post index capture period were compared using a2 medical visits, emergency department (ED) visits, and hospitalizations. Total healthcare costs in the 12 months post-index were quantified combining health plan– and patient-paid amounts and adjusted using the Consumer Price Index.

Results: Across the LN and control cohorts, 2326 patients met study criteria: 38.5% were 45–64 years of age, 44.1% were ≥65 years of age, 85.6% were female, 58.1% were located in Southern USA states, and 66.3% were covered by Medicare. The LN cohort had a significantly higher mean (standard deviation [SD]) number of ambulatory visits (53.9 [55.34] per year) compared to controls (14.87 [21.61]). ED visits (2.87 [7.91] vs 0.66 [2.31]), and hospitalizations (1.86 [1.48] vs 0.12 [0.51]) compared to the cohort control, respectively. Mean (SD) total costs were $50,958 ($86,100) for the LN cohort, which were significantly higher than $10,737 ($21,741) in the control cohort. Differences in cost were largely driven by mean (SD) medical expenses for the LN cohort versus the control cohort ($40,648 [$78,154] vs $6,781 [$14,773], respectively). All p-values were <0.001.

Conclusions: All-cause HRU and costs were higher for patients with LN than patients without SLE. This study quantifies the economic burden associated with LN.

Funding: Commercial Support - GSK

PO1767

A Novel Inflammatory Dendritic Cell in Lupus Nephritis

Laitha Prihla Ganesan,1 Ana Malvar,2 John P. Shapiro,2 James M. Turman,1 Haining Zhang,1,3 Bruce J. Lococo,2 Sethu M. Madhavan,1 Anjali A. Satoskar,1 Daniel J. Birmingham,1 Wael Jarjour,2 Brad H. Rovin,2 Samir V. Parikh,1 OSU Nephrology, The Ohio State University Wexner Medical Center, Columbus, OH; 2Hospital Fernandez, Buenos Aires, Argentina.

Background: Progress in Lupus Nephritis (LN) management has been limited and treatment outcomes remain sub-optimal. Knowledge on intra-renal changes during LN flare and the major immune cells that drive local inflammatory damage will lead to improved outcomes in LN.

Methods: We performed transcriptomic analysis on serial kidney biopsies of proliferative LN (n=58). Glomeruli and Tubulointerstitium (TI) were isolated using LCM, and 580 immune transcripts were analyzed using Nanostring human immunology panel. Guided by transcriptomic analysis, multi-color, high-resolution confocal immunofluorescence (IF) analysis using antibodies against various immune cell markers, was performed on LN flare kidney biopsies (n=5) and healthy nephrectomy controls (n=5), to identify the dominant intra-renal immune cell phenotypes present during LN flare.

Results: Transcriptomic analysis identified Fc receptor gamma chain (FeRγ), to be the most significantly overexpressed glomerular immune transcript (Fold change (FC): 3.5, P<1E-10) and also overexpressed in the TI (FC: 1.7, P<0.001) compared to controls. Confocal IF analysis found FeRγ to be abundantly present in the peri-glomerular (PG) region and to a lesser extent in the TI during LN flare. FeRγ was weakly expressed in controls. Further IF analysis identified the phenotype of FeRγ expressing cells to be CD11c+ , CD206+ , MHCIIC+ , CD68+ , CD16+ , CD206+ , CD68+ , CD123+ , CD3D+ , CD11b+ . This signature aligns with a dendritic cell (DC) phenotype but distinct from plasmacytoid dendritic cell (pDC). It is most consistent with an inflammatory dendritic cell (indDC) phenotype. Importantly, confocal IF identified CD3+ T cells present in close proximity to PG if indDC.

Conclusions: In this study, we identified a novel population of indDC not previously described for LN. During LN flares, indDC are present in abundance in the TI region. Their presence next to T cells suggests indDC dictates the nature of the T cell response during LN flare. Targeting indDC or their associated T cell phenotype may attenuate renal inflammation and improve outcomes in LN.

Funding: Other NIH Support - NIAIMS

PO1769

Clinico-Pathological Associations with Serum Thrombomodulin Level in Patients with Lupus Nephritis

Tak Mao,1 Chao, Kevin,2 Desmont Y. Yap, Susan Yang, The University of Hong Kong, Hong Kong, Hong Kong.

Background: Conventional serological markers do not always correlate with clinical activity or histopathology in lupus nephritis (LN). There is evidence of endothelial activation and injury in LN pathogenesis. Thrombomodulin (TM), a component of endothelial glycocalyx, is shed into the circulation in endothelial cell injury. We investigated clinico-pathological associations of circulating TM level.

Methods: TM level was measured by ELISA in sera collected serially every 3–4 months over ≥2 years (n=482) from 31 patients with biopsy-proven Class III/IV LN. Patients with non-renal SLE or non-lupus kidney diseases (CKD) and healthy subjects were included as Controls.

Results: Patients with active LN had the highest serum TM level, compared with LN patients in remission, patients with active non-renal SLE, CKD patients, or healthy subjects (P<0.001, for all). Serum TM level correlated with anti-dsDNA antibody titre, proteinuria, serum creatinine, SLEDAI-2K and renal SLEDAI-2K score; and inversely correlated with eGFR and P3 (P<0.05, for all). 8 patients had blood samples collected before disease flare, and 6 showed increased TM level (3.65±2.16 months before clinical flare). All episodes of LN flare were accompanied by elevated TM level, which decreased after treatment. A temporal relationship was noted between TM level and anti-dsDNA titers in the 12 months prior to index date. Proteinuria, SLEDAI-2K and renal SLEDAI-2K scores. TM level also correlated with renal interstitial inflammation score (r=0.54, P=0.0081). ROC analysis showed that serum TM level distinguished active LN from healthy subjects (sensitivity 100.00%, specificity 100.00%), from LN in remission (sensitivity 89.66%, specificity 99.93%), from patients with active non-renal SLE (sensitivity 90.91%, specificity 99.00%), and from CKD (sensitivity 89.66%, specificity 56.52%) (P<0.001, for all).

Conclusions: Determination of serum TM level may facilitate early diagnosis of active LN, and may be useful in monitoring the response to treatment.

Funding: Government Support - Non-U.S.
POI1770
Enhanced Na-K-ATPase Expression Mediates B-Cell Survival in Lupus Kidneys
Irene Chernova, Joseph Craft. Yale University School of Medicine, New Haven, CT.

Background: Systemic lupus erythematosus (SLE, lupus) is a multi-organ autoimmune disease characterized by antibody deposition in target organs, including the kidney. Kidneys of affected patients are characterized by lymphocytic infiltrates that correlate with tissue damage and disease severity. The kidneys are also characterized by a high salt environment not found elsewhere in the body. Thus, infiltrating lymphocytes are presented with the unique challenge of surviving in a high salinity environment which may define their phenotype and function. We now describe the molecular mechanisms utilized by immune cells when faced with this hypertonic microenvironment.

Methods: We utilized lupus-prone (MRL) and wildtype (C57BL/6) mice and renal biopsy samples from lupus nephritis patients for this study. B cells from mice were cultured in vitro standard versus high salt conditions. Kidney immune cell subsets were identified using flow cytometry and immunofluorescence techniques.

Results: B cells from lupus-prone (MRL) mice have enhanced survival when exposed in vitro to a high salt environment, compared to cells from control, non-autoimmune mice. The salt transporter Na-K-ATPase, and specifically its gamma subunit Fxyd2, is upregulated in the kidney and is necessary for kidney epithelial (tubular) cell survival under high salt conditions. We hypothesized that infiltrating lymphocytes also utilize Na-K-ATPase upregulation to survive in the hypertonic environment of the kidney. We found high expression of Na-K-ATPase alpha and gamma subunits on kidney-localized B cells of lupus-prone mice and high gamma subunit expression in B cells from human lupus kidney biopsies. Inhibition of Na-K-ATPase activity with a small molecule inhibitor obabain led to increased cell death when lupus-prone B cells, but not control B cells, were cultured in high salt conditions, suggesting a role for Na-K-ATPase in the enhanced survival of MRL B cells in high salt. In vivo treatment of MRL mice with obabain depleted renal-infiltrating B cells, but not T cells. MRL mice lacking the gamma subunit of Na-K-ATPase appear to phenocopy the obabain-treated mice in preliminary analyses.

Conclusions: These studies identify a novel role for Na-K-ATPase in B cell survival in the hypertonic renal microenvironment and suggest it is a potential therapeutic target in lupus nephritis.

Funding: Other NIH Support - R21 AI142145-01, R37 AR40072-28

POI1771
TNIP1/ABIN1 Mutation Contributes to Lupus Nephritis via Chemokine IP-10 Induction
David W. Fowell, Maklaya Brady, Michelle T. Barati, Dawn J. Caster. University of Louisville School of Medicine, Louisville, KY.

Background: We previously reported TNIP1 gene variants as risks for lupus nephritis (LN). TNIP1 encodes the protein ABIN1, which is a polyubiquitin binding protein that negatively regulates the prominent immune regulatory transcription factor NF-κB. We reported that transgenic mice with impaired ABIN1 ubiquitin binding function (ABIN1[D485N]) spontaneously develop SLE-associated autoimmunity and LN and that ABIN1 determines the severity of LN via activation of kidney and immune cell inflammation. Interferon gamma-inducible protein -10 (IP-10) is a pro-inflammatory chemokine and NF-κB target that has been implicated in the pathogenesis and as a diagnostic marker of LN. The current project tested a hypothesis that LN development is mediated by induction of IP-10 expression due to loss of cellular ABIN1 activity.

Methods: In order to test our hypothesis, we measured urine and serum IP10 in ABIN1[D485N] mice using ELISA and utilized IHC techniques to measure kidney IP10 expression. Additionally, we used ELISA to measure urinary IP10 levels in human subjects with LN (with and without TNIP1 variant rs9588881) and in healthy controls.

Results: We found that serum, urine, and kidney cell IP-10 expression is enhanced in ABIN1[D485N] mice. We also found that urinary IP-10 levels are higher in LN patients with TNIP1/ABIN1 variant rs9458881 when compared to LN patients without the TNIP1 variant and healthy controls. The rs9458881 variant also correlated with disease severity.

Conclusions: Our findings indicate that TNIP1/ABIN1 mutation contributes to the pathogenesis of LN via kidney and immune cell induction of IP-10 secretion and that serum and urinary IP-10 are promising diagnostic markers for LN especially in patients with TNIP1 variants. Further, successful Phase 2 clinical trials with IP-10 mAb for ulcerative colitis indicate its potential for effective LN treatment.

Funding: NIDDK Support

POI1772
Comparative Cross-Tissue and Cross-Species Transcriptome Analyses Predict Lupus Nephritis in Human Systemic Lupus Erythematosus and Guide Therapy in a Tissue-Specific Manner
Eleni A. Panagou,1,2 Panayiotis Garantziotis,2 Maria Grigorou,2 Aeggelos Banos,2 George Bertias,1 Anastasia Filia,1 Dimitrios Boumpas,1,2 Geniko Nokoskomeio Lemosou, Lemosou, Cyprus; 1Irymna Iatrobealti/Genome Ereneun tes Akademias Athoen, Athens, Greece; 2Ethniko Kai Kapodistriako Panepistimio Athenaon, Athens, Greece; Panepistimio Kretes Iatriko Schole, Heraklion, Greece.

Background: Despite advances, morbidity and mortality in systemic lupus erythematosus (SLE) and lupus nephritis (LN) remain increased. Most clinical trials on novel therapies failed to achieve their primary end-points, highlighting the need for therapeutic interventions targeting pathways enriched within individual tissues.

Methods: We applied RNA-sequencing to spleen, kidneys and brain from NZB/W-F1 lupus-prone mice at three stages: the pre-puberty, pre-autoimmunity and nephritic stage. Differentially expressed genes (DEGs) were analyzed with DESeq and functionally annotated with gProfiler. CHEA and Genes2Network were used to infer transcription factors and identify proteins that physically interact with them, respectively. KEA was used to link kinases predicted to regulate DEGs. Implications for human disease were explored in our whole-blood RNA-sequencing dataset of 120 SLE patients [55 LN and 65 non-LN SLE patients and 58 healthy individuals (HI)]. The L1000CDS2 engine was used to identify drugs/small molecules predicted to reverse DEGs. Human orthologs of DEGs were compared to human DEGs. Using machine learning, orthologs from the mouse dataset were used to predict LN in the human dataset, which was split in training and validation sets.

Results: We define lupus-susceptibility and lupus-progression signatures that reveal pathways and gene hubs, and a common cross-tissue signature that depicts transcription factors as putative upstream regulators and kinases as potential targets. Tissue-specific signatures uncover distinct tissue response and repair mechanisms in end-organ injury and distinct targets. 7 small molecules/drugs are predicted to reverse gene signatures in both murine and human SLE.193 orthologs accurately predict LN patients from HI (accuracy=0.86, sensitivity=0.82, specificity=0.91 in the validation set) and 30 orthologs with age and gender best predict LN from non-LN SLE patients (accuracy=0.71, sensitivity=0.73, specificity=0.69 in the validation set).

Conclusions: A murine cross-tissue transcriptome analysis uncovers genes, pathways and tissue-specific targets. The cross-species transcriptome analysis predicts LN in human SLE and guides therapy in a tissue-specific manner.
Efficacy and Safety of Non-Mitogenic Anti-CD3 in the Treatment of Lupus-Prone Mice

Masashi Morita, Masayuki Mizui, Satoshi Masuyama, Yoshitaka Isaka. Osaka University Graduate School of Medicine, Suita, Japan.

Background: Armenian hamster anti-mouse CD3e monoclonal antibody (145-2C11) is known to suppress T cell function in vivo by reducing T-cell receptor (TCR) expression and inducing T cell depletion. However, it has also mitogenic potentials through the functional Fc portion. Although in vivo administration of Fe-depleted 145-2C11 Fab'2 was reported to ameliorate lupus in mice, the detailed mechanisms are still unclear. Recently developed Fe-modified 145-2C11 (2C11 silent; 2C11S), which lacks the ability to bind complement or Fe receptors in vivo, is expected to be stable and safe in vivo as compared with native 145-2C11 (2C11N). Whether 2C11S has therapeutic potential in lupus remains to be elucidated.

Methods: Twenty micrograms of Armenian hamster anti-CD3 (hamster 2C11N), mouse anti-CD3e (mouse 2C11N), mouse anti-CD3e Fe-silent (2C11S), or isotype control IgG1 (IC) were injected intraperitoneally to C57BL6 mice. Lymphocyte number, TCR expression and plasma cytokines from peripheral blood were checked in time series. Next, 2C11S, 2C11N, and IC were administered (100 μg / week, 4 times, intraperitoneally) to NZB/W F1 mice at the age of 10 (early phase) and 29 (active phase) weeks, respectively. Renal histology, immune cell infiltration, and gene expression of cytokines/chemokines were evaluated.

Results: As compared with 2C11N, 2C11S reduced TCR expression on T cells in vivo for long-term period (more than 96 hours) without inducing cytokine release. In early phase of lupus, the rate of change in anti-dsDNA IgG titers (day28 / day0) were significantly reduced in 2C11S group (IC: 2.9±2.0, 2C11S: 2.1±3.0, 2C11N: 2.0±1.3, IC vs 2C11S; p=0.03), which was associated with the decreased number of both follicular helper-T cells and germinal center B-cells in spleen. In active phase, glomerular hypercellularity was diminished in 2C11S group (glomerular cell number: IC; 53±18, 2C11S; 44±6.1, 2C11N; 47±6.6, IC vs 2C11S; p=0.03) and lymphocyte infiltration into kidney was significantly reduced in 2C11S group. In addition, reduction of inflammation-related genes such as IFN-γ and IL-2 in kidney indicated improvement of lupus nephritis by 2C11S.

Conclusions: 2C11S, but not 2C11N, suppressed autoantibody production and ameliorated lupus nephritis, possibly through stable down-regulation of TCR. Targeting CD3 to modulate TCR expression could be a novel therapeutic approach in lupus.

Suboptimal Serological and Clinical Remission on Supportive Therapy in Lupus-Proteinuria Mice

Jennifer Pham, Juan Carlos Q. Ochse. Ochsner Nephrology Ochsner Health System, New Orleans, LA.

Background: A traditional notion is that one third of patients with primary membranous nephropathy (MN) are expected to achieve spontaneous clinical remission without immunosuppressive therapy (IST). Thus, Kidney Disease Improving Global Outcomes (KDIGO) recommends at least 6 months of supportive therapy (SUPPT) without IST in patients with primary MN with low risk for developing end-stage renal disease. Recently, phospholipase A2 receptor (anti-PLA2R) antibody titers have been added to decision-making algorithms. Our objective was to examine and compare rates of serological and clinical remission in patients with PLA2R-MN managed by either SUPPT or IST.

Methods: We retrospectively reviewed records of adult patients diagnosed with PLA2R-MN in native kidneys over the last 5 years at our single medical center. Trajectories of anti-PLA2R titers were extracted. Rates of partial remission (PR) (reduction in urine protein-to-creatinine ratio (UPCR) to 0.5 to 3.0 g/g) and complete remission (CR) (UPCR < 0.5 g/g) were assessed at varying time points within a 24 month interval and compared between patients managed by either SUPPT or IST.

Results: We included 25 patients, median age 59 years, 44% women, 60% black. Positive PLA2R antigen in kidney biopsy was verified in 18/27 (72%). Eight patients were managed by SUPPT and 17 by IST. The median serum creatinine at the time of biopsy was 1.0 mg/dl, for both groups (p=0.58), whereas the median UPCR was 5.6 ± g/g in the SUPPT arm and 10.5 ± g/g for IST (p=0.004). Median anti-PLA2R titer at baseline were 49 (17-76) and 258 (35 –>1500) RU/ml for the SUPPT and IST arms, respectively, p=0.0058. By the 18-month time mark, 19/35 (57%) in the IST group achieved serologic remission (negative anti-PLA2R titer) vs 0/6 (0%) in the SUPPT arm (p=0.02) (missing follow up-anti-PLA2R titer in 2 SUPPT patients). At 24 months, CR and PR was achieved in 1/6 (12.5%) and 3/8 (37.5%) of patients under SUPPT and in 3/17 (17.6%) and 8/17 (47%) of those under IST (p=0.75 and p=0.66, respectively).

Conclusions: Despite baseline characteristics denoting less aggressive disease, patients with PLA2R-MN under SUPPT therapy did not achieve greater rates of clinical remission and exhibited a lower rate of serological remission. Current algorithms dictating choice of SUPPT as initial treatment in low-risk PLA2R-MN should be revisited.

<table>
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<tr>
<th>Type</th>
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PO1778
Experimental Membranous Nephropathy in a Novel Transgenic Rat Model of Decay-Accelerating Factor Deficiency Generated by CRISPR-Associated Protein 9 (Cas9) Genome Editing
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Background: Decay accelerating factor (DAF), controls extent of formation of C3 and C5 convertases. Using clustered regularly-interspaced short palindromic repeats, CRISPR/ associated protein 9 (Cas9) genome editing a DAF deficient (daf-/-) rat model was generated. The present study describes the renal and extrarenal phenotype of this model and responses to podocyte injury in experimental membranous nephropathy (MN).

Methods: daf+/- rats were produced by injecting multiple CRISPRs targeting Cd55 exon 2 into Sprague-Dawley rat embryos. A founder harboring a net 4-bp deletion in exon 2 was backcrossed to the parental strain and litters were genotyped. 1 ml of anti-Fx1A serum was injected in daf+/+ and daf-/- rats to induce MN. Control rats received a single dose (1ml) of normal rabbit serum. DAF protein and mRNA levels were determined by western blotting and Real time PCR Renal function assessment involved measurement of serum urea and creatinine or in urine protein excretion. There was a significant increase in glomerular or tubulointerstitial lesions in daf-/- rats compared to daf+/+ and no change in C3 deposition was backconfirmed by immunofluorescence (IF) and western blot (WB) analysis.

Results: daf-/- rats were healthy, viable and able to reproduce normally. DAF was completely absent in renal and extrarenal tissues (lung, heart) at protein and mRNA level. There was no effect on glomerular Crry and CD59 protein expression. There were no glomerular or tubulointerstitial lesions in daf-/- rats compared to daf+/+ and no change in serum urea and creatinine or in urine protein excretion. There was a significant increase in proteinuria 14 days following anti-Fx1A injection in daf-/- rats accompanied by increased glomerular C3 deposition.

Conclusions: In experimental MN, DAF attenuates proteinuria. The daf-/- rat model provides a valuable tool to assess role of DAF in regulating complement activation in glomerular diseases, such as MN, which is best characterized in this species.

PO1779
T-Cell Epitopes of M-Type Transmembrane Phospholipase A2 Receptor in Primary Membranous Nephropathy
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Background: PLA2R is the major autoantigen of pMN. There is no information on T cell epitopes. We previously identified the risk HLA molecules DRB1*1501 and DRB1*0301. Methods: 123 linear peptides, each consisting of 15-22 amino acids and overlapping by 8-12 amino acids, were synthesized across PLA2R. Their binding capacity to molecules with high capacity. Among them, 11 peptides induced significant proliferations of CD4+ T cells from patients with anti-PLA2R positive pMN: PLA2R1129-1150(CysR3), PLA2R1080-1099(CysR10), PLA2R1112-1118(CysR7), PLA2R1102-1111(FnII-3), PLA2R1115-1124(CTLD3-9), PLA2R1119-1128(CTLD3-10), PLA2R1111-1120(CTLD3-11), PLA2R1117-1126(CTLD5-2-1), PLA2R1124-1133(CTLD7-1) and PLA2R1128-1137(CTLD7-2). Upon activation, PBMCs had similar pro-inflammatory cytokine profiles, predominantly IL-6, TNF-α and IL-10, and to a lesser extent IL-4/5/13 and IL-17.

Conclusions: Thus, we identified 11 potential T-cell epitopes on PLA2R.
PO1780

Investigating the Role of Complement in Membranous Nephropathy Using a Novel Ex Vivo Podocyte Model
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Background: Membranous nephropathy (MN) is an immune-mediated glomerular disease and is the commonest cause of nephrotic syndrome in adults. Progressive loss of kidney function leading to end-stage kidney disease occurs in up to one third of patients. We aimed to explore the potential functional link between antibody positive primary MN and the innate immune complement system using an ex vivo model of human podocytes.

Methods: Using a human podocyte ex vivo model, we evaluated complement activation via immunofluorescence staining for deposition of C3b and C5b-9, and functional alterations (demonstrated by cytoskeletal rearrangement) via IF staining for ActinGreen. Activation of complement via the classical pathway was used as positive control (incubation of podocytes with anti-C5b-9 and 50% NHS for 30 min), whereas NHS-only treated cells were used as negative control. Four patients with biopsy proven primary membranous nephropathy and detailed clinical phenotype were recruited from the Toronto GN Registry. To determine the role of complement in MN pathogenesis, podocytes were incubated with patient serum for 30 min.

Results: 2/4 patients who were nephrotic, antibody (aPLA2R or THSD7A) positive with no current immunosuppression demonstrated (1) positive C3b and C5b-9 staining confirming complement activation (Fig. 1A), and (2) reduced actin staining confirming impaired cytoskeletal organization (Fig. 1B). The remaining 2 patients with negative findings were Ab positive and treated with rituximab at the time of sample collection.

Conclusions: We successfully applied a new ex vivo model using podocytes to demonstrate complement activation in non-immunosuppressed MN patients. Further studies are needed to elucidate the detailed structural and functional consequences of complement activation in MN.

Figure 1

PO1781

Red Herrings: Delayed Immune Checkpoint Inhibitor-Associated Intestinal Nephritis with Membranous Glomerulonephritis and Myeloperoxidase-ANCA Antibodies
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Introduction: Immune checkpoint inhibitor (ICI) indications are expanding. The most common renal pathology is interstitial nephritis. Here, we report a late presentation of ICI-induced interstitial nephritis with concurrent membranous glomerulonephritis (MGN) and MPO-ANCA antibodies.

Case Description: A 52-year-old woman with stage IV small cell lung cancer and prior gastric sleeve surgery on PPI therapy presented with diarrhea and AKI 5 months after discontinuing nivolumab. Her serum creatinine (Scr) was 3.5 mg/dL on presentation, from a baseline of 1.6 mg/dL, along with 0.69 g/g proteinuria and an MPO-ANCA titer of 19. Her PPI was discontinued and her AKI rapidly improved with hydration to a Scr of 0.8 mg/dL, along with 0.69 g/g proteinuria and an MPO-ANCA titer of 19.

Discussion: We reported a late-manifestation of ICI-associated interstitial nephritis (6 months after last exposure) in the setting of PPI use. This case is unique because of its late presentation (>90% of cases present within 3 months from the last dose), and findings of MPO-ANCA antibodies and MGN. Given her mild proteinuria and down trending ANCA titer, we hypothesized that these were not the cause of AKI, but both were likely ICI-associated nonetheless. Nephrologists should be aware of these rare ICI-associated autoimmune conditions.
PO1784

Coexistence of Bullous Pemphigoid and Membranous Nephropathy

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Introduction: Bullous pemphigoid (BP) is an autoimmune disease with linear deposition of IgG and C3 in the skin basement membrane. BP is rarely associated with renal abnormalities like membranoproliferative glomerulonephritis (MN). We describe a rare case of MN in a patient with BP.

Case Description: 75-year-old male, intermittently treated with prednisone for upper extremity (UE) skin lesions, presents with bilateral UE puritic bullae, bilateral lower extremity (LE) and scrotal edema. He was previously treated for LE edema. Renal indices revealed nphrotic range proteinuria. Kidney biopsy showed subepithelial immune deposits consistent with primary MN (immunostain negative for PLA2R). He was treated with furosemide and lisinopril. Skin biopsies of his bullae were inconclusive. His LE edema and UE bullae progressed due to lack of follow up, leading to this hospitalization. Labs revealed eosinophilia, hypoalbuminemia and nphrotic range proteinuria. HIV, hepatitis and UE bullae progressed due to lack of follow up, leading to this hospitalization. Diagnosis of IgG4 immune complexes is more accurate to assess histological remission.

POI1785

Phospholipase A2 Receptor (PLA2R) Positive Membranous Nephropathy (MN) in Celiac Disease

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Introduction: In a 2011 study, PLA2R antibody (Ab) was detected in lupus MN, HBV MN, and solid tumor associated MN, with IgG4 stained glomeruli. PLA2R+ patients did not achieve remission with HBV treatment and tumor resection, suggesting a coincidental occurrence of primary membranous nephropathy (PMN). PLA2R Ab levels in cases of PMN were higher (87.5%) than non-membrane nephropathy (0%) in a 2018 study. PLA2R was positive in 40 cases of secondary membranous nephropathy SMN (25%), including lupus MN, HBV MN, and atypical MN. In 2014, a case of celiac disease (CD) and H. Pylori infection with PLA2R+ MN was reported. Remission was achieved by H Pylori eradication without immunosuppression. In 2002, 2007 and 2009, three cases of renal failure due to MN in CD patients were reported raising the possibility of a link between the two conditions. We report the fourth case on the association of CD and MN to date.

Case Description: 40-year-old male with iron deficiency anemia and small bowel biopsy proven CD presented with pleural effusions, hypoxia, and generalized anasarca. Infectious and rheumatologic work up was negative. Lung biopsy showed hemosiderosis reaching diagnosis of Lane-Hamilton Syndrome (LHS) (idiopathic pulmonary hemosiderosisis, IPH), CH, chronic anemia). Three years prior, he was diagnosed with PMN by PLA2R+ renal biopsy and had nephrotic range proteinuria >9g. He was treated with losartan and diuretics with improvement in his symptoms and decrease in proteinuria to 6g. Serum creatinine rose from baseline of 1.9 mg/dL. He was then started on high dose prednisone for IPH and cyclosporine for MN with further improvement in proteinuria to 2.6g and creatinine to 1.3 mg/dL. Anti-thrombospondin type 1 domain-containing 7A Ab was negative against PMN. He had been trying to adhere to gluten free diet but was not consistent.

Discussion: CD is known to cause IPH and chronic anemia. It was hypothesized that chronic gastrointestinal inflammation triggers auto antibody formation against PLA2R1, which is present in duodenum and gastric cells in addition to glomerular cells. This would favor a causal relationship rather than coincidence of two idiopathic processes. Gluten free diet and steroids are the mainstay of therapy for LHS. We hope to prove that adherence to strict gluten free diet in our patient in addition to sustained low dose prednisone would lead to remission of MN without need for cyclosporine.

PO1786

Hydralazine-Induced Membranous Nephropathy

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Introduction: Hydralazine is associated with a variety of rare renal diseases including drug-induced lupus, ANCA vasculitis and membranous nephropathy (MN) with associated crescentic GN. We present a case of a patient with features of hydralazine-induced MN with some FSGS but no features of vasculitis. This would be the first such reported case to the best of our knowledge.

Case Description: This 67-year-old female with a medical history of HTN, DMT2, anti-C1q disease, presented with urinary symptoms and proteinuria. She had rapidly worsening Cr rising from 1.9 to 2.69 mg/dL over 1 month, prompting a renal biopsy and stopping hydralazine therapy. The biopsy showed areas of scarring and FSGS on light microscopy and membranous nephropathy on EM but demonstrated none of the classic necrotizing or crescentic lesions associated with drug-induced vasculitis or any of the typical findings of lupus nephritis. Follow-up PLA2R, thrombospodin, and Hsp returned negative. Age appropriate cancer screening was negative. Repeat blood work showed Cr returning to prior baseline after 1 month off hydralazine. We decided together with the patient to continue to monitor and forgo more aggressive therapy. Renal function remained baseline for the next 6 months.

Discussion: This case represents an up-to-now unreported case of hydralazine-induced MN without associated vasculitic lesions. Patient fit the classic serological findings for a drug-induced vasculitis and her renal function stabilized upon cessation of exposure to hydralazine, giving us a high suspicion for causality. Given renal decline during workup, re-exposure was not attempted. This patient never demonstrated any clinical or lab findings of MN disease: no severe proteinuria, no sequela of nephrotic syndrome, and no associated diseases. Additionally, no lupus-like findings were appreciated on biopsy. We believe we have identified a novel association of hydralazine-induced MN.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Lupus nephritis (LN) complicates 20-49% of systemic lupus erythematosus (SLE) patients. Vascular lesions are not considered in the activity index of LN pathology classification. We report a case of LN with severe necrotizing arteritis without proliferative glomerular lesions, prompting a more aggressive intervention.

Case Description: A 49-year-old female was referred for asymptomatic hematurnia and nephrotic-range proteinuria (4.9 g/g) in March 2014. Her creatinine (0.77 mg/dL), C4, ANA, dsDNA, and Rheumatoid factor were normal with low C3. Labs were normal for Hepatitis B, C, HIV, ANCA, RNP, and Sm antibodies. She was started on lisinopril, and initially the proteinuria improved (2.3 g/g) and renal functions were stable. Hematurnia was initially suspected to be secondary to MPGN. Renal biopsy immunofluorescence showed IgG, C3, IgM, kappa/lambda, and C1q (in lesser quantity). EM showed deposits in subendothelial, subepithelial and mesangium. She was diagnosed with immune complex glomerulonephritis without evidence of systemic lupus. Over the next 2 years, proteinuria worsened from 1.9 to 5.7 g/g despite increasing lisinopril to maximum dosage (40 mg/day). Hematurnia and low C3 levels persisted. In February 2017, creatinine worsened (1.33 mg/dL). Cellcept (1000 mg/day) was started in March; by June, there was no response. Lisinopril was stopped in May due to low BP. A second renal biopsy (November 2017) showed a lupus picture with a full house pattern (3+ IgG, 1+ IgM, 2+ C3, 3+ C1q, 2+ kappa/lambda, IgA+ tubular casts). EM showed subendothelial and scattered subepithelial deposits, and GBM duplication. She was diagnosed with Class IV Lupus Nephritis. She was started on Cytoxan (500 mg q 2 weeks x6 weeks) and prednisone (60 mg/day). She showed improvement and was started on Imuran in May 2018 for maintenance. Her proteinuria (400mg/g) and creatinine (0.93mg/dL) improved, C3 normalized, and hematurnia resolved.

Discussion: Diagnosis of lupus nephritis can be missed on the basis of atypical labs and requires a high degree of suspicion and a biopsy. This case represents such an atypical presentation without systemic lupus. Initially, thought to have C3 nephritis; but later, the diagnosis was confirmed by renal biopsy and electron microscopy. The Full House immunofluorescence pattern seen in this patient is characteristically indicative of lupus nephritis, and she was responsive to immunosuppressive therapy.

Hepatitis B-Associated Lupus-Like Nephritis
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Introduction: The spectrum of renal disease with hepatitis B virus (HBV) is broad including different glomerular lesions related to the presence of viral antigens. HBV-associated lupus-like nephritis (HBLN) is characterized by immune deposits of polyclonal immunoglobulins linked to polytropic complements in glomeruli, structures reminiscent of lupus nephritis (LN). There is a dearth of literature regarding differentiation of HBLN and LN along with differing management and outcomes.

Case Description: We report a 46-year-old male with known HBV infection with 3 weeks of progressive dyspepsia and edema. The serum creatinine (Scr) rose from a baseline of 0.8 mg/dl to 5.2 mg/dl with proteinuria of 1.7 g/g and microscopic hematuria. Serology showed transiently positive ANA, negative anti dsDNA, and low levels of C3. Hepatitis B e Ag and hepatitis B surface Ag were positive, and the viral load was 2483 IU/mL with normal liver enzymes. A renal biopsy revealed severe diffuse endocapillary hypercellularity, a “full house” immunofluorescent pattern, and numerous subendothelial and mesangial immune deposits ultrastructurally, findings consistent with a diagnosis of HBLN. The patient was started on Entecavir for treatment of hepatitis B. After 2 months of treatment, the Scr improved to 1.97 mg/dl with improvement in initial symptoms.

Discussion: Our case highlights the inherent difficulty in recognition of renal failure secondary to HBLN with associated pathology findings consistent with LN in the presence of hepatitis B infection. Although the full-house immunofluorescent pattern generally implies a diagnosis of LN, renal biopsy findings have to be interpreted in the clinical context. All the findings in renal biopsies of LN can also be seen in HBLN. Renal manifestations in both groups, including proteinuria and Scr, can be similar. Although considerably lower C3 levels in patients with lupus may suggest more widespread extrarenal disease, low C3 levels have also been reported in HBLN. The distinguishing feature between HBLN and LN is the presence of HBsAg and hepatitis B DNA. Our case is an unusual presentation of hepatitis B with renal involvement with effective diagnosis and management. While there is limited data for the treatment of HBLN with most studies excluding patients with an elevated Scr, small studies suggest first-line treatment with antiviral agents to achieve viral clearance.

A Unique Case of Autoimmune-Mediated Cryoglobulinemic Glomerulonephritis
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Introduction: Cryoglobulinemic syndrome is a disease in which immunoglobulin components are deposited within tissues, resulting in various end-organ damage. Subtypes Type II and III contain mixed monoclonal and polyclonal immunoglobulins, thereby referred to as Mixed Cryoglobulin Syndrome (MC). MC is often associated with infections such as Hepatitis C; however, it can also be secondary to autoimmune diseases. While the most common associations are with Systemic Lupus Erythematosus and Sjogren’s disease, occasionally, MC can be seen with other rheumatologic conditions. We examine a rare case of Overlap Syndrome (OS) induced cryoglobulinemic glomerulonephritis (CG).

Case Description: A 44-year-old woman with a history of OS, presented with symptoms of fatigue, generalized edema, weight gain of 20lbs, and found to have an acute kidney injury (AKI). She was admitted to the hospital with a diagnosis of decompensated heart failure. The diagnosis of OS was confirmed with elevated ANA, SSA, RNP antibodies, as well as negative dsDNA and anti-smith antibodies. Previously, she was unsuccessfully treated with methotrexate and hydroxychloroquine. She was on hydroxychloroquine monotherapy at the time of admission. During the investigation for her AKI, she was found to have hematuria and non-nephritic range proteinuria (UPCR 2.65g/dL), raising concerns for glomerulonephritis. Subsequent renal biopsy showed autoimmune-mediated cryoglobulinemic glomerulonephritis. She was treated with a combination of methylprednisolone/prednisone and rituximab, which resulted in normalization of renal function.

Discussion: This case illustrates a patient with a history of OS with biopsy proven autoimmune mediated CG. The patient’s underlying diagnosis of OS is likely the leading risk factor for renal impairment secondary to immunoglobulin deposits. Treatment
is focused on immunosuppression, including steroids, rituximab, or mycophenolate mofetil. Combination therapy with a non-steroid immunosuppressant is preferred over monotherapy with steroids. The patient was treated with steroids and rituximab, with recovery of renal function. Given the varying presentation of CG, physicians should be mindful of keeping a broad differential, particularly in patients with rheumatological history presenting with proteinuria, hematuria, and signs of renal dysfunction.

PO1791
Bartonella Buried in the Aortic Valve

Introduction: Bartonella species are the most common cause of culture-negative endocarditis in the United States. We report a case with culture negative Bartonella endocarditis masquerading as Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis.

Case Description: A 46 year old male presented with leg rash and swelling. Physical exam was notable for diastolic murmur in the aortic area and a systolic murmur in the mitral area and non blanching purpura on the lower extremities. Labs showed BUN 39mg/dl, creatinine 1.54 mg/dl. Urinalysis showed non nephrotic range proteinuria and microcytic anemia. ANA was 1:160, RF was 541 IU/mL, complement C3 and C4 levels were low and serum cryoglobulin was positive. ANCA titer was elevated with myeloperoxidase ANCA of 38 AU/mL and serum proteinase 3 ANCA of 580 AU/mL. Anti-Smith antibodies were 68AU/mL. Echocardiography showed severe mitral and aortic regurgitation with mitral and aortic vegetations. Ceftriaxone and vancomycin were started after blood cultures were obtained which remained negative. The aortic valve was replaced with mitral and tricuspid valve repair.

Discussion: Bartonella is the most common cause of culture-negative endocarditis in the United States with a reported association with pauci-immune glomerulonephritis. Intense serological testing and valve PCR were helpful in establishing the diagnosis.

Conclusion: Heterogenous glomerular lesions were found in our cohort. Previous cohort study showed that membranous nephropathy was rare, but in this study, two out of eight cases turned out to be membranous nephropathy. In addition, analysis of IgG subclass suggests that either IgG1 or IgG2 was dominant in secondary membranous nephropathy due to Castleman disease and that deposition of immunoglobulin complex could be associated to the onset of proteinuria of Castleman disease.

PO1793
Is It Systemic Lupus Erythematosus Nephritis or Not?
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Introduction: IC-MPGN (immune complex-mediated glomerulonephritis) is a histopathological finding that is associated with infection, immune-complex deposition, monoclonal gammapathies as well as autoimmune disorders such as lupus, Sjögren’s, and rheumatoid arthritis. MPGN traditionally has been classified as I-III depending on the pathology findings. More recently, an alternative classification system based on the pathological process has been developed (immune complex-mediated vs complement-mediated).

Cases: In cases of IF showing IgG +/- C3, a tentative diagnosis of immune-complex mediated MPGN can be made. MPGN treatment is aimed first at treating the underlying cause. In the case where a cause cannot be found, as in our case of biopsy-proven IC-MPGN with negative serologies, the underlying mechanism is not clear.

Conclusion: Diagnosis: 71 year-old female with PMHx aortic valve replacement, HTN, CKD-I presented with constitutional symptoms, and AKI on CKD with proteinuria. She was found to have biopsy-proven immune complex mediated MPGN, but the etiology was unclear due to negative: ANA, anti-Smith, anti-Ro/SS, anti-La/SSB, Hep B/C, cryoglobulins, CCP, CRP, ESR. K/L. The biopsy pattern was consistent with Lupus Type IV/V, with EM findings showing scattered sub endothelial dense deposits and full house IF staining pattern. CT abdomen/pelvis was negative. Further testing and workup for malignancy were negative. She was started on high-dose steroids for initial treatment of presumptive seronegative lupus nephritis. Serologies were repeated and all were negative. Patient showed improvement with initiation of mycophenolate ± steroids; proteinuria and creatinine improved on follow-up.

Discussion: The optimal initial treatment of idiopathic/seronegative immune complex-mediated MPGN has not been established. In this case, the patient improved with aggressive steroid treatment with a tapering dose after starting mycophenolate. Proteinuria which was initially nephrotic at 14 g/g is now near 0.2 g/g.

PO1794
Role of the IgA Immune Complexes Bound to FcαRI/CD89 in IgA Nephropathy
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Background: Studies have demonstrated the pathogenic role of circulating polymers IgA immune complexes (poly-IgA ICs) in IgA nephropathy (IgAN). In this study we aim to evaluate the role of poly-IgA ICs specifically bound to FcαRI/CD89 in the kidney development of IgAN.

Methods: rCD89 protein was produced from a HEK293 cell expression system. A novel ELISA method that using rCD89 as the ‘capturing’ probe was established for detecting poly-IgA ICs. The plasma levels of poly-IgA ICs were measured in 181 IgAN patients and 35 patients with glomerular diseases of unrelated etiologies. Another 85 age-, gender-, and geographically-matched healthy individuals were enrolled as controls.

Results: A total of 268 proteins were identified in mass spectrometry. The plasma levels of poly-IgA ICs in IgAN (26.67, 17.06 to 42.61 units/ml) were significantly higher than healthy controls (15.46, 10.73 to 20.04 units/ml; P<0.001) or disease controls (13.99, 10.35 to 24.22 units/ml; P<0.001). Patients with higher levels of poly-IgA ICs had lower eGFR, higher proteinuria and higher Oxford scores in E and T lesions. Accuracy parameters and concordant statistics showed good discrimination between IgAN and healthy controls for poly-IgA ICs levels (AUC, 0.775; 95% CI, 0.720–0.832; P<0.001), significantly better than IgA1 levels (AUC, 0.710; P=0.015) and galactose deficient-IgA1 levels (AUC, 0.702; P=0.048). A total of 268 proteins were identified in mass spectrometry analysis. The protein abundance of fibrinogen alpha chain, protein AMBP and C4H were higher in IgAN group.

Conclusion: Higher level of rCD89-bound poly-IgA ICs was a potential useful diagnostic biomarker in patients with IgAN which was also associated with the severity of the disease. The findings suggest that the role of CD89 in eliminating IgA ICs and it may be a new approach to improve the clinical progress of patients with IgAN.

PO1795
Proteinuria and the Role of IgA Deposition in the Pathogenesis of IgA Nephropathy
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Introduction: Proteinuria and the role of IgA deposition in the pathogenesis of IgA nephropathy may be a new approach to improve the clinical progress of patients with IgAN.

Methods: Case-series was designed for analyzing the clinicopathological features of renal dysfunction accompanied with Castleman disease. Inclusion criteria of the object was renal biopsy performed between 1990 and 2019 and the patients who were diagnosed as Castleman disease. Clinical and pathological data was collected from the electrical medical record.

Results: Eight patients were eligible to the study. Seven out of eight cases were plasma cell type, while anti-HIV anti-gp120 was negative in all cases. Laboratory data at the time of renal biopsy showed: median serum creatinine was 0.75(0.6-5.0) mg/dL, urine protein was 1.28(0.04-8.9) mg/dL. In glomerular lesion, following involvement were found: two cases of AA amyloidosis and membranous nephropathy respectively, while

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
The baseline clinical and pathological characteristics of IgA nephropathy patients

PO1795
Racial Heterogeneity of IgA Hinge Region O-Glycoforms in Patients with IgA Nephropathy
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Background: IgA with galactose (Gal)-deficient hinge region (HR) O-glycans (Gal-Gd-IgA1) plays a crucial role in the pathogenesis of IgA nephropathy (IgAN). The microRNAs, namely let7b and miR-148b, which affect IgA1 HR O-glycosylation, showed differences in serum levels between Caucasians and Asians, suggesting a racial difference in HR O-glycosylation. To understand race-specific IgA1 HR O-glycoform heterogeneity at the molecular level, we compared Greek and Japanese profiles of IgA1 HR O-glycoforms in patients with IgAN.

Methods: IgA1 from sera of 10 Japanese healthy controls (J-HC), 36 Japanese IgAN patients (J-IgAN), 16 Greek HCs (G-HC), and 23 Greek IgAN patients (G-IgAN) were subjected to liquid chromatography-high-resolution mass spectrometry, and the HR-binding Gal and GalNAc B-glycoforms in patients from both racial groups, compared with healthy subjects, and in Greek individuals. The amount of GalNAc per HR showed a common tendency to decrease in patients from both racial groups, compared with healthy subjects, and in Greek individuals. The amount of Gal per HR decreased in patients from both racial groups, compared with healthy subjects, and in Greek individuals. The disease-specific IgA1 HR (Gal-Gd-IgA1) on glomerulus were examined by immunohistochemistry.

Results: No significant difference in the grades of urinary protein and hematuria was observed between CD-IgAN and NOS-IgAN, but CD-IgAN had elevated serum creatinine (sCr) and lower rate in clinical remission after steroid treatment as compared to NOS-IgAN. Pathologically, CD-IgAN had remarkably higher levels of global glomerulosclerosis (%), grades of interstitial fibrosis and tubular atrophy (IFTA) than NOS-IgAN. Immunohistochemically, IgA1 was a dominant subclass and Gd-IgA1 was frequently detected in glomerular mesangium in both groups. No difference was noted in the extents of IgA1, IgA2 and Gd-IgA1 deposition, depending on the presence or absence of CD.

Conclusions: From the results of the subclasses and galactose-deficiency of the IgA molecule, no difference was suggested in the etiology and pathogenesis between CD-IgAN and NOS-IgAN. However, advanced glomerulosclerosis and tubulointerstitial fibrosis in renal pathology and highly resistant clinical features to medical treatments in CD-IgAN suggest that the intestinal immunity and other clinical factors associated with CD may promote and activate the inflammatory process of IgAN.

PO1797
Antibody Sequencing Analysis After Flu Vaccine Response in IgA Nephropathy Patients Reveals Enhanced IgA Variable Regions of the Heavy Chains Lineage Diversity
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Background: IgAnephropathy (IgAN), the most common primary glomerulonephritis in the world, is characterized by mesangial immunodeposits consisting of galactose-deficient IgA1 (Gal-Gd-IgA1) and Gd-IgA1-specific IgG autoantibodies. IgG autoantibodies in IgAN patients have variable regions of the heavy chains (VH) with long complementarity-determining region 3 (CDR3) that contains a key amino-acid residue important for binding Gd-IgA1. This CDR3 modification is not due to a genetic variant of a VH gene but is thought to originate from somatic mutations. To determine whether IgAN patients have generally enhanced rates of VH somatic mutations, we have assessed responses to influenza-vaccine antigen in IgAN patients and healthy controls.

Methods: Peripheral blood (PB) from 4 IgAN patients and 4 healthy controls (HC) was collected 7 d after flu vaccination (i.m.), the peak of plasmablasts in PB. Plasmablasts were isolated after enrichment with CD138-coated beads. cDNA from plasmablasts was used for VH gene amplification with VH and isotype-specific primers, and sequenced on an Illumina MiSeq. Sequences were filtered, aligned, and grouped using an in-house workflow, with further analyses performed in Matlab.

Results: Isotype-specific nucleotide mutation rates were similar in IgAN and HC plasmablasts, except for IGHV3-1, with a higher rate in HC for IgM (p=0.01). Average nucleotide mutation rate for CDR3 was 1.6% higher in HC compared to IgAN, almost reaching significance (p=0.06). Further analysis revealed that number clonotype-specific VHsequences was increased for IgA in plasmablasts from HC vs. IgAN for IGHV2-5p (p=0.02), IGHV3-7p (p=0.04), IGHV3-3p (p=0.02), IGHV3-21p (p=0.03), IGHV3-48p (p=0.02), IGHV4-32p (p=0.05), IGHV4-56p (p=0.04), and IGHV4-61 (p=0.02).

Conclusions: Analysis of influenza-vaccine-specific immune responses showed that IgAN patients and HC exhibit similar VH repertoire diversity. Unexpectedly, we also observed thatIgAN patients produced fewer IgF VHsequences than healthy controls after flu vaccination, indicating a possible disparity of IgA responses in IgAN.

Funding: NIDDK Support, Private Foundation Support
Identification of Proteins Associated with IgA1-Containing Circulating Immune Complexes in Patients with IgA Nephropathy
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Background: IgA1-containing immune complexes (IgA1-ICs), consisting of galactose-deficient IgA1 (Gd-IgA1) bound by IgG specific for Gd-IgA1, are central to the pathogenesis of IgA nephropathy (IgAN). We have shown that Gd-IgA1 alone is not sufficient to induce mesangial-cell proliferation and that additional serum proteins are required for IgA1-ICs to become nephritogenic. To elucidate the composition of IgA1-ICs, we have developed a novel proteomic-bioinformatic workflow to identify proteins in IgA1-ICs in patients with IgAN.

Methods: IgA1-ICs from sera of 20 patients and 20 healthy controls were isolated by lectin affinity chromatography followed by size-exclusion chromatography (SEC). Quality-controlled test confirmed that most IgA1-ICs and free IgA1 were captured by affinity chromatography. IgA1-ICs were separated by SEC from monomeric and polymeric IgA1. After IgA-specific protease and LC-MS/MS sequencing trypsin digestion, each IgA1-IC sample was analyzed by liquid chromatography coupled on line with mass spectrometry (LC-MS). After standard proteomic database searches, LC-MS results were extensively curated by use of Scaffold perSpectives to identify proteins enriched in IgA1-ICs of IgAN patients vs. healthy controls. Additional comparisons included polymeric and monomeric IgA1.

Results: Seventy-nine proteins were identified in IgA1-ICs samples from IgAN patients, with a false discovery rate of 1%. After proteomic-bioinformatic curation, we generated a list of 38 proteins with high-confidence identification that were uniquely enriched in the IgA1-ICs from patients with IgAN. Using Principle Component Analysis, we confirmed that protein content differentiated the three molecular forms of IgA1, monomeric, polymeric, and IgA1-IC. Pathway analysis indicated that proteins in IgA1-ICs were part of the complement cascade, with seemingly more enrichment in the regulation of complement, and the plasma lipoprotein pathway.

Conclusions: Our new workflow enabled targeted identification and evaluation of proteins associated with IgA1-ICs in IgAN. These proteins represent new targets to be evaluated for their roles in the formation and activity of the nephritogenic IgA1-ICs in IgAN.

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Low Serum IgG4: A Remarkable Diagnostic Biomarker for IgAN Nephropathy
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Background: Reports regarding IgG subclasses in IgAN nephropathy (IgAN) are scarce. Low serum IgG4 levels in IgAN patients were evident in our preliminary experiment. We aim to verify the low IgG4 levels in IgAN and investigate the related immune mechanism.

Methods: Three groups of IgAN patients were enrolled, including the newly diagnosed IgAN-N (n = 58), IgAN-NF (n = 28) with a follow-up interval of (19 ± 11) months, and IgAN-10 patients (n = 27) who have been diagnosed over 10 years. Healthy individuals (n = 56) and patients with idiopathic membranoproliferative nephropathy (IMN, n = 30) were enrolled as controls. Serum IgG4, IgG, galactose-deficient IgA1 (Gd-IgA1), and urinary IgG4 levels were detected by ELSA. The IgG4/B, Th1, and Th2 cells were measured by flow cytometry. Receiver operating characteristic curves and logistic regression analyses were performed to evaluate the diagnostic and predictive abilities of IgG4.

Results: The serum IgG4 levels in IgAN patients differ with course, severity, and outcomes, and were all significantly lower than those of healthy controls and IMN (all \( P < 0.001 \)). The catalytic value of IgG4 in differentiating IgAN from healthy individuals and IMN was respectively 0.26mg/ml (sensitivity 98.3%, specificity 82.1%, AUC 0.938, \( P < 0.0001 \)) and 0.24mg/ml (sensitivity 96.6%, specificity 73.3%, AUC 0.869, \( P < 0.0001 \)). The risk of IgAN in subjects with low IgG4 levels was 28 times higher than that of normal individuals (OR 281.11, 95%CI 34.33 - 2301.97, \( P < 0.001 \)), and a negative correlation between serum Gd-IgA1 and IgG4 levels was observed in healthy controls (\( r = -0.240, P = 0.077 \)) and IgAN-N patients (\( r = -0.066, P = 0.629 \)). Similar results were obtained when IgG4/GD was analyzed in the same patients and controls. The urine IgG4 levels \( \mu g/\mu l \) in IgAN-N (278 ± 210.80) were higher than healthy controls (278.87 ± 210.89, \( P < 0.001 \)), but similar to IMN (1153.53 ± 208.40, \( P = 0.341 \)). The IgG4/B1/B2 cells (0.29 ± 0.17 vs. 0.61 ± 0.56, \( P = 0.017 \)) and Th2/Th1 (0.54 ± 0.27 vs. 0.87 ± 0.44, \( P = 0.037 \)) of IgAN were significantly lower than those of healthy controls.

Conclusions: Serum IgG4 levels of IgAN patients are generally low, and the low IgG4 level may be a risk factor for IgAN. Serum IgG4 may be a remarkable diagnostic biomarker for IgAN. Decreased IgG4/B and Th2 cells may contribute to the low IgG4 levels.

Comparing the Lectin and Mass Spectrum-Based Approaches to Quantify Galactose-Deficient IgA, in IgA Nephropathy
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Background: Abnormalities in O-glycosylation of circulating IgA, are implicated in the pathogenesis of IgAN. We initially demonstrated altered binding of lectins with specificity for O-linked glycans and confirmed later by mass spectrometry. Nevertheless, combining and interpreting the results from these two orthogonal techniques is difficult, due to their different levels of complexity. We applied the two approaches to quantify galactose-deficient IgA, (Gd-IgA) in plasma samples of IgAN patients and matched controls. We aim to identify potential sources of discrepancy between the two analytical methods.

Methods: IgAs were affinity purified from plasma samples from 23 patients with IgAN and 36 controls. We used enzyme-linked lectin assay and the lectin from Vicia villosa (VVL) to measure defective galactosylation of O-linked oligosaccharides. Monomeric (mIgA) and polymeric (pIgA) forms of IgA, were size-separated by gel electrophoresis. IgA-containing bands were in-gel digested with trypsin, the released glycopeptides were analyzed by electrospray ionization liquid mass spectrometry.

Results: A significantly larger fraction of IgA, molecules in the circulation of IgAN patients exist as high molecular mass complexes, as compared with the control group (48.8 ± 42.8%, \( p = 4.25E-02 \)). The reactivity of VVL lectin with unfractonated IgA, was higher in the IgAN group compared with healthy controls (10.9 ± 9.1 A.U., \( p = 6.06E-02 \)). By contrast, binding to IgA, binding was much stronger for pIgA than mIgA. Mass spectrometry showed that the level of Gd was higher in pIgA than in mLgA (3.66 ± 3.54 Gal/Heavy Chain, \( p = 7.63E-05 \)). However, no significant differences in glycan composition was detected between patients and controls. In all the experiments, the inter-individual differences in glycan composition were large, which may have obscured the signals from the disease-related galactose-deficient IgA.

Conclusions: Our results suggest that the apparent increased abundance of Gd-IgA, in circulation of patients with IgAN, is at least in part, attributable to a greater abundance of polymeric IgA, compared with controls. However, the glycosylation profile of each form of IgA, appeared indistinguishable in the IgAN group when compared to the corresponding form in the control group.

Developing Molecular-Specific Biomarker Assays for IgA Nephropathy and IgA Vasculitis with Nephritis
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Background: Patients with IgA nephropathy (IgAN) develop characteristic glomerular immunodeposits containing IgA that is enriched for IgA1 glycoforms with galactose-deficient hinge-region O-glycans (Gd-IgA1). Blood levels of Gd-IgA1 are elevated in patients with IgAN and those with IgA vasculitis with nephritis (IgAV-N), suggesting a key role of Gd-IgA1 in pathogenesis of these diseases. In contrast, patients with IgA vasculitis (IgAV) without renal involvement do not have elevated blood levels of Gd-IgA1. These observations suggest potential prognostic role for a minimally invasive biomarker based on profiling serum/plasma IgA1 O-glycoforms. Here, we describe a novel workflow to qualitatively and quantitatively assess molecular IgA1 phenotype(s) in IgAN by profiling serum IgA1. This validated approach can be extended to IgAV-N patients.

Methods: Isolation of IgA1 from sera is based on lectin-affinity chromatography followed by size-exclusion chromatography to separate IgA1 monomeric and polymeric forms and IgA1 bound in immune complexes. IgA1-glycoform analysis was analyzed by liquid chromatography-high-resolution mass spectrometry (LC-MS). In a pilot study, we used monomeric IgA1 from sera of 10 healthy controls and 10 IgAN patients. LC-MS runs were standardized using internal and external calibration methods.

Results: Quantitative LC-MS analysis revealed variations in the abundance of individual IgA1-\( O \)-glycoforms in the tested samples. We used quantitative data for 10-15 IgA1 glycoforms, expressed as relative ratios, to distinguish IgA1 from patients with IgAN vs. healthy controls. Furthermore, the LC-MS assay was standardized with internal and external calibration methods, an approach that will enable sample normalization, internal validation studies, as well as evaluation of IgA1 from patients with IgAV-N.

Conclusions: Quantitative profiling of IgA1 clustered O-glycosylation can determine molecular IgA1 phenotype(s) and identify IgA1 glycoforms as biomarkers related to disease pathogenesis. These approaches are applicable to differential profiling of IgA1 from patients with IgAN vs. IgAV vs. healthy controls to identify pathogenic IgA1 glycoforms involved in the formation of nephritogenic immune complexes in IgAV-N.

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PO1802
Mass Spectrometric Analysis of IgA, O-Glycans and Glomerular Diseases: IgA, C3G, and FSGS

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PO1804
TLR9 Signaling Pathways in Nasal-Associated Lymphoid Tissue Have a Crucial Role in the Pathogenesis of IgA Nephropathy

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Background: The pathogenesis of IgA nephropathy (IgAN) is closely associated with immuno-regulation of mucosal immune system. However, it is unclear which nasal-associated lymphoid tissue (NAL) or gut-associated lymphatic tissue (GALT) is more involved in the pathogenesis of IgAN. In present study, we examined whether NALT or GALT is the major responsible site for the nephritogenic immune complexes in murine IgA nephropathy.

Methods: We examined the effect of broad-spectrum antibiotics in the IgAN onset ddY mice. In addition, we assessed disease phenotypes of the IgAN onset ddY mice housed in germ free condition (GF-ddY) and transferred to specific pathogen free condition (SPF-ddY). The levels of aberrantly glycosylated IgA and IgG-IgA immune complexes (IC) in serum and supernatant of cultured cells purified from NALT and mesenteric lymph node (MLN) were measured using the IgAN onset and the quiescent ddY mice (n=15). To identify dysregulation of mucosal immune response site in IgAN, NALT and GALT were immunized separately in GF-ddY mice, i.e., nasally challenged with TLR9 ligand (CpG-ODN) stimulation andecal transplantation.

Results: Broad-spectrum antibiotics depleted microbiota efficiently, resulted in ameliorating clinopathological changes in IgAN onset ddY mice. Moreover, the GF-ddY mice did not develop IgAN, meanwhile, the GF-ddY mice showed an aggravation of renal injury with mesangial IgA deposition after transferred to SPF condition. In the IgAN onset ddY mice, the levels of aberrantly glycosylated IgA and IgG-IgA IC in serum and supernatant of cultured cells purified from NALT are significantly higher than those in the quiescent ddY mice. However, the levels of supernatant aberrantly glycosylated IgA and IgG-IgA IC produced by cultured cells purified from MLN showed no significant difference between the IgAN onset and the quiescent ddY mice. Although the GF-ddY mice nasally immunized with Cpg-ODN also showed an aggravation of renal injury with mesangial IgA deposition, the GF-ddY mice which received fecal transplant did not develop IgAN.

Conclusions: Present study indicated that the dysregulation of mucosal immune response due to exogenous antigen exacerbated the pathogenesis of IgAN. TLR9 signaling pathways in NALT may be mainly involved in the pathogenesis of IgAN.

PO1803

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Background: Chronic Kidney Disease (CKD) is an emerging global health challenge, affecting 10-15% of the population. Lack of reliable biomarkers precludes the early diagnosis of CKD. The progression of CKD is known to be dictated by renal tissue changes. For example, in the case of Diabetic Nephropathy, disease progression is accompanied by considerable changes to the glomeruli including the thickening of the glomerular basement membrane and mesangial expansion, extracellular matrix accumulation, reduced podocyte number, inflammation of the renal tissue, the influx of immune cells which ultimately lead to tissue damage and progression to CKD. Understanding these tissue-centered events on a deeper level is imperative to reduce morbidity associated with CKD and for early diagnosis.

Methods: To aid high-level multiplex staining of these tissues by immunofluorescence, we developed a novel multiplex staining method called SeqStain. The SeqStain multiplex platform uses DNA tagged antibodies and Fab fragments to stain while endomucinases are used to achieve gentle de-staining after each round. We designed a SeqStain multiplex platform with antibodies to probe different histological regions relevant to the kidney. Antibodies or Fab fragments were tagged with DNA oligonucleotide duplex which carries multiple fluorophores. Labeled Fab fragments were pre-complexed with primary antibodies for staining.

Results: SeqStain modified antibodies and Fab fragments efficiently labeled multiple markers in tissue sections. Kidney tissues were stained with the SeqStain reagents and de-stained using endomucinases and provided a simple, gentle, and rapid technique for multiplex imaging of the tissues. The method was implemented using a custom flow chamber and allowed the labeling of tens of antigens on a single tissue section. Image alignment and overlay were performed to spatially orient multiple cell types in the tissue.

Conclusions: SeqStain method offers a robust yet gentle multiplex staining method to profile the CKD kidney tissues and comprehend the tissue-centered events that could play a role in the disease progression. Currently, we are profiling the CKD tissues in multiple staining experiments and comparing it to healthy human kidney tissues to generate the spatial maps.

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PO1805
Functional Studies of IgG Autoantibodies in IgA Nephropathy

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Background: IgA nephropathy (IgAN) is an autoimmune disease wherein galactose-deficient IgA1 (Gd-IgA1) is recognized by IgG autoantibodies (autoAbs), resulting in the formation of immune complexes (ICs), some of which deposit in the kidneys and induce glomerular injury. We have shown that a recombinant IgG (rIgG) autoAb derived from an IgAN patient can bind to Gd-IgA1, form ICs, and induce pathologic mesangioproliferative changes in a passive mouse model of IgAN. However, the interaction between the key elements, Gd-IgA1 and IgG autoAbs, has not been fully clarified. After solving the Fab structural studies of different variants of this rIgG will elucidate the nature of autoantigen.

Methods: Based on solved 3-D structure of the Fab of rIgG autoAb, we used site-directed mutagenesis to replace specific amino-acid (aa) residues in the rIgG autoAb. rIgGs were expressed in Expi293F cells and purified by affinity chromatography. ELISA was used to assess the binding of rIgGs to Gd-IgA1. Fab fragments of two selected mutants of rIgG were purified and used for hanging-drop crystallization. Liquid chromatography coupled with mass spectrometry (LC-MS) analysis was used to identify Gd-IgA1 O-glycosforms recognized by rIgG autoAb.

Results: We generated rIgG variants with aa replacements in several heavy-chain segments: junction of framework 1 (FR1) and complementarity-determining region 1 (CDR1) and in the CDR3. The FR1-CDR1 mutations reduced or disabled rIgGs binding to Gd-IgA1 depending on the specific aa residue used for replacement. Mutations in CDR3 completely impaired the binding of rIgG to Gd-IgA1. LC-MS analyses indicated that rIgG autoAb preferentially binds to a subset of IgA1 molecules, resulting in enrichment of the glycoforms recognized by rIgG autoAb.

Conclusions: Our study identified specific aa residues in the FR1-CDR1 and CDR3 regions of the rIgG autoAb that are critical for Gd-IgA1 binding. The ongoing structural studies of different variants of this rIgG will elucidate the nature of autoantigen recognition by IgG autoAbs. This knowledge, together with the understanding what are the major glycoforms that will allow us to develop future therapeutic approaches based on blockade of these pathogenic IgG autoAbs in IgAN.

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Underline represents presenting author.

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PO1806

Can the Cross-Talk Between PDGF Receptor and Axl in Mesangial Cells Represent a Possible Therapeutic Target in IgA Nephropathy? Qi Biao,1 Zhi qiang Huang,2 Joshua C. Anderson,3 Xianwen Zhang,4 Kerstin Ebe,4 Boris N. Ebe,4 Peter St. John,1 Christof Ebling,5 Kerstin Ebe,4 Jenny C. Nystrom,4 Stacy D. Hall,6 Lea Novak,6 Bruce A. Julian,6 Christopher D. Willey,6 Jan Novak,6 Changbai Hospital, Chinese University, Second Military Medical University/Naval Medical University, Shanghai, China; 7University of alabama at Birmingham, Birmingham, AL; 8Long Hua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China; 9University of Gothenburg, Gothenburg, Sweden.

Background: PDGF is involved in the pathogenesis of IgA nephropathy, namely in the activation of mesangial cells (MC). Our kinomic profiling revealed that receptor tyrosine kinase Axl and non-receptor tyrosine kinase ABL were the top upregulated protein-tyrosine kinases in MC stimulated by PDGF-AB. In this study, we describe crosstalk between Axl and PDGF receptor (PDGFR-β) in human MC stimulated with PDGF.

Methods: Quiescent primary human MC were stimulated with PDGF-AB for 15 min. Cell lysates were analyzed with SDS-PAGE/Western blotting to probe for phospho-PDGFR-β, phospho-Axl, and downstream signaling. Immunoprecipitation with antibodies specific for PDGF-φ or Axl was used to assess association of Axl and PDGFR-β. To test the role of Axl in crosstalk with PDGFR-β, the Axl/ABL inhibitor R428 and an Axl-specific siRNA knock-down (k/d) were used. Cellular signaling was measured by BEad1 incorporation —20 h after PDGFB-AB stimulation.

Results: PDGF-AB stimulated cellular proliferation of MC. PDGF-AB induced phosphorylation of multiple kinases, including Axl, PDGFR-β, Akt1, and ERK1/2 in MC. Immunoprecipitation experiments revealed association of Axl and PDGFR-β. The Axl/ABL inhibitor R428 inhibited PDGF-AB-induced phosphorylation of Axl, PDGFR-β, Akt1, and ERK1/2, and partially reduced PDGF-AB-induced MC proliferation. siRNA k/d of Axl reduced expression of Axl, but did not prevent PDGF-AB-induced phosphorylation of Akt1, ERK1/2 and PDGFR-β, and did not reduce proliferation of MC.

Conclusions: In summary, PDGF-AB induced multiple signaling events in cultured human MC that included crosstalk between PDGFR-β and Axl. MC cellular signaling induced by PDGF-AB was blocked by the Axl/ABL inhibitor R428 but not by Axl siRNA k/d. These findings suggest a role for the non-receptor tyrosine kinase ABL in a crosstalk between the two receptors. We postulate that the PDGFR-β/Axl/ABL pathway may represent a possible therapeutic target in the treatment of IgA nephropathy.

Funding: NIDDK Support

PO1807

Galactose-Deficient IgA1-Containing Immune Complexes Deposit with Complementary Activity in Mesangium Through Endothelial Cell Injuries Yasuko Makina,1 Hitoshi Suzuki,1 Daisuke Nakano,1 Toshiki Kano,1 Akira Nishiyama,2 Yusuke Suzuki.1 1Department of Nephrology, Juntendo University Faculty of Medicine, Tokyo, Japan; 2Department of Pathology, Kagawa University, Kagawa, Japan.

Background: IgAN is defined by the presence of dominant mesangial IgA immune deposits, accompanied by C3 deposits, and deposition of IgA1 includes galactose-deficient IgA1 (Gd-IgA1). However, the pathogenic role of Gd-IgA1-containing IC with regard to mesangial immune deposits is still unclear. The endothelial surface glycocalyx modulates microvascular function. Loss of the glomerular endothelial glycocalyx is involved in albuminuria. In this study, we hypothesize that Gd-IgA1-containing IC deposit in mesangium through endothelial cell injuries.

Methods: Gd-IgA1 and recombinant α2-macroglobulin IgG were used to form IC (Gd-IgA1-IgG IC) to inject i.v. into nude mice. After various time intervals, mice were sacrificed and kidney was harvested to determine mesangial deposition and kidney injuries. To investigate that Gd-IgA1-IgG IC stimulation increases permeability of glomerular microvascular resulted in renal injuries, the renal microvascular endothelial glycocalyx removal was estimated by real-time glycocalyx imaging. Furthermore, human renal glomerular endothelial cells (HRGEC) were co-cultured with Gd-IgA1 alone or Gd-IgA1-IgG IC for 72 h to test the potential capacity of these IC to activate endothelial cells.

Results: After injection of Gd-IgA1-IgG IC, but not Gd-IgA1 alone induced proteinuria and hematuria in nude mice. Gd-IgA1-IgG IC deposited with murine C3 in the mesangium as well as subendothelial area of the glomerular capillaries. Furthermore, electron microscopic examination showed that injection of Gd-IgA1-IgG IC induced endothelial injuries. In fact, real-time glycocalyx imaging showed that renal microvascular glycocalyx were reduced after injection of Gd-IgA1-IgG IC in nude mice. After co-culture of Gd-IgA1-IgG IC with HRGEC, transcript levels of endothelial adhesion factors such as ICAM-1, VCAM-1, and E-selectin were significantly overexpressed (P<0.01). Transcript levels of TNFα and IL-6, proinflammatory mediators which are able to induce expression of adhesion factors on endothelial cells, were also increased (P<0.01).

Conclusions: Present data suggested that Gd-IgA1-containing IC deposition and subsequent complement activation may induce renal damage and overexpression of pathogenic cytokines and adhesion molecules resulting in glomerular injuries in IgAN.

PO1808

Sparstaurtin Protects Against Development of Albuminuria and Glomerulosclerosis in the gddY Mouse Model of IgA Nephropathy Hajime Nagasawa,1 Hitoshi Suzuki,1,2 Yusuke Fukao,1 Maiko Nakayama,1 Tomoyuki Otsuka,1 Kai Liu,1 Radko Komerus,1 Yusuke Suzuki.1 1Department of Nephrology, Juntendo University Faculty of Medicine, Tokyo, Japan; 2Department of Nephrology, Juntendo University Faculty of Medicine, Chiba, Japan.

Background: gddY mice are an IgA nephropathy (IgAN) model that develops albuminuria by 8 weeks (W) of age with glomerular IgA, IgG, and C3 deposits and progressive mesangio-proliferative glomerulonephritis. A previous study in the ddy mouse model (the predecessor to gddY mouse) using the endothelium type A receptor blocker valsartan resulted in significant protection from glomerulosclerosis (GS) without a significant prevention in proteinuria. We examined the effect of sparstaurtin (SP), a dual ET, R, and AT, R blocker, on development of albuminuria and GS in gddY mice.

Methods: 8 W old gddY mice were fed with control (C) chow (n=5) or chow containing 900 ppm (n=10) or 1800 ppm (n=10) SP (180 and 360 mg/kg/day) for 8 W. Albuminuria (U-Alb) was assessed at 4, 6, 8, 10, and 12 W of age and plasma levels of SP were determined at 8 am and 4 pm at 6, 8, 10, and 12 W. Kidney biopsies were taken at the end of the study at 12 W of age and 30 glomeruli/animal were scored for the percentage of GS. Serum IgA and glycosylation of IgA was measured using ELISAs.

Results: gddY mice fed SP for 8 W from 4 W of age demonstrated significantly decreased U-Alb (0.4±0.9 mg/100 ml vs 1.5±0.8 mg/100 ml for the control group, P<0.005) and decreased U-Alb vs C diet (Fig 1). Development of GS in SP-fed mice was significantly reduced (P<0.005) attenuated vs C diet (Fig 2). Plasma levels of SP taken at 8 am and 4 pm after 8 W of treatment were (means±SD) 281±107 and 105±26 ng/ml respectively for 900 ppm SP and 774±176 and 304±176 ng/ml respectively for 1800 ppm SP. Weight gain in mice fed SP was not different from mice receiving C diet. There was no difference in serum levels of IgA or aberrantly glycosylated IgA.

Conclusions: 8 weeks of treatment with SP significantly attenuated increases in albuminuria and GS associated with the development of IgAN in gddY mice. If translated to the clinic, these data support SP as a new approach to the treatment of IgAN.

PO1809

Dysregulation of B-Cell Differentiation in IgA Nephropathy Model Mice Yoshihito Nihei,1 Hitoshi Suzuki,2 Yusuke Fukao,1 Maiko Nakayama,1 Mingfeng Lee,1 Rina Kat0,1 Toshiki Kano,1 Yuko Makita,1 Yusuke Suzuki.1 1Department of Nephrology, Juntendo University Faculty of Medicine, Tokyo, Japan; 2Department of Nephrology, Juntendo University Faculty of Medicine, Chiba, Japan.

Background: Several novel drugs targeting B cells are reported to be effective in the treatment of IgA nephropathy (IgAN). On the other hand, we have reported that the abnormal B cells expressing APRIL (a proliferation-inducing ligand) are present in tonsils of human IgAN. Given these reports, dysregulation of B cells may be involved in the pathogenesis of IgAN. To elucidate the abnormality in B cells of IgAN, we analyzed characteristics of B cells by using IgAN prone mice with (O-dyD) or without (NO-dyd) full onset of this disease. Furthermore, we recently developed a novel culture system mimicking germinal center in mucosa, by which nearly 50 % of B cells undergo class switch (CS) to IgA. Here, we aim to evaluate characteristics of B cells in O-dyd mice using this novel B cell culture system.

Methods: Splenic B cells from O-dyd or NO-dyd mice were stimulated with membrane-bound IgM and CD40 for 48h and then proliferation of B cells was evaluated by Thymidine-uptake analysis. To examine CS to IgA, naïve splenic B cells from O-dyd or NO-dyd mice were cultured for seven days under the newly developed culture system. The frequency of IgA CS was evaluated by flow cytometry.

Results: We found that naïve B cells of O-dyd proliferated more than those of NO-dyd mice in response to stimuli through CD40 and membrane-bound IgM. There was no significant difference in the frequency of class switch to IgA between splenic B cells from O-dyd and NO-dyd mice. However, we found that the frequency of IgA CS was significantly lower in NO-dyd mice than those from O-dyd mice.

Conclusions: These data indicate that B cells in O-dyd mice are hyper-sensitive to Th and T-cell help without increasing the expression of APRIL in O-dyd mice and suggest that such dysregulation of B cells may be involved in the pathogenesis of IgAN.
PO1810
Novel Model for IgA Nephropathy Using Synthetic Polymeric IgA
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**Background:** IgA nephropathy (IgAN) is characterized by polymeric IgA deposition in the glomerulus. The mechanism for IgA deposition remains elusive. We constructed a recombinant IgA polymerized by streptavidin to model the initiation and development of IgAN.

**Methods:** To model IgA complex, we produced recombinant rat and human IgA CH2-CH3 segments. By fusing them with Avi-tag, adding biotin and tetrameric streptavidin to form 4-8 unit multimers. Both dimeric IgA and polymeric IgA constructs were IV injected in rats. Renal deposition of the IgA was detected by immunofluorescence. Polymer IgA was used to stimulate mesangial cells and IL-6 production was measured by ELISA.

**Results:** Through BirA enzymatic reaction, single biotin was added to the Avi-Tag at the N-terminus of IgA. The total molecular size of IgA with and without streptavidin were measured by size-exclusion chromatograph. As expected, uninduced IgA was a standard dimer of 65 kDa, whereas streptavidin-induced IgA formed multimers of 4-8 units, resembling poly-IgA in IgAN. These dimeric and polymeric IgA at 2 mg/kg. BW were injected in 5 week old Wistar rats. 1h, 3 hrs and 24 hrs after injection, the kidney and the liver were harvested for detection of IgA. Exclusively IgA deposition in the glomeruli mesangial areas was found (Figure). In general, the staining intensity gradually diminished over 24 hrs period. However, rats received daily doses of the induced IgA for 2 and 5 days showed enhanced intensity of IgA deposition. In contrast, the dimeric IgA was not detectable in kidney. Furthermore, EM and PAS staining of the renal sections showed mesangial proliferation. Ex vivo stimulation of human mesangial cells also showed increased levels of IL-6 in the medium.

**Conclusions:** The findings indicate that streptavidin-induced poly-IgA causes specific renal mesangial deposition and mesangial cell proliferation, which can be used to study ongoing serologic biomarker abnormalities.

PO1811
Nephritic Factor Function Over Time
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**Background:** Nephritic factors (Nef) are autoantibodies that stabilize and dysregulate the function of the C3 convertase, the cornerstone of complement amplification. Their association with renal inflammation central to the C3 Glomerulopathies (C3G) is well reported; however, it is unknown whether Nefs 1) change over time, 2) correlate with serologic biomarker assessments, and/or 3) are useful for predicting risk for relapse of C3G. We aimed to create a novel assay that allows comparison of Nef properties over time. We further sought to correlate these results with an array of serologic biomarkers.

**Methods:** The test subject was a C3G patient with disease recurrence 7 months after renal transplant. Reagent C3 convertase was formed by injecting factor B, factor D, and patient-derived IgG (versus normal pooled human IgG as a control) over a C3b-immobilized CM5 chip (Biacore X100) followed by injection of Decay Accelerating Factor (DAF) to reconstitute the C3 convertase. Data was allowed to dissociate for 3600 minutes. Kinetic data were collected at five time points during dissociation. Data for each clinical time point were normalized to the amount of stabilized convertase at t=0. Serologic biomarker assays were performed as previously described.

**Results:** Qualitatively, test subject Nef stabilized the convertase 1.32 to 1.44 fold longer than unstabilized convertase. Between sample time point variability at 800s was less than 13%. Nef function correlated with serologic biomarker abnormalities at all 4 study points.

**Conclusions:** Using a novel assay, we show that Nefs isolated from a test subject remained remarkably stable over a 28-month period. In addition, the stabilizing effect of Nef on C3 convertase consistently correlated with serologic biomarker abnormalities. We propose that this approach to additional C3G patients with and without recurrence of disease in transplant in order to provide a method for comparing Nefs over time, thereby defining the role of Nef-stabilizing function as an at-risk biomarker for C3G recurrence in transplant.

PO1813
C3 Glomerulopathy Recurrence After Kidney Transplant: A Systematic Review
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**Background:** C3 glomerulopathy (C3G) is a recently defined entity, characterized by the dysregulation of the complement pathway, leading to deposition of C3 component in the glomeruli, with no or few immunoglobulin deposits. While it is known that membranoproliferative glomerulopathies carry a risk of recurrence after transplant, no large-scale meta-analysis was done after 2015 to assess the precise recurrence risk and remission duration for C3 glomerulopathies. The goal of this work is to determine if there is currently enough literature specific for C3G to conduct such a metaanalysis.

**Methods:** Our research protocol was guided by the PRISMA protocol, and the Joanna Briggs Institute Critical Appraisal Tools. A search was conducted in 3 databases using a specific search string, at the conclusion of which, 230 papers were found. The identified papers were subsequently screened by the 2 authors independently using precise inclusion and exclusion criteria. The screening resulted in the final inclusion of 6 papers, on which a qualitative synthesis was performed. The information extracted was organized on the basis of demographics, time of transplantation, disease recurrence, and disease-free period post-transplantation.

**Results:** Among the 6 papers selected, 2 were case series and 4 were case reports. In total, 25 patients were reported as having a recurrence of C3G. The age of the patients ranged between 7 and 60 years of age. Among the 25 patients, 11 of them were male, while 6 of them were females. The C3G subtype was determined for 25 patients, with 16 were classified as having C3GN, and 8 having DDD. The age of transplant was reported for 14 patients, ranging from 11 to 64 years old. The disease-free period post-kidney transplant and the recurrence of the disease ranged from 14 days to 91 months, with 1 case series paper only reported the median time to recurrence in months (59[27-91]) for C3G patients and 41[0-71] for DDD patients.

**Conclusions:** While C3G, with its 2 subtypes, have been well-defined entities for a decade, our review reveals that little research about the post-transplant evolution and recurrence of these diseases has been done. While extensive research can be found on the recurrence risks of Membranoproliferative Glomerulonephritis, we believe that with the new classification, more data on the new subtypes is necessary to guide the decision-making of clinicians and their patients.

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Underline represents presenting author.
plasmapheresis were continued. Renal function improved and dialysis discontinued, with Cr at last follow up 1.9. Chemotherapy for CLL has been ordered. Lymphocytes were negative for CD3, CD10, Bcl6, and cyclin D1; with a MIB1 nuclear proliferation rate within the lymphoid infiltrates less than 5%.

Discussion: We present a case of C3GN and DAH secondary to CLL autoimmune etiology, a rare complication of CLL which usually affects the kidney by infiltration and by toxicity of the CLL treatment. Recent case reports suggest improved outcomes of CLL associated C3GN when CLL is treated.

Fibrillary Glomerulonephritis or Complement 3 Glomerulopathy: A Rare Case of Crescentic Glomerulonephritis with C3 Dominant Deposition and Positive DNAJB9

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Introduction: Fibrillary glomerulonephritis (FGN) and complement 3 glomerulopathy (C3G) are two rare forms of GN. FGN is diagnosed by electron microscopy (EM) showing randomly oriented fibrils ranging in diameter from 15-25 nm. Immunofluorescence (IF) in FGN typically is IgG-predominant. C3G is diagnosed by isolated C3 (>3+ intensity) or dominant C3 in a pattern consistent with CSG but EM findings suggestive of FGN.

Case Description: A 57-year-old female with history of HTN, type 2 DM, ESRD, and C3GN associated C3GN when CLL is treated. Her kidney biopsy undertaken revealed monoclonal gammopathy–associated diffuse proliferative glomerulonephritis with C3 deposits deposits with light-microscopy. However, repeat immunofluorescence was consistent with diffuse proliferative immunotactoid glomerulonephritis with “masked” monoclonal IgG kappa deposits. Congo red stain was negative, ruling out amyloidosis. The patient was continued on daily high-dose steroid treatment. He was referred to Hematology/Oncology for bone marrow biopsy for concern of monoclonal gammopathy of renal significance (MGRS). Dialysis was discontinued at the time of discharge as patient’s kidney function improved with steroid treatment.

Discussion: It is important to keep ITG in the differential diagnosis as high-dose steroid or cyclophosphamide might prevent rapid glomerulonephritis progression. Treatment of underlying disease such as light-chain deposition disease might have some benefit on renal disease.

Rare Association of Monoclonal Gammopathy of Renal Significance with Acquired Angiodema

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Introduction: Acquired angiodema (AA) due to deficiency of C1 esterase inhibitor is also abbreviated as C1INH-AAE. This rare syndrome presents with recurrent angiodema episodes, without urticaria, and sometimes is associated with B-cell lymphoproliferative disorders. Kidney involvement is rare with AA. The monoclonal immunoglobulins are secreted by a non-malignant B-cell or plasma cell clone, causing renal damage representing a group of disorders called monoclonal glomerulopathy of renal significance (MGRS). We present a rare association of these two entities.

Case Description: 64 year old female patient came to the emergency department with complaints of 2 week duration waxing, waning maculopapular rashes in all extremities, chills, hoarseness of voice and lower extremity swelling. She had no family history of angiodema. Positive examination findings were rashes and bilateral pedal edema. With a normal baseline creatinine, admission serum creatinine was high at 2.4 mg/dl. Positive laboratory findings were very low complements level (C4< C3), low C1q level, high C1 esterase inhibitor level. Other immunological workup including serum, urine immunoelectrophoresis, kappa lambda ratio, serum immunofixation were normal. Kidney biopsy undertaken revealed monoclonal glomerulopathy–associated diffuse proliferative glomerulopathy. She responded well to steroids only and is in clinical remission with normal renal function.

Discussion: Paraproteinemia is characterized by clonal proliferation of B-cells and/or plasma cells resulting in overproduction of monoclonal proteins and can cause secondary renal dysfunction. Paraprotein-induced renal disease can occur without malignancy, now termed as monoclonal glomerulopathy of renal significance. MGRS includes a wide spectrum of disorders like light/heavy chain deposition disease, C3 glomerulopathy, proliferative glomerulonephritis with monoclonal immunoglobulin deposition(PGNMID), and primary amyloidosis. MGRS necessitates strict monitoring,
early interventions to prevent renal damage. Acquired angioedema generally presents with headache, neck stiffness, and vomiting. A BMI biopsy with C4d deposits was performed. A had low C1q levels unlike hereditary angioedema. Systemic manifestations are far common with AA than hereditary angioedema. No literature has shown an association of MGRS/PGNMID with AA and low complement levels. Further case studies need to be done to discover any large-scale association of MGRS with AA.

PO1817
Clinical Biomarker Trend in C3 Glomerulopathy
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Background: There is a paucity of data defining the natural history of the clinical and complement biomarker characteristics of C3 Glomerulopathy (C3G) patients. Whether there are disease defining trends and/or relationships between the markers of disease is unknown. In a series of C3 patients, we sought to describe the trend in three commonly available markers of disease: complement C3, urine protein-to-creatinine ratio (UPCR), and GFR. We hypothesized that lower C3 levels, as a reflection of ongoing complement activity would be associated with progressive renal disease as represented by changes in UPCR and/or GFR.

Methods: All patients met the consensus, renal biopsy definition of C3G. Thirty-two native kidney disease subjects with an age ≥ 12 years and GFR ≥ 30 ml/min were included. Trends in C3, UPCR and GFR were monitored in 1-year spans. Ninety spans were matched with C3, UPCR and GFR data were identified. Mean and median statistics across all spans were reported as percent change per year and standard regression analyses were used to explore the relationship between variables.

Results: 54% of patients retained a C3 within 10 mg/dL of their span entry C3; 86% had a C3 within 25 mg/dL of their entry C3. In only three 1-year spans did a patient start with a low C3 and finish with a normal C3. Mean and median change in GFR per year were a decrease of 4.5% and 2.9% respectively, with the greatest GFR decreases in those spans with the lowest C3. Mean and median change in UPCR per year was a decrease of 8.3% and 10.9%. When considering baseline GFR, baseline UPCR, baseline C3 and change in UPCR, loss of GFR most closely correlated with baseline C3 (Figure, p<0.01).

Conclusions: These data indicate that C3 levels vary little from baseline over a 1 year period and that loss of GFR correlates with baseline C3. These results suggest that treatment approaches that effect an improvement in C3 may have a beneficial effect on GFR.

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PO1818
A Case Series of Proliferative Glomerulonephritis with Monoclonal Immune Deposits
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Introduction: Monoclonal gamopathy of renal significance (MGRS) comprises B-cell and plasma-cell clonal proliferative disorders that do not require treatment for the clonal disease but produce nephrotic monoclonal immunoglobulins (miG) that elicit a variety of kidney manifestations. One such presentation is proliferative glomerulonephritis associated with monoclonal immune deposits (PGNMID), typically presenting as membranoproliferative glomerulonephritis (MPGN) and non-organized glomerular miG deposits. We describe 3 unique cases of PGNMID from our institution.

Case Description: Case-1: A 16-year old female presented with abdominal pain, gross hematuria, nephrotic proteinuria, edema and normal renal function. Protein electrophoreses and bone marrow (BM) biopsy were unremarkable. Kidney biopsy showed MPGN with monoclonal IgG3 lambda deposits. She had inadequate response to R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone) and was referred to the second investigator (mycophenolate+monomethylauracil) achieving complete response. Case-2: A 39-year old woman with history of antiphospholipid syndrome and 2 miscarriages developed persistent nephrotic proteinuria after un complicated third pregnancy. Kidney biopsy showed membranous glomerulopathy with mesangial hypercellularity and monoclonal IgG lambda deposits. She was currently being treated with plasma cell targeted therapy with good response. Case-3: A 28-year old male with nephrotic proteinuria found on routine examination. Further evaluation showed unremarkable BM biopsy and protein immunohistochemistry. Kidney biopsy showed mesangial biopsy sclerosis and monoclonal-IgG kappa deposits. He is currently being treated with rituximab.

Discussion: PGMID is a subset of MGRS with variable histologic pattern and histological features of immune complex glomerulonephritis; however, the immune deposits are monoclonal and are seldom associated with serum paraprotein. Our patients were younger than those reported in literature and had variable histologic patterns. None had M spike or clonal B or plasma cells. The response to treatment was variable. Two patients showed no response to B-cell depleting therapy. One patient did not respond to plasma-cell directed therapy, but the other did. The third patient is currently receiving B-cell depleting therapy.

PO1819
Role of SIRT1 in HIV-Associated Kidney Disease
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Background: HIV infection of kidney cells can lead to HIV-associated nephropathy (HIVAN) and aggravate the progression of other chronic kidney diseases. Thus, a better understanding of the mechanisms of HIV-induced kidney cell injury is needed for development of effective therapies against HIV-induced kidney disease progression. We previously showed that the acetylation and activation of key inflammatory regulators, NF-kB p65 and STAT3 were increased in HIVAN kidneys. Here, we examined the key role of SIRT1 deacetylation in regulation of NF-kB and STAT3 in HIVAN.

Methods: We analyzed expression of SIRT1 in glomeruli of human and mouse HIVAN kidneys, and then we explore the role of SIRT1 on acetylation of NF-kB p65 and STAT3 and expression of HIV genes by overexpression or knock-down of SIRT1 or using SIRT1 agonist, BFI73 in cultured podocytes. In vivo, we examined the effects of SIRT1 on HIVAN progression by administration of BFI75 for four weeks and inducible podocyte-specific SIRT1 overexpression in Tg26. We also assessed whether miR34a was associated with SIRT1 expression.

Results: SIRT1 expression was reduced in the glomeruli of human and mouse HIVAN kidneys and that HIV-1 gene expression was associated with increased acetylation of NF-kB p65 and STAT3 in cultured podocytes. Interestingly, SIRT1 overexpression in turn reduced the expression of Nef in podocytes stably expressing the HIV-1 proviral genes, which was associated with the inactivation of NF-kB p65 and reduction in the HIV-1 LTR promoter activity. In vivo, the administration of small molecule SIRT1 agonist BFI75 or inducible overexpression of SIRT1 specifically in podocytes markedly attenuated albuminuria and kidney lesions in Tg26 mice. Finally, the reduction in SIRT1 expression by HIV-1 in part mediated through miR-34a expression.

Conclusions: These findings provide a new mechanism of SIRT1 regulation and its downstream effects in HIV-1 infected kidney cells and indicate that SIRT1/miR-34a are potential drug targets to treat HIV-related kidney disease.

Funding: NIDDK Support, Veterans Affairs Support

PO1820
Protein Kinase R Inhibition Ameliorates Tg26 HIV-Associated Nephropathy Mouse Model

Background: HIV-associated nephropathy (HIVAN) has become less common with widespread use of antiretroviral therapy but has not yet disappeared. Double-stranded RNA (dsRNA)-activated protein kinase (PKR) is a sensor for dsRNA in response to viral infection such caused by HIV. We previously reported that APOL1 risk alleles damages podocytes through double-stranded RNA-activated protein kinase (PKR) activation. Thus, we hypothesized that PKR activation could be an activated pathway shared in the pathology of HIV- and APOL1-mediated nephropathies. We tested this hypothesis by investigating whether PKR inhibition would ameliorate HIVAN using the well-established Tg26 mouse model.

Methods: We evaluated the kidney phenotype of Tg26 mice and wild type mice treated with or without the PKR inhibitor (C16) from 6 to 12 weeks of age. We quantified albuminuria after treatment and evaluated kidney pathology after 6-week treatment. We confirmed the knockdown of PKR in Tg26 mice kidneys by Western blot. We saw a significant decrease in kidney disease development in the PKR inhibitor (C16) treatment group compared to the vehicle control group. Urine albumin/creatinine ratio (mg/gCr, mean [IQR]) was 668 [60-1064] in the treatment Tg26 group and 2564 [1786-5646] in the vehicle control Tg26 group (P=0.026). Kidney pathology showed fewer sclerotic glomeruli and tubular microcystic lesions in the treated Tg26 group than in the vehicle control Tg26 group.

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Underline represents presenting author.
Interleukin 22 Attenuates Renal Tubular Cells Inflammation and Fibrosis Induced by TGF-β1 Through Notch1 Signaling Pathway

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Background: Transforming growth factor-β1 (TGF-β1) is a crucial factor implicated in the development of renal inflammation and tubulointerstitial fibrosis. The cytokine interleukin 22 (IL-22) was previously reported to involve in the pathogenesis of chronic inflammatory diseases. In the present study, we aim to investigate the role and mechanisms of IL-22 in renal tubular cells inflammation and fibrosis induced by TGF-β1.

Methods: HK-2 cells were treated with TGF-β1 in the presence of IL-22 or the Notch inhibitor dibenzazepine (DBZ) for 48 h. Cell proliferation was determined by MTT assay, Cytotoxicity was assessed by LDH assay. Collagen I (Col I), fibronectin (FN), α-smooth muscle actin (α-SMA), vimentin and E-Cadherin were detected by western blot, proinflammatory factors (TNF-α, IL-6) and chemokines ( MCP-1, RANTES) in the supernatant of cell cultures were evaluated by ELISA. Jagged1, Notch1, NICD1, and Hes1 were also detected by western blot.

Results: In our study, IL-22 (10–40 ng/ml) did not affect cell proliferation and cytotoxicity. Then IL-22 (20 ng/ml) incubation for 48 h was chosen for subsequent experiment. We found TGF-β1 increased the levels of Col I, FN, α-SMA and vimentin in HK-2 cells compared with control, and decreased E-Cadherin level, however, IL-22 restored their expressions partly. IL-22 reduced over expression of proinflammatory factors (TNF-α, IL-6) and chemokines (MCP-1, RANTES) levels induced by TGF-β1, along with down-regulation of Jagged1, Notch1, NICD1 and Hes1. Fibrosis and inflammation in renal tubular cells induced by TGF-β1 could be attenuated by IL-22, and the effects were similar to DBZ treatment.

Conclusions: Collectively, our study shows that IL-22 exerts a protective role in renal fibrotic and inflammatory responses induced by TGF-β1 in vitro, which may be through inhibiting Jagged1/Notch1 signaling pathway activation.

Funding: Government Support - Non-U.S.
**PO1825**

**Minimal Change Disease Relapse Following Administration of an Anti-IgE Monoclonal Antibody, Omalizumab**

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**Introduction:** Minimal Change Disease (MCD) is incompletely understood with immune cells, circulating factors, and glomerular basement membrane all considered potential precipitants. We present the first reported case of reactivation of MCD following administration of omalizumab.

**Case Description:** A 59-year-old lady presented with lower limb oedema two days following a second dose of Omalizumab for treatment of severe eosinophilic asthma. Her background was significant for two previous episodes of biopsy-proven MCD. Exam was static, a blood pressure of 138/86 mmHg, and proteinuria on urine dipstick. Urine PCR was 473 mg/mmol on presentation with preserved GFR. Treatment for a presumed MCD relapse was commenced with prednisolone and diuresis and omalizumab was discontinued indefinitely. Clinical and biochemical remission was achieved and she remained well at 2-weeks and maintained at 6-month follow-up.

**Discussion:** Omalizumab is indicated as add-on therapy in patients with severe persistent allergic asthma, the primary mechanism of which is that of the binding of the active drug to IgE. The clinical effects of omalizumab are not accounted for solely by IgE antagonism with further immune regulatory effects hypothesised. Notably reduction in IL4, IL13, and IL8 have been described post-treatment. Immune system dysregulation, a hypothesised circulating factor, medications, and atopy are all considered to play a role in development of MCD. Studies have supported an imbalance of T-cell subpopulations and cytokines in MCD. Of note, Th2 cytokines IL4 and IL13 can interact directly with the glomerular basement membrane and are acted upon by omalizumab. In particular IL13 has been described as being related to a nephrotic syndrome in animal studies, and high levels are seen in paediatric nephrotic syndromes, with IL13 levels increasing following omalizumab administration. This is the first reported case of MCD in the context of omalizumab administration. IL13 and IL4 appear key to the hypothesised pathophysiology of MCD and mechanism of action of omalizumab. This case provides an insight into the interactions between MCD, atopy, and biologic medications, presenting MCD as a novel complication of omalizumab.

**PO1826**

**Neurorenal Syndrome: Two Cases of Tip-Variant Focal Segmental Glomerulosclerosis Associated with Guillain-Barré Syndrome**

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**Introduction:** Glomerular disorders have been associated with immune-mediated polyneuropathies in previous case reports. We present two cases of tip-variant focal segmental glomerulosclerosis (FSGS) associated with a variant of Guillain-Barré syndrome (GBS) in Winnipeg, Manitoba.

**Case Description:** Two previously healthy males aged 62- and 55-years old presented to our hospital with extremity weakness and paresthesias. They each progressed to flaccid lower extremity weakness. Both cases responded to high-dose corticosteroids initially. Case one relapsed during his taper requiring re-initiation of steroids and addition of mycophenolate mofetil (MMF). He was discharged following thirteen months in hospital with complete remission of proteinuria and ongoing neurologic recovery. Case two achieved complete remission of proteinuria and was discharged after six months with ongoing neurologic recovery.

**Discussion:** Our cases have similar presentations and responses to therapy suggesting they may share a common circulating autoantibody reacting against shared neural and glomerular podocyte antigens. Circulating autoantibodies including anti-contact-1 and neurofascin have previously been implicated in chronic inflammatory demyelinating polyneuropathy (CIDP), a chronic variant of GBS. Identifying the culprit immune target in primary FSGS is limited due to the absence of immune complex deposition. The timing of podocytopathy development compared to GBS is highly variable in cases reported throughout the literature. The onset and diagnosis of FSGS in Case 1 was either delayed or unrecognized illustrating the importance of educating clinicians about this neuro-renal syndrome. Although not routinely used in GBS, corticosteroids have led to favorable outcomes in our cases and those reported throughout the literature. Recognition of a co-existing nephrotic syndrome with GBS could significantly change management and impact treatment outcomes.

**PO1827**

**Hemophagocytic Lymphohistiocytosis Presenting as Nephrotic Syndrome**


**Introduction:** Minimal change disease (MCD) is a podocytopathy resulting from systemic T cell dysfunction. Although frequently a primary disease, MCD can be secondary to immune dysregulation in malignancy or autoimmune disease. Hemophagocytic...
PO1829
Collapsing Glomerulopathy in Mixed Connective Tissue Disease: Case Report
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Introduction: Collapsing glomerulopathy (CG) is a form of podocytopathy with segmental or global wrinkling and collapse of capillary walls and overlying epithelial cell proliferation but may be distinct from other forms of focal and segmental glomerular sclerosis (FSGS). CG may be idiopathic or associated with infections, autoimmune diseases, malignancies, genetic diseases, certain drugs and in post-transplant setting. Although CG has been reported in lupus nephritis, it was rarely reported in the setting of mixed connective tissue disease (MCTD).

Case Description: A 30 y/o African American male with a history of muscle aches, nontraumatic rhabdomyolysis, evanescent skin rash and weight loss was found to have a creatinine of 5.1 mg/dl (1.4 1 year earlier) with urine protein/creatinine ratio (uPCR) of 10,136 mg/g. CPK was 1697 U, erythrocytes sedimentation rate > 120, a positive speckled ANA of 1:640, positive anti-SSA 5.9, anti-chromatin >8, anti-sm RNP >8, anti-RNP >8. Kidney biopsy showed mesangial immune complex deposition, collapsing glomerulopathy and diffuse podocytopathy, immunofluorescence showed global mesangial IgG staining (3+), IgM (1+), C3 (2+), and kappa (2-3+) and lambda (3+) light chains. Electron microscopy revealed several mesangial electron-dense deposits with mild increase in mesangial matrix and hypercellularity and severe epithelial foot processes effacement without glomerular or tubular basement membrane deposits. Muscle biopsy confirmed the diagnosis of dermatomyositis. The patient was treated with pulse methylprednisolone 1 gm IV for three days followed by prolonged prednisone taper. Later, MMF was started at 500 mg bid, lisinopril 40 mg daily, hydroxychloroquine 200 mg bid and bumetanide 2 mg bid. By 4 months creatinine had stabilized at 2.6 mg/dl, uPCR was 1,824 mg/g, and CPK was 55 U.

Discussion: Here we describe a case of collapsing glomerulopathy in the setting of MCTD (SLE and dermatomyositis), with at least partial response to high dose prednisone for 16 weeks, hydroxychloroquine and late initiation of MMF. CG can present in association with autoimmune diseases including but not limited to SLE. This case represents the second such as this case of CG in the setting of MCTD and is notable for its response to immunosuppressive therapy.

PO1830
A Case of AKI with Nephrotic Syndrome After Intraperitoneal Infection with Methicillin-Sensitive Staphylococcus aureus (MSSA)

Introduction: Postinfectious glomerulonephritis (PIGN) causes acute nephritic syndrome complicated with urinary protein and hematuria after infection but rarely leads to nephrotic syndrome. The effectiveness of steroid for PIGN has been reported, but still controversial. We report a case of refractory nephrotic syndrome caused by PIGN treated with steroid.

Case Description: A 78-year-old man presenting with nausea and dizziness was admitted. He had pancreatitis for intraductal papillary mucinous tumor two months before. He was diagnosed as postoperative pancreatic fistula with intraperitoneal infection caused by MSSA. During treatment for the infection, he presented acute kidney injury with nephrotic range proteinuria and hematuria, and required hemodialysis. Renal biopsy revealed diffuse endocapillary proliferative glomerulonephritis with cellular crescents. He was diagnosed as nephrotic syndrome caused by PIGN after intraperitoneal infection with MSSA. Since renal failure was persistent despite infection resolution, he started steroid treatment, lead to improve kidney injury.

Discussion: Antibacterial treatment is important for treatment of PIGN, but if the improvement is still poor, steroid treatment may be effective.

PO1828
Case of FSGS in a Patient on Pembrolizumab
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Introduction: Pembrolizumab, a humanized antibody directed against human cell surface receptor PD-1 with immune checkpoint inhibitory and antineoplastic activities, has been reported to cause minimal change disease (MCD). Here we report a case of focal segmental glomerulosclerosis (FSGS) glomerular tip lesion (GTL) in a patient on pembrolizumab.

Case Description: A 55 year old man with a history of HTN, ex-smoker, and bladder cancer in 2014, presented with leg edema and raised creatinine. His bladder cancer was treated with guadecitabine and atezolizumab (6/2018-12/2018). Pembrolizumab was given again Dec 2018-July 2019. On physical examination he had 3+ edema up to his knees. Labs showed creatinine 1.4 mg/dl (baseline 1.0 mg/dl). Urinalysis showed proteinuria without hematuria. Urine protein excretion was 19.5 g/day. Kidney biopsy showed 8 out of 24 glomeruli were globally sclerotic. Of the remaining 16 glomeruli, 4 displayed cellular lesions of FSGS and one glomerular tip lesion (GTL). There was GBM duplication and focal endothelial swelling, suggestive of mild endothelial injury (i.e. thrombotic microangiopathy).

Discussion: Glomerular tip lesion (GTL) is a prognostically favorable variant of FSGS with presenting features intermediate between FSGS and MCD. There are reports of MCD with pembrolizumab but no reports of GTL. Given the clinical presentation and similarities between MCD and GTL, it is likely that pembrolizumab contributed to the development of GTL in this case. His FSGS was treated with steroids and pembrolizumab was withheld. His proteinuria started to improve and renal function stabilized.
Mitochondrial Injury May Be a Ubiquitous Finding in the Pathogenesis of Various Glomerulonephritis

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Background: Previous study showed that mitochondrial injury is associated with IgA nephropathy (IgAN). It is not clear whether mitochondrial injury is a unique finding in IgAN or a ubiquitous finding in various glomerulonephritides (GN). To clarify this, we analyzed urinary mitochondrial DNA (mtDNA) levels and expression of the stimulator of interferon genes (STING) pathway activated by mtDNA leakage in various GN.

Methods: We prospectively enrolled age-sex matched healthy volunteers (HV) and biopsy-proven IgAN, minimal change disease (MCD), acute tubulointerstitial nephritis (ATIN), and minor glomerular abnormalities (MGA) (n=30, 8, 10, and 7 each, respectively). Urinary copy number of the mtDNA genes cytochrome-c oxidase-3 (COX3) and nicotinamide adenine dinucleotide dehydrogenase subunit-1 (ND1) were measured by quantitative polymerase chain reaction. We analyzed STING expression in prostatic cancer specimen as control and kidney tissues obtained from each GN patients by immunohistochemistry staining.

Results: Log10ND1/nDNA and log10COX3/nDNA were significantly higher in IgAN (p<0.001, p<0.001, MCD) (p<0.001, both), ATIN (p<0.001, both), and MGA (p<0.001, both) compared with HV (Figure 1). Although there was a difference in signal intensity and site of kidney structures, positive staining for STING was observed in the kidney tissue of each GN patients. Characteristically, STING was strongly stained in the tubulointerstitium for ATIN and in the distal tubule for MGA (Figure 2).

Conclusions: Elevated urinary mtDNA copy numbers and STING activation were observed in various GN. These results suggest that mitochondrial injury would be a ubiquitous finding in the pathogenesis of various GN.

Funding: Government Support - Non-U.S.
Methods: NeffGard is a randomized, double-blind, placebo-controlled trial with two parts, recruiting a total of 360 patients across 150 nephrology clinics in 20 countries. Patients must be aged 18 years with biopsy-confirmed primary IgAN, proteinuria >1 g/24 h and eGFR 35–90 ml/min/1.73 m² (CKD-EPI) despite optimized renin–angiotension system blockade. Part A of the study, comprising the first 200 dosed patients, will form the basis for submission for accelerated/conditional regulatory approval to the FDA and EMA. The primary outcome will assess the effect of NEFECON® 16 mg/day on UPCR at 9 months vs placebo, consistent with the 2019 Kidney Health Initiative White Paper “Proteinuria Reduction as a Surrogate End Point in Trials of IgA Nephropathy”. Part B is a post-approval confirmatory trial to validate the superiority of the Surrogate A UPCR endpoint. For this purpose, and based on the 2018 NKF/FDA/EMA workshop supporting NEFECON® on a 2-year eGFR-based endpoint vs placebo.

Results: In 2019 the 200 patients needed for Part A were randomized, with top-line data expected in Q4 2020.

Conclusions: Randomization will continue until 360 patients are reached for Part B, which is expected to report in 2022.

Funding: Commercial Support - Calliditas

POI1834

Effect of Hydroxychloroquine in Patients with IgA Nephropathy with Insufficient Responses to Immunosuppressive Therapy: A Retrospective Case-Control Study

Chen Tang, Jiecheng Lv, Sufang Shi, Yuqin Chen, Lijun Liu, Hong Zhang. Peking University First Hospital, Beijing, China.

Background: Hydroxychloroquine, a well-known immunomodulator, has recently been used in IgA nephropathy (IgAN) due to its antiproteinemic effects. We aimed to verify the effect of HCQ in patients with IgAN whose proteinuria remained above 1 g/d after conventional immunosuppressive (IS) therapy.

Methods: This was a retrospective case-control study. Twenty-six patients with IgAN who received HCQ and had insufficient responses to IS therapy (corticosteroid (CS) therapy with/without IS agents) were included. 26 matched historical controls who received conventional IS therapy were selected by propensity score matching. The clinical data from 6 months were compared

Results: Proteinuria at baseline was comparable between the “IS therapy plus HCQ” and “conventional IS therapy” groups (2.35 [interquartile range (IQR), 1.47, 2.98] vs. 2.35 [IQR, 1.54, 2.98] g/d, p = 0.920). There was a significant reduction in proteinuria in patients with IgAN with HCQ treatment (2.35 [IQR, 1.47, 2.98] vs. 1.10 [IQR, 0.85, 1.61] g/d, p = 0.002). The percent reduction in proteinuria in 6 months was similar between the two groups (-39.81% [-66.26, -12.37] vs. -67.9% [-70.08, -9.14], p = 0.968). The cumulative frequency of patients with a 50% reduction in proteinuria during the study was comparable between the two groups (53.8% vs. 57.7%, p = 0.780). No serious adverse events were observed during the study.

Conclusions: HCQ could further reduce proteinuria in patients with IgAN who had insufficient responses to conventional IS therapy.

Proteinuria of enrolled patients

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>IS therapy plus HCQ</th>
<th>Conventional IS therapy</th>
<th>P-value</th>
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<tr>
<td>Baseline</td>
<td>2.35(3.9, 5.69)</td>
<td>2.27(5.6, 3.5)</td>
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<tr>
<td>6 months</td>
<td>1.10(2.07, 2.98)</td>
<td>2.28(5.6, 3.5)</td>
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POI1835

IgA Nephropathy Study: A Multicentric Study in Portugal

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Background: In the last decade, an attempt to correlate the histopathological lesions with renal prognosis in IgA Nephropathy (IgAN) was developed in order to identify patients that benefit from IS therapy.

Methods: A multicentric, longitudinal and retrospective (2007-2019) study was developed in Portugal: adult patients with histological diagnosis of IgAN. Biopsy date defined study entrance and data was collected.

Results: 167 patients were analyzed. The cohort was divided in 2, according the use of steroid therapy: 105 in group of no steroids (noCST) and 62 in the group with steroids (wCST). Endocapillary hypercellularity (29% vs 16%, p=0.049) and crescents (34% vs 10%, p=0.001), were significantly more frequent in wCST group. Median time until the beginning of steroids was 55 days (IQR 7-251), and median duration was 195 days (IQR 96-239). Follow up time was 39 months (IQR 15.1-65.8), significantly superior in wCST group (56.6 vs 29.8 months, p=0.004). No difference between groups concerning infections, AKI, CV disease or death. Renal survival at 7 years was 70% in noCST group and 85% at wCST group, p=0.184. Multivariable analysis identified HT (OR 3.81), proteinuria (OR 2.80) and crescents (OR 2.72) as significant factors associated with steroids use. Table 1 defines the independent predictors for ESRD (Cox regression analysis). When we analyze the steroids effect on renal survival, we saw that the average time until renal replacement therapy (RRT) was 47.7 months (IQR 34.6-60.7) in noCST group and 81.6 months (IQR 63.8-99.3) in wCST group. The average treatment effect with steroids was 33.9 months (11.9-55.9, p=0.002), that means that if we treat all, this was the time that we could delay beginning of RRT.

Conclusions: In this group of patients, use of steroids was an independent predictor for delaying CKD progression and the beginning of RRT. HT, degree of proteinuria and crescents presence were significant predictors for its use. In spite of the controversy about the use of steroids therapy in IgAN, this study showed their effectiveness without risk increase.

POI1836

Corticosteroid Therapy Improves Renal Prognosis in IgAN Patients with Crescent

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Background: IgA nephropathy (IgAN) has been identified as having an inflammatory basis leading to the biological rationale of immunosuppressive therapy. However, little is known about the clinical indication of immunosuppressive therapy related to each histological finding. Recently, Haas et al reported that the crescent lesion is an independent predictor for renal survival in IgAN especially with no immunosuppressive therapy. We assessed the effect of corticosteroid therapy on renal survival of IgAN with crescent based on the Japanese dataset used in the recently published IgAN prediction tool from multinational multi-ethnic cohort (Barbour SJ, JAMA Intern Med. 2019), given it was almost all corticosteroids.

Methods: We extracted the 566 Japanese adults with biopsy-proven IgAN patients (male 45.9%, median age 34.7) from original cohort. Baseline characteristics were evaluated at the biopsy, and clinical data including serum creatinine, urinary findings, use of RAS blockers (RASB) and corticosteroid therapy and tonsillectomy were collected at every visit. The outcome was defined as 50% decline in eGFR or end-stage kidney disease. Cox proportional hazard models were used to investigate the association between corticosteroid therapy and renal survival with adjustments of confounders including the Oxford classification. Treatment options were included in the model as time-dependent covariates.

Results: At biopsy, median eGFR and proteinuria and proportions of the patients with crescent were 73.2(14.7-14.7) cm/day, 0.67g/day, and 59.9%, respectively. Patients received a median follow-up of 3.79 years, 57 patients (10.1%) reached the outcome. RASB and corticosteroid were used in 377 patients (66.6%) and 368 patients (65.0%), respectively. 241 (42.6%) patients were performed tonsillectomy. Hazard ratio (HR) of corticosteroid...
therapy was reversed by presence of crescent (no crescent: HR 1.75 95% confidence interval 1.07–2.84; presence of crescent: HR 0.26 95% CI 0.11–0.64), in finding the interaction between corticosteroid therapy and presence of crescent (p<0.001). Tonsillectomy had also a favorable effect on renal survival (HR 0.43 95%CI 0.20–0.91).

Conclusions: Present findings revealed that corticosteroid therapy improved renal survival in Japanese IgAN patients with crescent and are thus suggestive for the indication of this therapy.

V0183

Rituximab in IgA Vasculitis with Aggressive Glomerulonephritis: A Real-Life Experience

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Background: IgA-vasculitis (IgAV) is a systemic small vessels vasculitis characterized by deposition of underglycosylated IgA1 immune complexes. Presently, no treatment is specifically recommended in IgAV Glucocorticoids (GC) have been traditionally thought to be effective in tempering systemic symptoms, but did not show long-term benefits either in reducing flares or progression of kidney disease. Recently Rituximab (RTX) has been proved to be effective in a few case series of adults with IgAV. Aim of the study: to evaluate the effectiveness of RTX as first line therapy in induction and maintenance of remission of adults with IgAV with biopsy-proven crescentic glomerulonephritis.

Methods: We reviewed the clinical records of patients (pts) with adult-onset IgAV treated with RTX at our Center. Patients included 8 males and 4 females, mean age 45 years with mean follow-up duration of 31 months. All pts had a biopsy proven IgAV- severe nephritis. Pts received 4 weekly doses of RTX given alone (8 pts) or in combination with CS (4 pts). Disease activity was evaluated by BVAS version 3 at the onset and at 1, 6 and 12 months and at the end of follow up. Complete remission (CR) was defined as BVAS of 0.

Results: Eleven pts (91.7%) achieved a clinical response at 6 months. 10 pts had a CR while 1 pts had a partial response and was given an additional dose of RTX after 12 months from induction due to persistent proteinuria (1g/24 hrs), despite systemic remission. He achieved a CR 6 months later. One patient did not respond to RTX and was switched to MMF. Among the 10 pts with CR, 1 patient needed maintenance doses of RTX every 6 months due to relapse of palpable purpura; 1 relapsed after 15 months and received a new induction course showing a CR again. Significant decrease in 24-hour proteinuria, BVAS, and CRP level was detected. RTX was generally well tolerated. One patient, who had a CR with RTX alone died after 6 months of follow-up for cardiovascular cause.

Conclusions: This extended experience confirms our initial results supporting the use of RTX in the treatment of IgAV with severe renal involvement. Indeed, RTX proved to be effective and safe for induction and maintenance of long-lasting remission. Present data also suggest that RTX is not only effective for severe and refractory IgAV, but can be also proposed as a first line therapy.

V0184

External Validation of International IgA Nephropathy Prediction Tool in a Singapore Cohort (EXIST Study)

Ru Sin Lim, Su mein Goh, See Cheng Yeo. Tan Tock Seng Hospital, Singapore, Singapore.

Background: IgA Nephropathy (IgAN) is the most common cause of glomerulonephritis worldwide, including in Singapore. Although IgAN may lead to end-stage kidney disease (ESKD), the risk of progressive kidney function decline is extremely heterogeneous; a reliable risk prediction model is important to inform both patients and physicians of renal prognosis and to guide clinical treatment decisions. A newly validated International IgAN prediction tool has been published recently and we aim to externally validate this model in our Singapore cohort.

Methods: We validated the predictive performance of the two full models (with or without race) derived from the International IgAN Prediction Tool study in our IgAN patient dataset over 11 years (Jul 2009 to Oct 2020) using external validation of survival prediction models (Royston and Altman). The discrimination and calibration of the models were tested using the R² measure, C statistics, Akaike Information Criterion (AIC), and calibration plot.

Results: The study included 119 patients; mean age of 43.3 (± 16.66) years; 62 (52.1%) were male; 90 (75.6%) Chinese, 12 (10.1%) Malay, 7 (5.9%) Indian and 10 (8.4%) other ethnicity. Complete case analysis was done with 93 patients. The 5-year risk of the primary outcome (50% reduction in estimated glomerular filtration rate or ESKD) in our Oxford T2 histologic score was removed from the full model analysis as the number of observations is low (n=2). The original study reported AIC of 6338 for full model with race, 6379 for full model without race, vs 107.35, and 111.90 respectively in our study. The R² for the full models with and without race when applied to our validated cohort were 39% and 32%2 respectively, both were similar or better than the R² for the same models applied to the original derivation and validation cohorts (26.3%, 25.3%, and 35.3%, respectively). The C statistics for the full model with race was 0.858 (95% CI, 0.687-1.000), without race was 0.811 (95% CI, 0.599-1.000), comparable to the C statistics from the original derivation and validation analysis. Both full models were well calibrated in our cohort, with good agreement between predicted and observed risk of the primary outcome at 5 years post-biopsy.

Conclusions: The 2 full models with or without race were shown to be validated in our multi-ethnic Singapore IgAN cohort for predicting disease progression.
Background: Gut microbiota is observed to be associated with IgAN, as immune response in the gut is assumed to be one of the triggers of its development. And because the microbial composition is heritable, we hypothesize that genetic variants controlling gut microbiota composition may associate with susceptibility to IgAN or clinical phenotypes.

Methods: 175 gut-microbiome-associated genetic variants were retrieved from GWAS Catalog. Genetic associations were examined in 1511 patients with IgAN and 4469 controls. Sub-phenotype associations and microbiome annotations were undertaken for better understanding how genes shaped phenotypes. Likely candidate microbes suggested in genetic associations were validated using 16s rDNA sequencing in 29 patients with IgAN and 20 controls.

Results: Nine genetic variants associated with susceptibility to IgAN (P values from 4.1×10^-3 to 1.39×10^-2). The rs1889714-AA/AG risk genotypes associated with higher serum levels of Gd-IgA1 (A). Other significant findings included the associations between rs14830122-CC risk genotype and early age of onset (B), rs6665904-AA/AG risk genotypes and worse kidney function (C), rs9363741-GG/AA risk genotypes and severer hematuria (D). Besides, rs1889714-AA/AG risk genotypes associated with decreased abundance of beneficial Dialister; whereas rs6665904-AA/AG and rs9363741-GG/AA risk genotypes associated with increased abundance of detrimental Erysipelotrichaceae and Lachnobacterium, respectively. 16S rDNA sequencing data validated the decreased Dialister (E), and a tendency of increased Erysipelotrichaceae and Lachnospiraceae abundance in faeces from IgAN (F/G).

Conclusions: Our results provided supporting evidence that gut microbiota in IgAN was affected by host genetics and shed light on candidate bacteria for future pathogenesis studies.

Funding: Government Support - Non-U.S.
PO1844
Clinical Significance of Intensity of Galactose-Deficient IgA Deposition in Patients with IgA Nephropathy
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Background: Galactose-deficient IgA (Gd-IgA) has a crucial role in the pathogenesis of IgA nephropathy (IgAN). It was reported that Gd-IgA1 specifically deposit on glomeruli of primary IgAN using Gd-IgA1-specific monoclonal antibody (KM55 mAb). However, the association between intensity of Gd-IgA1 deposition and histological severity and clinical parameters are not clear.

Methods: We performed immunostaining with anti-IgA and KM55 mAbs in 74 patients who were diagnosed as IgAN at Juntendo University Hospital. We quantified the intensity of glomerular Gd-IgA1 by Image J software, and analyzed its association with histological findings. We also analyzed the association of intensity of glomerular Gd-IgA1 with serum levels of Gd-IgA1 and creatinine, urine Gd-IgA1 and proteinuria.

Results: Glomerular Gd-IgA1 was positive in all 74 primary IgAN cases, we divided into high-intensity (n=45) and low-intensity groups (n=29) by Image J software. In the Gd-IgA1 high-intensity group, acute lesions such as cellular crescents are dominant compared with low-intensity group (P<0.01). Moreover, the levels of proteinuria and urinary Gd-IgA1 were significantly higher compared with Gd-IgA1 low-intensity group (P<0.05). Next, we analyzed the pathogenic significance of merge ratio of glomerular IgA and Gd-IgA1. Interestingly, levels of proteinuria and urinary Gd-IgA1 were correlated with high merge ratio of glomerular Gd-IgA1 deposition associated with histological severity, especially acute lesions. Moreover, levels of proteinuria were correlated with high merge ratio of glomerular IgA and Gd-IgA1. Thus, glomerular Gd-IgA1 staining may be considerable index for therapeutic intervention.

PO1845
Glomerular Galactose-Deficient IgA, Expression Analysis in Pediatric Patients with Glomerular Diseases
Shinya Ishioka,1 Kandai Nozu,1 Rika Fujimaru,2 Yako Shimia,2 Hiroshi Kaito,3 Ryojiro Tanaka,4 Shingo Ishimori,5 Yuya Aoto,1 Nana Sakakibara,5 China Nagano,1 Tomoko Horinouchi,1 Tomohiko Yamamura,1 Takeshi Ninhoji,1 Koichi Nakashishi,5 Norishige Yoshikawa,6 Kazumoto Bija,1 Kobe University Graduate School of Medicine, Kobe, Japan; 2Wakayama Medical University, Wakayama, Japan; 3University of Rikkyu, Nishikawa, Japan; 4Takatsuki General Hospital, Tatsukichi, Japan; 5Osaka City General Hospital, Osaka, Japan; 1Hyogo Prefectural Kobe Children’s Hospital, Kobe, Japan.

Background: Galactose-deficient IgA (Gd-IgA1) has been identified as a key molecule in the pathogenesis of IgA nephropathy (IgAN). Using a Gd-IgA1-specific monoclonal antibody (KM55), glomerular Gd-IgA1 deposition has been detected in patients with IgAN and IgA vasculitis with nephritis (IgAV-N), but not other glomerular diseases. However, this specificity is controversial and there are currently no studies in pediatric cases.

Methods: We conducted a retrospective, multicenter study to examine double-immunofluorescence staining of IgA and Gd-IgA1 (KM55) in 60 pediatric patients with various glomerular diseases.

Results: Glomerular Gd-IgA1 deposition was detected in all cases of IgAN (n=17/17) and IgAV-N (n=6/6), and in patients with immunocomplex-mediated glomerulonephritis, including lupus nephritis (n=9/9), membranoproliferative glomerulonephritis (n=3/4), and membranous nephropathy (n=1/1). However, Gd-IgA1 was negative in patients with non-immune related glomerular diseases with IgA deposition, including idiopathic nephrotic syndrome (n=6/6), oligomeganephropenia (n=2/2), Alport syndrome (n=1/1), dense deposit disease (n=1/1), and crescentic glomerulonephritis (n=1/1). Both IgA and Gd-IgA1 were negative in patients with idiopathic nephrotic syndrome (n=5/5), membranoproliferative glomerulonephritis, membranous nephropathy, oligomeganephropenia, Alport syndrome, C3 glomerulonephritis, poststreptococcal acute glomerulonephritis, and hemolytic urmic syndrome (n=1/1 each).

Conclusions: Gd-IgA1 positivity in patients with IgAN and IgAV-N was consistent with previous reportings. However, Gd-IgA1 was also positive in patients with IgA-positive immunocomplex-mediated glomerulonephritis. KM55 may have the potential to distinguish incidental IgA deposition in pediatric cases. We speculate that Gd-IgA1 may be involved in the pathogenesis of these immune-related diseases, or KM55 may recognize IgA-related immunocomplex non-specifically.

PO1846
Urinary Exosomal MicroRNAs Are Potential Diagnostic and Prognostic Biomarkers in IgA Nephropathy Patients
Kyungohan Jeong, Jin Sug Kim, Hyeon Seok Hwang, Ji Yoon Kong, Shinyaegong Kang, Ji Ra Yang, Yun Kim, Ju Young Moon, Sanghee Lim. Division of Nephrology, Department of Internal Medicine, College of Medicine, Kyung Hee University, Seoul, Republic of Korea.

Background: Micro-RNAs (miRNAs) are small non-coding RNA molecules which regulate disease pathophysiology by modulating target gene expression. miRNAs are derived from tissues and biofluids such as serum, saliva, and urine. Recently, emerging evidence suggests urinary exosomal miRNAs as non-invasive biomarkers of various kidney diseases. However, few studies investigated clinical relevance of miRNA in IgA nephropathy (IgAN). In this study, we evaluated urinary exosomal miRNA expression and analyzed its clinical significance in patients with IgAN.

Methods: Urine samples were collected from 93 patients with biopsy-proven IgAN and 14 normal controls. We identified mRNA differential expression of renal tissue between IgAN and normal subjects in the gene expression omnibus database, and selected 884 glomerular and 67 tubulointerstitial genes through meta-analysis. We then used the miRtarBase, TargetScan, micorRNA database to predict potential miRNA targets. Finally, 11 urinary exosomal miRNAs were selected. We observed urinary exosomal expression of miRNAs and analyzed their diagnostic and prognostic accuracy for IgAN.

Results: The expression of miR-16-5p, miR-26b-3p, miR-29a-3p, miR-29c-3p, miR-126-3p, miR-199a-3p, miR-615-3p, and miR-29b-3p were significantly upregulated in IgAN patients as compared with normal controls. miR-16-5p, miR-26b-3p, miR-29a-3p, miR-29c-3p, miR-126-3p, miR-199a-3p, and miR-29b-3p have good diagnostic accuracy for IgAN (area under curve of receiver operating characteristic curve > 0.8). Baseline renal function significantly correlated with miR-16-5p, miR-29a-3p, miR-199a-3p, miR-199b-5p, miR-335-3p, and miR-615-3p. During follow-up period, 43 (46.2%) IgAN patients experienced adverse renal outcomes defined as a greater than 25% reduction in estimated glomerular filtration rate (eGFR), decline in eGFR category from the value determined at the time of renal biopsy, or start renal replacement therapy. miR-16-5p, miR-29a-3p, miR-199a-3p, and miR-335-3p were independently associated with increased risk of adverse renal outcomes.

Conclusions: Urinary exosomal miRNAs might be potential non-invasive biomarkers for diagnosis and prediction of disease progression of IgAN. Further studies are needed to clarify our results and ascertain the underlying mechanisms.

PO1847
Urinary Sediments Could Differentiate the Endocapillary Proliferative Lupus Nephritis and Endocapillary Proliferative IgA Nephropathy
Mo Yuan, Ying Tan. Institute of Nephrology, Peking University, Beijing, China.

Background: The role of manual urine sediment examination in the diagnosis and prognostication of endocapillary proliferative glomerulonephritis remains to be elucidated. This study aims to investigate the differences of urinary sediment findings between lupus nephritis and IgA nephropathy with endocapillary proliferative glomerulonephritis and further evaluated associations of leukocyturia with disease activity, pathological features and prognosis.

Methods: The urinary sediments of 126 patients, including 92 patients with lupus nephritis and 34 patients with IgA nephropathy with a renal biopsy-proven endocapillary proliferative glomerulonephritis were examined in the morning before renal biopsy according to a standardized method. The urinary elements investigated including various cells, casts and crystals. The associations of the level of leukocyturia and disease activity, pathological features and prognosis were further analyzed.

Results: In the patients with endocapillary proliferative glomerulonephritis, normal to mild leukocyturia (<12 HPF), and moderate to severe leukocyturia (>12 HPF) were found in 52(41.27%) and 74 (58.73%) patients, respectively. The proportion of moderate to severe leukocyturia, the frequency of urinary white blood cells casts and waxy casts were significantly higher in endocapillary proliferative lupus nephritis patients compared with endocapillary proliferative IgA nephropathy patients (P<0.001, P=0.020, P=0.010, respectively). In the proliferative lupus nephritis group, the levels of leukocyturia was significantly correlated with serum creatinine (r=0.288, P=0.005), eGFR (r=−0.284, P=0.006), serum C3 (r=−0.275, P=0.009), SLEDAI scores (r=0.383, P<0.001) and glomerular leukocyte infiltration (r=0.285, P=0.002). A multivariate analysis showed that leukocyturia was identified as an independent risk factor for renal outcome in proliferative lupus nephritis (HR: 1.456, 95% CI: 1.083-1.957, P=0.013) but not in IgA nephropathy (HR: 1.069, 95% CI: 0.404-2.312, P=0.866).

Conclusions: Urinary sediments of the endocapillary proliferative lupus nephritis and endocapillary proliferative IgA nephropathy differed in many aspects. Leukocyturia and endocapillary proliferative IgA nephropathy with endocapillary proliferative glomerulonephritis differed in many aspects. Leukocyturia was identified as an independent risk factor for renal outcome in proliferative lupus nephritis.
A Single-Center Retrospective Study of Thrombotic Microangiopathy

Miguel Obrador, Joan S. Carter, Senthil Sukumar, Vedat O. Yildiz, Clarissa A. Cassol, Sergey V. Brodsky, Tibor Nadasy, Spero R. Cataland, Samir V. Parikh, The Ohio State University Wexner Medical Center, Columbus, OH.

Background: Thrombotic microangiopathies (TMAs) are a rare group of clotting disorders of various origin, including infectious, idiopathic, autoimmune or drug-induced. This group shares common clinical manifestations that include low red blood cell and platelet counts. Although the disease is rare but treatable if clinician is aware about its manifestations. To increase the awareness and understand the disease better we conducted a retrospective study to characterize and assess TMAs in our institution

Methods: An observational retrospective study of patients with a diagnosis of TMA at Westchester Medical Center in the past 5 years was conducted. Data was collected from electronic medical records. Demographic, clinical and therapeutic variables were extracted, tabulated and analyzed

Results: A total of 43 patients with a diagnosis of TMA were identified and included in the study. The cohort had a mean age of 39.9 years; 20 were male and 23 females. As shown in Table 1. Thrombotic thrombocytopenia purpura (TTP) (n=14, 32%), systemic lupus erythematosus (SLE) (n=5, 11.6%), and hemolytic uremic syndrome (HUS) (n=5, 11.6%) are the most common etiologies. Other identifiable etiologies were atypical HUS (9%), use of calcineurin inhibitors (9%), acute myeloid leukemia (4.6%). About 6.9% cases didn’t have any identifiable cause (6.9%). Patients with TTP had a mean age of 48 years, mean platelet count of 17 k/mm3, and most were female (71%). Fifty-seven percent had hematuria, 21% proteinuria and 85% had schistocytes in the blood smear.

Conclusions: Most common cause of Thrombotic Microangiopathies is TTP which is what we found in our institution. It is essential to aware about the manifestation of this disease since early recognition and prompt treatment is the key for better outcome

Table 1

<table>
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PO1850

Does Kidney Histology Predict Renal Response or Complement Status in Atypical Hemolytic Uremic Syndrome?

Jessamyn S. Carter, Senthil Sukumar, Vedat O. Yildiz, Clarissa A. Cassol, Sergey V. Brodsky, Tibor Nadasy, Spero R. Cataland, Samir V. Parikh, The Ohio State University Wexner Medical Center, Columbus, OH.

Background: Atypical Hemolytic Uremic Syndrome (aHUS) is diagnosed based on clinical evidence of microangiopathic hemolytic anemia, thrombocytopenia and renal failure and histologic evidence of thrombotic microangiopathy (TMA). However, these characteristics are not specific and cannot differentiate aHUS from other causes. Whether specific histologic lesions of TMA can predict complement mutation status (CM +/-), guide treatment, or predict renal outcomes has not been explored. Here, we evaluate the potential of using kidney histology to predict CM status and renal response in aHUS.

Methods: A retrospective analysis of aHUS patients (N=35) who achieved a hematologic response after treatment with anti-C5 therapy was conducted. Clinical and demographic data were recorded and two blinded Nephropathologists scored native kidney biopsy findings independently. Seventeen histologic lesions of TMA were scored.

Results: In this cohort, 13/29 (45%) were CM+. Of the 17 histologic variables studied, only glomerular intracapillary fibrin differentiated CM+ from CM- (P<0.05), suggesting that histologic features were also similar between patients who achieved renal response (RR) and non-responders (NR). Although not statistically significant, NR had a higher percentage of global glomerulosclerosis (38 vs 16%, P=0.07) and concentric fibros intimal thickening (onion skinning) (70% vs 29%, P=0.08) compared to RR.

Conclusions: Glomerular intracapillary fibrin was the only histologic variable different in CM+ versus CM- TMA. When present, this variable may suggest patients with TMA will be CM-. Percentage of glomerulosclerosis and presence of fibros intimal thickening was higher in NR compared to RR but this did not reach statistical significance. A larger study is needed to determine the value of these features in predicting complement mutation status and renal response in aHUS.

PO1851

Comparative Efficacy of Ravaluzumab and Eculizumab in the Treatment of Atypical Hemolytic Uremic Syndrome: An Indirect Comparison Using Clinical Trial Data

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare disease that can cause organ damage or death if not suitably treated. Eculizumab (EUC), a C5 inhibitor, was approved, to treat aHUS in 2011. Ravaluzumab (RAV), approved in 2019, was engineered from EUC to reduce dosing frequency (every 8 weeks [for patients weighing ≥ 20 kg] vs 1 week, respectively) and minimise treatment burden. Both drugs have established safety and efficacy via pivotal single armed studies. We indirectly compared the efficacy of RA V vs ECU using clinical trial data.

Methods: Patient-level data from a pivotal RAV trial (NCT02949128) and pivotal EUC trials (NCT00844428, NCT01194973) for adults with aHUS without kidney transplant were used. Propensity scores were calculated based on baseline characteristics of the ECU trials (NCT00844428, NCT01194973) for adults with aHUS without kidney transplant or acute dialysis program who showed neurologic damage. The mean cost per patient-year changed from 319,931 to 150,878 euros from the pre- to post-MDT period. The number of patients-dialysis or in kidney transplant program (KTx) and the milligrams of Eculizumab used at the pre-MDT implementation.

Results: After balancing patient characteristics between study groups, no significant differences were seen between outcomes for ECU and RAV at 26 weeks.

Conclusions: After balancing patient characteristics between study groups, no significant differences were seen between outcomes for ECU and RAV at 26 weeks.
C3 Inhibition with Pegcetacoplan Targets the Underlying Disease Process of C3 Glomerulopathy (C3G) and Improves Proteinuria

PO1852

C3 Inhibition with Pegcetacoplan Targets the Underlying Disease Process of C3 Glomerulopathy (C3G) and Improves Proteinuria

Pegcetacoplan also appeared to be well-tolerated. Further studies are warranted to No serious or severe adverse events were reported and no TEAEs led to discontinuation.

to Week 48. Serum albumin and C3 increased, and serum creatinine was stable (Table).

administration. Data showed a greater than 65% reduction in 24-hour uPCR from baseline

as 360 mg daily subcutaneous infusions with transition to 1080 mg twice weekly from

Xin

C3 Glomerulonephritis Associated with Monoclonal Gammopathy: A Process of C3 Glomerulopathy (C3G) and Improves Proteinuria

PO1854

The Prognostic Value of Chronic Histopathological Lesions in Monoclonal Immunoglobulin Deposition Disease: A Clinicopathological Analysis of Patients from a Single Institution

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Background: Kidney is the most common involved organ in monoclonal immunoglobulin deposition disease (MIDD), which could lead to end stage renal disease (ESRD). Few studies have evaluated the association between the irreversible chronic histopathologic lesions and clinical features, and its prognostic value in renal outcomes in MIDD.

Methods: A series of 20 patients with MIDD and 20 patients with renal AL amyloidosis proven by renal biopsy between January 2001 and December 2018 were reviewed retrospectively. The degree of chronic changes including glomerulosclerosis, interstitial fibrosis, and arteriosclerosis were semiquantitatively scored and the overall chronic lesions were also graded based on the grading system proposed in 2017. The association between histopathological lesion and clinical manifestations, and the correlation with risk of progression to ESRD were investigated.

Results: MIDD patients presented more significantly overt ischemia-related global glomerulosclerosis and a more severe tendency of interstitial fibrosis(Figure 1). The significantly higher extent of overall chronic changes was also seen in MIDD compared with AL amyloidosis, which was independently correlated with worse baseline estimated glomerular filtration rate (β coefficient (95% CI): -4.618(-8.238 to -0.999), P=0.017). And the overt interstitial fibrosis predicted the increased risk of developing ESRD in MIDD.

Conclusions: The extent of chronic changes provide information both about baseline manifestation and renal survival. Carefully grading and evaluating the chronic changes in MIDD may help guiding the treatment and accessing the renal outcomes.

Figure 1. Comparison of overt histopathological lesions between AL and MIDD at kidney biopsy

PO1855

Development of Atypical Hemolytic Uremic Syndrome in a Patient with Complement 3 Glomerulonephritis

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Introduction: Uncontrolled hyperactivity of alternative complement pathway has been implicated in development of two distinct pathological processes, namely C3 glomerulonephritis (C3GN) and atypical hemolytic uremic syndrome (aHUS). Here we present a unique case which initially started as C3GN on kidney biopsy and progressed to aHUS.

Case Description: 68-year-old female presented with progressive weakness and palpitations over a month. She denied any fever, chills, dysuria, chest pain, dyspepsia or abdominal pain. Her past medical history was significant for hypertension and coronary artery disease, with no family history of end stage renal disease. On admission, her medications included hydrochlorothiazide for hypertension, levothyroxine for hypothyroidism and intermittent steroids for gouty arthritis. On exam, her vital signs revealed tachycardia with heart rate 119 beats/min and hypotension with blood pressure 97/59 mmHg. Exam was significant for dry mucosa and irregular heart rate. Initial laboratory evaluation was significant for acute kidney injury (AKI), with creatinine (Cr) of 2.6 (baseline Cr of 1.2). Urinalysis demonstrated 21-50 RBC/hpf and urine protein/Cr of 12.5 g/g. A renal biopsy was performed which showed endocapillary proliferation with dominant staining for C3 in the mesangium and along the capillary wall, consistent with C3GN. The patient was started on prednisone 60 mg daily.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Hemodialysis was initiated for uremic symptoms. Complement function test was consistent with ongoing complement dysregulation at C3 convertase level and C5 convertase level without the presence of autoantibodies towards complement proteins. 2 months after her kidney biopsy, she developed worsening anemia and thrombocytopenia, elevated lactate dehydrogenase and undetectable haptoglobin. Direct coombs test was negative, peripheral smear showed schistocytes, ADAMTS13 level was 65%, consistent with diagnosis of atypical hemolytic uremic syndrome. Patient was started on Eculizumab therapy with stabilization of hemoglobin and platelets but remains dialysis dependent.

**Discussion:** In our growing understanding of alternative complement pathway, it is thought that dysregulation at fluid state is associated with C3GN, while solid state dysregulation is associated with widespread endothelial injury leading to aHUS. Our patient developed both pathologies, suggests further research is needed in understanding the details of complement system.

**PO1856**

**Acute Renal Failure from Thrombotic Microangiopathy: Is IgA Vasculitis to Blame?**

Dipal Patel.

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**Introduction:** Thrombotic microangiopathy (TMA) has been associated with several cases of IgA nephropathy. In most cases the clinical significance of the TMA is uncertain. We describe a case of acute renal failure in a patient with systemic IgA vasculitis, who was found to have severe renal-limited TMA treated with eculizumab for the possibility of underlying complement dysregulation.

**Case Description:** A 34 year old male presented with abdominal pain and bloody bowel movements, and was found to have extensive duodenitis. Infectious testing of stools was negative, though he later tested positive for H. pylori. While hospitalized he developed acute kidney failure, with creatinine rising from 1.5 to 11.7 within four days. Urine sediment demonstrated granular casts consistent with acute tubular injury, though he also had white cell casts for which acute interstitial nephritis was considered. Blood counts were normal on admission, but he developed anemia and thrombocytopenia with mildly positive markers of hemolysis (haptoglobin 25, LDH 269, no schistocytes). Serum complements were profoundly low (C3 33, C4 9). A kidney biopsy revealed severe TMA. Given the rapidity of progression to renal failure requiring dialysis, he was started on eculizumab for a presumed atypical hemolytic uremic syndrome (aHUS). Since he did not have evidence of active hemolysis, he was not started on plasmapheresis. Kidney biopsy demonstrated proliferation and expansion of the mesangium with IgA deposition. Endoscopy was later performed with biopsy consistent with systemic IgA vasculitis, for which he was started on steroids. Abdominal symptoms improved and he was discharged home. He continues on eculizumab with normalization in complements, but without improvement in renal function.

**Discussion:** There have been case reports of complement factor dysregulation resulting in both IgA vasculitis and TMA. Given the extent and acuteness of renal failure in this case, we treated our patient with eculizumab for presumed aHUS.

**PO1857**

**Proliferative Glomerulonephritis with Monoclonal IgG Deposits (PGNMID): A Report of Two Cases Managed with Renin-Angiotensin-Soldosterone System (RAAS) Inhibition Alone**

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**Introduction:** PGNMID is a relatively rare disorder with monoclonal immunoglobulins (Ig) deposition in glomeruli that resembles immune complex glomerulonephritis (GN), after exclusion of other related disorders such as amyloidosis and cryoglobulinemia. The pathogenesis and management of PGNMID remains uncertain, especially if no systemic clonal disorder is found, which is frequently the case. Some groups have recommended anti-plasma cell or anti-B cell therapy in most if not all cases, even if a clone is not identified. We present two cases of PGNMID that were managed with RAAS blockade alone and whose renal disease remained stable over 6 and 10 years of follow up.

**Case Description:** Two cases were identified who had prolonged follow up with PGNMID and no immunosuppressive treatment. Charts were reviewed retrospectively and data collected from time of biopsy until most recent follow up. Case 1 is a 25 year old obese black woman with recent onset of hypertension who presented with serum creatinine (sCr) 1.4mg/dl. Urinalysis (UA) showed 1+ protein and no blood. 24hr urine protein was 296mg. Renal biopsy (done as she had positive antiphospholipid antibodies) revealed PGNMID (IgG kappa) with diffuse mesangial proliferation and focal sclerosing GN with focal fibrous crescents. There was no evidence of thrombotic microangiopathy. Serum and urine immunofixation (IF) were negative for monoclonal protein. Bone marrow biopsy was unremarkable. The patient was treated with angiotensin-receptor blocker (ARB) without immunosuppressive therapy. Six years later the most recent sCr was 1.5mg/dl and urine protein-creatinine ratio (PCR) was 1100mg/g. Case 2 is a 41 year old white woman who presented with sCr 0.6mg/dl. UA had 3+ protein and no blood. 24hr urine protein was 2.3g. Renal biopsy showed PGNMID (IgG kappa) with mesangial and endocapillary proliferation. Serum and urine IF were negative for monoclonal proteins. Bone marrow biopsy was not done. The patient was treated with an angiotensin-converting enzyme inhibitor (ACEI) alone. After ten years of follow up, her sCr was 0.7mg/dl, and urine PCR was 0.2mg/g.

**Discussion:** We report 2 cases of PGNMID with stable renal function and proteinuria after 6 and 10 years of RAAS therapy alone. This suggests that not all patients with PGNMID may require immunosuppression.

**PO1858**

**Use of Proneur-Treated Paraffin Immunofluorescence to Unmask a Reclusive Glomerular Disease**

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**Introduction:** Interpretation of renal biopsy depends on light, IF and electron microscopy. Direct IF on unfixed frozen tissue sometimes fails to pick up immunoglobulins. Treatment of paraffin embedded formalin-fixed tissue with pronase renders such Igs more amenable to detection. We present a case of a young woman where use of this “unmasking” technique allowed the correct diagnosis to be made.

**Case Description:** A 24 YO WF presented to our Gn Clinic with intermittent edema, IF and electron microscopy. Direct IF on unfixed tissue sometimes fails to pick up immunoglobulins. Treatment of paraffin embedded formalin-fixed tissue with pronase renders such Igs more amenable to detection. We present a case of a young woman where use of this “unmasking” technique allowed the correct diagnosis to be made.

**Discussion:** A 24 YO WF presented to our GN Clinic with intermittent edema, proteinuria and hematuria noticed about a year ago. Her creatinine was 1.5 mg/dl. Urine P/C ratio was 1.8 g/g. Her ANA was 1:320 but the rest of the antibody panel was negative. C3 and C4 were normal. Lupus Anticoagulant, beta 2 GPI, antiphospholipid IgG and IgM were positive. Screens for paraproteins and relevant viruses were negative. Renal Biopsy: 20/31 glomeruli were globally sclerotic. Intact glomeruli showed mesangial proliferation and hypercellularity. IF showed C3+ but all other stains were negative. IF on pronase digested, paraffin embedded tissue stained IgG, C3 and kappa with no lambda. Stain for SAP was positive. EM showed numerous mesangial deposits, some sub-epithelial but no sub-endothelial deposits. Based on above, she was diagnosed with Membranous like glomerulopathy with masked IgG-kappa deposits. Her age, race, gender, Ab profile as well as biopsy findings all supported the diagnosis. She was started on immunosuppression therapy to attempt salvage of renal function and delay progression.

**Discussion:** Refinedment in IF techniques has expanded our diagnostic ability and mechanistic understanding of glomerular disease. Use of paraffin embedded tissue for IF after pronase treatment helps discover Ig deposits not picked up by traditional IF. This can prove critical in correctly diagnosing glomerular disease, as exemplified in this case. This patient could have been misdiagnosed as C3 glomerulopathy based on traditional IF. Unmasking IgG-kappa deposits allowed us to correctly diagnose her with a rare disease, MGNMID. This technique expands our ability to correctly diagnose glomerular disease and should be applied routinely.

**PO1859**

**Fibrillary Glomerulonephritis: A Case Series with Clinical Features and Outcomes**

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**Background:** Fibrillary glomerulonephritis (FGN) is a rare cause of chronic glomerulonephritis with a poor prognosis. We evaluated a series of patients with FGN, most of whom were treated with rituximab, low-dose cyclophosphamide, and prednisone (RCP).

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.**

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Methods: Patients were included if they had FGN treated at Massachusetts General Hospital between 2008-2020 with a minimum of six months of follow up. The primary outcome was achievement of remission, defined as serum creatinine that remained stable, improved or increased <25% of the original value after treatment, and a 50% reduction in proteinuria at the end of follow up.

Results: We identified 11 consecutive patients with FGN. ANCA-associated vasculitis (n = 3), rheumatoid arthritis (n = 1), chronic hepatitis C (n = 1), and monoclonal B lymphocytosis (n = 1) were concurrently present. At the start of therapy, the median (IQR) serum creatinine, GFR, and proteinuria was 2.31 mg/dL (1.25 – 4.69), 30 mL/minute/1.73 m² (11 – 68), and 6.68 g/L (5.5 – 8.4), respectively. Of the 31 patients, 10 were treated with RCP, and one patient with rituximab monotherapy. The median (IQR) follow-up was 2.6 years (2.0 – 3.9). Seven of 11 patients achieved remission. Of the 4 patients who did not achieve remission, one received pre-emptive transplantation, two initiated hemodialysis, and one had >25% rise in serum creatinine not reaching ESRD. Five serious adverse events occurred over 33 patient years.

Conclusions: Remission was achieved in most patients with FGN treated with rituximab, low-dose cyclophosphamide, and prednisone. Larger studies evaluating this regimen are warranted.

POI1860
An Atypical Case of Fibrillary Glomerulonephritis
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Introduction: Fibrillary glomerulonephritis (FGN) is a rare glomerular disease associated with multiple disease associations such as hepatitis C, malignancy, and dysproteinemia. Despite these known associations, little is known about the interaction between FGN and other comorbidities. We present a case of FGN that presented years after successful eradication of hepatitis C virus infection treated with DAAs with SVR for years referred to nephrology clinic for evaluation of CKD and nephritic syndrome. She also reported pain and a purpuric papular rash on her legs. Labs showed hypocomplementemia and high levels of RF. Cryo was suspected, but repeated testing of serum cryoglobulins was negative. Renal biopsy showed membranoproliferative GN with endocapillary hypercellularity and endocapillary “cryo-plugs” by LM, and IgM dominant with kappa greater than lambda capillary loop and mesangial staining by IF, and subendothelial and mesangial deposits by EM. These findings suggest cryo GN. Patient was treated with a prednisone taper and rituximab.

Case Description: Our patient is a 49-year-old Filipino female, hypertensive, diagnosed case of Immune Complex-Mediated Glomerulonephritis presenting with elevated blood pressure and nephrotic-range proteinuria. Initial adjustment of her anti-hypertensive regimen controlled her blood pressure. Subsequently, she developed resistant hypertension and increasing proteinuria. Creatinine increased to 2.1 mg/dL from a baseline of 1 mg/dL in 12 months. A second renal biopsy was done showing globally widespread podocyte foot process effacement and mesangial fibrillary deposits measuring 13 mm in mean diameter suggestive of Fibrillary Glomerulonephritis. Patient was worked up for an underlying malignancy, autoimmune disease and infectious causes but none turned out positive. At this time, proteinuria has increased to 7596.05 grams from 1622.08 grams with a creatinine clearance of 39.80 ml/min/1.73 m². After discussing with the patient, she was given Rituximab as four weekly doses of 375 mg/m² intravenously. After five months, there was significant reduction in proteinuria at 373 mg/m² intravenously. Further rash, there was significant reduction in proteinuria at 1734.32 grams with stable creatinine clearance of 31.99 ml/min/1.73 m².

Discussion: In general, FGN prognosis is poor and majority of patients progress to ESRD. Treatment options are currently limited and conclusions regarding immunosuppressive therapy cannot be drawn from limited published data. Rituximab may offer benefit particularly in patients with relatively normal baseline renal function.
Renal Biopsy. Cryoglobulinemic Glomerulonephritis

PO1863
Clinico-Biological Characteristics and Treatment of Hepatitis B Virus-Related Mixed Cryoglobulinaemia: Current Clinical Evidence

Introduction: Hepatitis B virus (HBV)-related mixed cryoglobulinaemia (MC) was considered to be a rare disease, presented as mild clinical symptoms just like purpura to severe organ damage such as glomerulonephritis. We aimed to clarify the clinico-biological characteristics and treatment of HBV-related MC.

Methods: We reported a case of HBV-related MC, enrolled 41 HBV-related MC cases from literature, and summarized demographic, clinical, laboratory, treatment group, patients in remission and refractory were compared. Kidney involvement, death and time to death were included for survival analysis.

Results: Of the 42 HBV-related MC, Mean age was 53±14 years, and 47.6% patients were male. Extraglomerular clinical manifestations mainly included cutaneous lesions, kidney involvement, peripheral neuropathy, arterial involvement, which accounted for 78.6%, 54.8%, 35.7%, 19.0%, respectively. 87.1% (27/31) patients had low serum C4, and 92.6% (25/27) patients’ rheumatoid factors (RF) were positive. Renal pathology showed membranous proliferative glomerulonephritis, the capillary lumen disclosed hyaline thrombi and electron microscope found microtubular substructure. 36 (85.7%) patients received antiviral therapy. Corticosteroids were used in 22 (52.4%) patients, immunosuppressive agents were given to 13 (31.0%) patients, and plasma exchange (PE) were used in 9 (21.4%) patients. At the end of follow-up, 52.4% (22/42) patients were in remission, 47.6% (20/42) patients had refractory disease, and 11.9% (5/42) patients died. The patients who had cutaneous necrosis, peripheral neuropathy and kidney involvement had correlation with overall survival (log rank $P=0.034$).

Conclusions: Extraglomerular clinical manifestations of HBV-related MC were varied. Anti-HBV treatment, corticosteroids, immunosuppressive agents and PE were useful for some patients. The patients with kidney involvement may be related to poor prognosis.

PO1864
Membranoproliferative Glomerulonephritis (MPGN) Associated with Epstein Barr Virus (EBV)


Introduction: Immune complex-mediated MPGN has been commonly associated with viral infections including Hepatitis B, C, HIV and Hantavirus. We present a rare case of EBV associated MPGN successfully treated conservatively.

Case Description: A 19-year-old female, previously healthy, presented with fatigue, sore throat and periorbital swelling for 3 weeks. Vitals were stable on presentation. Her EBV IgM and IgG serologies were positive while CMV was negative. UA showed proteinuria (>300mg/dl) and microscopic hematuria. Albumin was 2.9 g/dl. Spot urine protein to creatinine ratio was 2.6g/g. Urine sediment was bland. SCr was 0.72 mg/dl. Extensive serological work up was negative. Renal biopsy showed mesangial hypercellularity, double contours of capillary loops with intramembranous, subendothelial and subepithelial immune type electron dense deposits. Immunofluorescence revealed segmental globular to coarsely granular staining in the glomerular capillary walls for IgG (3+), IgA (1+), IgM (3+), kappa (2+), lambda (3+), C3 (1-2+), C1q (3+), and C4 (1+). Mesangial regions showed segmental granular staining for IgG (1+), kappa (1+), lambda (1+) and C4 (1+). She was treated with furosemide 20mg daily as needed for swelling and linsinopril 5mg daily. Her symptoms resolved within 2 weeks of initiating treatment. She self-discontinued her medications after 4 months. On 6 month follow up, she remained asymptomatic and urine protein was undetectable.

Discussion: Infectious Mononucleosis (IM) is caused by EBV. EBV primarily infects human B cells via the CD21 receptor and may infect renal tissue since the CD21 molecule has been detected in proximal tubular cells of kidneys. Further, acute EBV infection may cause immune-mediated response with deposition of immune complexes and subsequent glomerulopathy. Renal involvement is reported with 3-16% cases of acute IM. Common renal lesions include acute tubulointerstitial nephritis, membranous nephropathy, minimal change disease and vasculitic lesions. MPGN is a rare presentation of EBV and should be considered in patients with IM and proteinuria. Previous case reports have suggested that nephritic syndrome in patients with an acute EBV infection is usually self-limiting. Our case report also suggests that MPGN associated with EBV may have a relatively benign course.

PO1865
Infection-Related Glomerulonephritis Mimicking Lupus Nephritis

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Introduction: Differentiating infection vs auto-immune related GN is crucial in order to avoid inadvertent immunosuppressive therapy that can be harmful and even lead to fatal consequences. This case illustrates the dilemma of medical management in lupus like-GN.

Case Description: A 66 year old man with mitral valve prolapse, was found to have elevated creatinine of 3.59 mg/dl from a baseline of 1 mg/dl. He complained of leg rash and dark urine. His rash was symmetric and non blanchable petechiae. Urine sediment showed 20 dysmorphic RBC per high-power field and RBC casts. Urine protein/creatinine ratio was 1.35 g/g. Serum creatinine peaked at 14.0 mg/dl. Hemodialysis was begun. Further testing was significant for pancytopenia, low complements (C3 was 40 mg/dl, C4 10 mg/dl) and positive MPO-ANCA. Kidney biopsy was performed (Fig 1). On light microscopy 2 glomeruli were globally sclerotic. One glomerulus showed crescentic and necrotizing lesion. There was diffuse ATN. Some tubules showed red blood cell casts. Interstitial inflammation was mild. Direct IF showed a full house pattern with bright IgG, IgM, kappa, lambda, C1q, C3 and mild to moderate IgA staining. EM identified few mesangial and subendothelial deposits with a single subepithelial hump. During his hospitalization, streptococcus bacteremia was documented. Echo showed mitral valve vegetation. In setting of bacterial endocarditis, the Biopsy is consistent with infection related glomerulonephritis (IRGN).

Discussion: Crescents as well as ANCA positivity have been described in IRGN. However a full-house immunostaining pattern is not typical of IRGN and has never been reported in IRGN. Instead, this is typical of lupus-like GN. The patient didn’t have positive ANA, however he developed pancytopenia and hypocomplementemia which can be manifestations of both SLE even at an old age as well as infection. The dilemma is that auto-immune mediated GN warrants immunosuppressive therapy which is contraindicated in IRGN. Our patient received penicillin and underwent mitral valve replacement His kidney function gradually improved and dialysis was discontinued after 4 months.

PO1866
Hypocomplementemic Urticarial Vasculitis: Interstitial Nephritis with New Microtubular Deposits and Successful Response to Rituximab

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Introduction: HUV is caused by antibodies to C1q complement and has many features of systemic lupus and cryoglobulinemia. Different patterns of GN often occur such as the mesangial GN, MPGN or membranous GN but interstitial nephritis has never been described.

Case Description: A 57 year old female in 2007 developed recurrent hives, and asymptomatic leukocytoclastic vasculitis on skin biopsy & 5 g proteinuria with RBC casts. C1q complement was 2 mg/dl, C3 20 mg/dl, C4 6 mg/dl & C1q antibody was 35 mg/ml (NL=10). All other serology and cryos were negative. Serum creatinine was 0.6mg/dL.

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Her 1st renal biopsy showed mesangial proliferative GN with +3 IF for IgG, IgA, C1q & C3, subendothelial, subintimal, subperitubular, subepithelial, and focal location of subintimal inflammation. Parallel microtubular structures, 25 nm wide with hollow cores, were present in interstitial capillaries and hilar arterioles but not in the glomeruli. Tubular basement membranes & peritubular capillaries were +3 positive for IgG & C1q with granular, subendothelial & subperitubular deposits. Tubulointerstitial fibrosis & chronic inflammation were minimal. She had 4 weekly doses of Rituximab 375 mg/m^2; she rapidly went into remission within 2 months which was sustained for 6 years. HU flared in 2016 with new onset nephrotic syndrome, hives, angioedema, COPD & AKI. Serum creatinine was 2.2 mg/dl & urine total protein/creatinine ratio was 4.2 g/mmol. C1q was 4 mg/dL, C3 33 mg/dL, C4 4 mg/dL & C1q antibody > 100 mg/mL. A 2nd renal biopsy showed diffuse endocapillary proliferation with membranous GN similar to lupus Class IV & V & interstitial inflammation. IF was +3 for IgG, IgA, C1q and kappa and lambda in the same locations as biopsy 1. Tubular basement membranes & peritubular capillaries were positive for IgG & C1q. Peritubular capillaries had 25 nm hollow microtubule structures as before. Rituximab was initiated at 375 mg/m^2 for 4 doses. It induced a complete renal remission after 3 months with a serum creatinine of 0.6 mg/dl & urine total protein of 210 mg.

Discussion: We conclude: In addition to glomerulonephritis HUV can cause interstitial nephritis with +1IF for IgG & C1q. HUV causes unique microtubular structures in the interstitium but not the glomeruli. Rituximab rapidly induces clinical renal remission in HUV.

UAB867
Unusual Aggregation of Different Glomerulopathies in a Family Resolved by Genetic Testing

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Introduction: Glomerulonephritis (GN) is a major cause of chronic kidney disease (CKD) in children. The conventional approach to diagnosis of GN includes clinical evaluation and in most cases kidney biopsy to make a definitive diagnosis. However, in many cases, clinical presentations of different GNs can be indistinguishable leading to uncertainty in diagnosis and management even after renal biopsy. In this report we identify a family with clinical diagnoses of post infectious glomerulonephritis (PIGN) and IgA nephropathy in a parent and two children. Renal biopsies were inconclusive and we were only able to make all the diagnoses in each of the family members after genetic testing and reverse phenotyping.

Case Description: A previously healthy 7 year old male presented to the emergency department with hematuria, fever, and sore throat. Apart from being obese, his physical examination was unremarkable. Laboratory studies were remarkable for microscopic hematuria and non-nephrotic range proteinuria. C3/C4 complements, ASO, anti-DNase b, anti-ssDNA, ANCA, and anti-GBM titers were all normal. A presumptive diagnosis of PIGN was made. However, he had persistent hematuria and proteinuria over the next 10 months. Further history at follow up revealed a history of IgA nephropathy in his mother and CKD of unclear etiology in his maternal grandfather. Renal biopsy was initially reported to be consistent with IgA nephropathy. However, because of the family history we carried out genetic testing and identified a rare hemizygous variant [c.3437G>A (p.Gly1146Glu)] in the gene COL4A5 of his brother and mother.

Discussion: This case highlights the utility of genetic testing and reverse phenotyping in resolving clinical diagnosis in families with unusual presentations of different glomerulopathies. We propose that clustering of different glomerular disease phenotypes in a family should be an indication for genetic testing.

UAB868
Unusual Case of Histiocytic Glomerulopathy in the Setting of Sarcoma-toid Malignancy

Faris Al faris, Majid Al-Ahmad, Llwellyn A. Foulke, Mauricio Monroy, Kelly H. Beers. Albany Medical Center, Albany, NY.

Introduction: We present a case of histiocytic glomerulopathy and pauci-immune ANCA negative glomerulonephritis (GN) in the setting of sarcomatoid malignancy.

Case Description: An 83-year-old female presented to our hospital for evaluation of abdominal pain. Her vital signs were normal and her physical exam was only significant for mid-abdominal tenderness on palpation. Aortic angiography revealed occlusion of the superior mesenteric artery, celiac artery and left renal artery, in addition to a mass engulfing the celiac artery. She later developed acute kidney injury (AKI) with creatinine rising to 1.5mg/dl from baseline of 1.2mg/dl. Work up revealed bland urine sediment and 24-hour proteinuria. Although c-AKNI is a rare and aggressive cause of AKI with 10% of the cases being ANCA-negative. Few case reports linked ANCA-negative pauci-immune GN to non-small cell lung cancer. To our knowledge this is the first case of histiocytic glomerulopathy, ANCA-negative pauci-immune GN and arthritis in the setting of sarcomatoid malignancy.

PO1869
Bilateral Renal Infarctions: A Perplexing Presentation of Polyarteritis Nodosa

Alissa Lee, Matthew Foy. Louisiana State University Health Sciences Center, Baton Rouge, LA.

Introduction: Classic polyarteritis nodosa (c-PAN) is an autoimmune necrotizing vasculitis with predilection for medium-sized vessels. Although c-PAN can be associated with renal involvement, acute renal failure or extensive renal infarctions are exceedingly uncommon. We report a rare case of c-PAN manifested by bilateral renal infarctions on initial clinical presentation.

Case Description: A 40 year old man with no known medical issues presented to the emergency department with encephalopathy in the setting of one month of reported myalgia, fevers, chills, night sweats, and unintentional ten lb. weight loss. Upon physical examination, his vitals were 95.1°F, 101 beats/min, 145/101 mmHg, with no evidence of trauma or skin abnormalities. His lab results were notable for Cr 1.83 mg/dL, AST 116 mm/hr, and he had transient worsening of his Cr (2.96 mg/dL) and Hbg (6.7 g/dL). CT/CTA revealed bilateral renal infarctions with perinephric and retroperitoneal hematomas, right renal artery aneurysm, thrombosis of one of three left renal arteries, and splenic hematoma, while MRI demonstrated a small parietal hematoma and thoracic intrathoracic epidural hemorrhage. He was initiated on monthly cyclophosphamide and prednisone. One month later, he had symptomatic resolution and a Cr of 1.89 mg/dL.

Discussion: Given his fulfillment of five American College of Rheumatology (ACR) criteria, he was diagnosed with c-PAN as a constellation of clinical findings can be used, and biopsy results are not always necessary, especially given the risk of hemorrhage. Although it is a rare condition, it is important to remain cognizant and consider c-PAN in the differential due to its significant implications and the importance of timely treatment.

Right Renal Artery Aneurysm and Renal Infarctions

PO1870
Clinical Predictors of Response to Rituximab in the Nephrotic Syndrome Study Network (NEPTUNE) Cohort

Daniella Levy Eroz, 1,2 Kevin E. Meyers, 1,2 Jarcy Zee, 1 Abigail R. Smith, 3
1Division of Nephrology, Children’s Hospital of Philadelphia, Philadelphia, PA; 2University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; 3Arbor Research Collaborative for Health, Ann Arbor, MI.

Background: Rituximab, an anti CD20 monoclonal antibody, is one of the alternative medications offered to children and adults with Nephrotic syndrome. Despite the growing knowledge regarding this medication, there are still concerns regarding long-term safety that need to be considered prior to initiation of therapy. Given these risks there is a need to identify characteristics of patients who will respond best to rituximab therapy.

Methods: We identified all patients who received rituximab within NEPTUNE, a prospective study of adults and children with glomerular disease enrolled at the time of first biopsy or at initial presentation. Remission was defined as UPC<0.3 mg/mg
after rituximab initiation. Kaplan-Meier plots and log-rank tests were used to compare the probability of response among various levels of demographic and clinical variables.

**Results:** Of 734 patients enrolled in NEPTUNE, 57 (34 adult, 23 pediatric) received rituximab after enrollment and were eligible for analysis. In the adult cohort, average age at initiation was 45.8 (SD−15.4), majority were male (79%) and white (88%) and diagnosed with membranous nephropathy (MN) (74%). In the pediatric cohort, most had Minimal change disease (MCD) disease on biopsy or nephrotic syndrome not specified (not biopsied) (NSNS) (83%), mean age was 6.96 yrs (SD−4.25), 57% were male, and 74% were white. Remission was achieved in 18 (53%) adults and children 19 (83%) respectively, with a median time to remission of 25.4 months and 4.8 months respectively. Probability of achieving remission was higher in patients with MCD/NSNS compared to MN (p<0.001, Figure). Among patients with MCD/NSNS, probability of remission was higher in <6 yrs vs. ≥6 yrs and adults (p=0.036).

**Conclusions:** Rituximab response rate in patients with MCD/NSNS were higher and quicker than in those with MN. Young children with MCD/MSNS had the highest rates of response. Future work is now targeted at identifying additional biomarkers (specifically lymphocyte profile) to predict response to rituximab.

**Funding:** NIDDK Support, Private Foundation Support

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**Figure:** Remission probability by age and disease diagnosis.

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**POI871**

**Tobacco Exposure in the Nephrotic Syndrome Study Network (NEPTUNE)**

Linda Wang, Kevin E. Meyers, Christine B. Sethna. NEPTUNE Cardiovascular Working Group 1The Children’s Hospital of Philadelphia, Philadelphia, PA; 2Cohen Children’s Medical Center, Queens, NY.

**Background:** Tobacco exposure is associated with cardiovascular disease (CVD) risk and chronic kidney disease (CKD) progression. Risks of tobacco exposure in proteinuric glomerulopathies are not known. The objectives were to describe the prevalence of tobacco exposure and determine the longitudinal associations between tobacco exposure and CVD risk factors and kidney outcomes in adults and children with proteinuric glomerulopathies in NEPTUNE.

**Methods:** Tobacco exposure was self-reported at study enrollment as non-smoker, active smoker, past smoker and passive smoker. Baseline characteristics were compared by t-test, ANOVA and chi square. Using adjusted generalized estimating equations and time-varying Cox survival analysis, tobacco exposure was analyzed for association with blood pressure (BP), lipids, urine protein/creatinine ratio (UPCR), glomerular filtration rate (eGFR), complete remission (UPCR <0.3), kidney failure (eGFR <15 or Kidney Replacement Therapy [KRT]) and CKD progression (40% eGFR decline and eGFR <90, or KRT).

**Results:** Included were 371 adults (45.9±16.0 yrs; 60.6% M; 23.0% black, eGFR 66.4 [IQR 42, 91]) and 192 children (9.9±5.0 yrs; 57.3% M; 39.4% black, eGFR 93.1 [IQR 78.1,114]) with median 45 (IQR 27,55) months of follow up. Among adults, there were 14.6% active smokers, 29.1% past smokers and 4.9% passive smokers. In children, percentages were 0.5%, 1.6%, and 16.7%, respectively. In adults, there were significant differences in age, sex, race, and employment among groups. In children, non-smokers were significantly older than passive smokers (10.1±4.9 vs. 8.0±4.9, p≤0.01). Tobacco exposure was associated with greater total cholesterol in adults and UPCR in children in adjusted models (Table).

**Conclusions:** In NEPTUNE, tobacco exposure was associated with higher levels of cholesterol in adults and proteinuria in children.

**Funding:** NIDDK Support

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**Table: Association of Tobacco Exposure with Cardiovascular Risk Factors and Kidney Outcome in Adjusted Regression Models**

<table>
<thead>
<tr>
<th>Reference Population</th>
<th>Adult Active Smokers</th>
<th>p-value</th>
<th>Adult Passive Smokers</th>
<th>p-value</th>
<th>Pediatric Active Smokers</th>
<th>p-value</th>
<th>Pediatric Passive Smokers</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (%)</td>
<td>35.7 (95%)</td>
<td>0.89</td>
<td>35.4 (95%)</td>
<td>1.00</td>
<td>32.0 (95%)</td>
<td>0.49</td>
<td>29.0 (95%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>12.4 (95%)</td>
<td>0.20</td>
<td>12.6 (95%)</td>
<td>0.99</td>
<td>13.0 (95%)</td>
<td>0.53</td>
<td>13.0 (95%)</td>
<td>0.66</td>
</tr>
<tr>
<td>UPCR (%)</td>
<td>2.8 (2.0, 4.0)</td>
<td>0.48</td>
<td>2.8 (2.0, 4.0)</td>
<td>0.09</td>
<td>2.8 (2.0, 4.0)</td>
<td>0.03</td>
<td>2.8 (2.0, 4.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>HDL cholesterol (%)</td>
<td>43.7 (43.0, 44.4)</td>
<td>0.18</td>
<td>43.7 (43.0, 44.4)</td>
<td>0.18</td>
<td>43.7 (43.0, 44.4)</td>
<td>0.18</td>
<td>43.7 (43.0, 44.4)</td>
<td>0.18</td>
</tr>
<tr>
<td>Glucose (%)</td>
<td>8.4 (7.5, 9.4)</td>
<td>0.02</td>
<td>8.4 (7.5, 9.4)</td>
<td>0.02</td>
<td>8.4 (7.5, 9.4)</td>
<td>0.02</td>
<td>8.4 (7.5, 9.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Kidney failure (%)</td>
<td>4.7 (3.5, 5.9)</td>
<td>0.54</td>
<td>4.7 (3.5, 5.9)</td>
<td>0.54</td>
<td>4.7 (3.5, 5.9)</td>
<td>0.54</td>
<td>4.7 (3.5, 5.9)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

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**POI872**

**Validating a Computable Phenotype for Nephrotic Syndrome in Children and Adults Using PCORnet Data**

Andrea L. Olives1, Dorotha Marchel1, Cheryl L. Tran1, Isabella Ayoub2, Salem Almanani2, Jessica M. Greco1, Michelle Denburg3, Debbie S. Gipson1, Laura H. Marian1. 1University of Michigan Medical School, Ann Arbor, MI; 2The Ohio State University Wexner Medical Center, Columbus, OH; 3The Children’s Hospital of Philadelphia, Philadelphia, PA; 4Mayo Clinic Minnesota, Rochester, MN.

**Background:** Primary nephrotic syndromes (pNS) are rare diseases which can be a barrier to adequate sample size for observational patient-oriented research. A computable phenotype may be powerful in identifying patients with these diseases for research while leveraging data from millions of patients in the PCORNet Common Data Model (CDM).

**Methods:** A comprehensive algorithm of ICD-9 and ICD-10 codes indicative of pNS was developed based on prior work in the University of Michigan Health System. Cases of pNS were defined as subjects that were seen for at least one encounter with more than 1 NS code, and did not have codes for diabetes mellitus, systemic lupus erythematosus, or amyloidosis. Non-cases were individuals not meeting case criteria who were seen in the same calendar year and within 2 years of age of a case. The algorithm was executed on the PCORnet CDM at 3 institutions from Jan 1, 2009 to Jan 1, 2018, where a random selection of 50 cases and 50 non-cases were reviewed by a nephrologist, for a total of 150 cases and 150 non-cases reviewed. The classification accuracy (sensitivity, specificity, positive and negative predictive value, F1 score) of the computable phenotype was determined.

**Results:** The algorithm identified a total of 2,708 patients with NS from 4,305,092 distinct patients in the CDM at all sites. For all sites, the sensitivity, specificity, PPV, and NPV of the algorithm were 99.1%, 81.0%, 76.7%, and 99.3%, respectively. The accuracy of the algorithm was 88.0% with an F1 score of 86.5%. The most common cause of false positive classification was secondary FSGS (27%), followed by class V lupus nephritis (9.3%).

**Conclusions:** While prior computable phenotypes for glomerular diseases have used IMC and SNOMed codes, this computable phenotype had good classification in identifying both children and adults with pNS utilizing only ICD-9 and ICD-10 codes, which are universally available. This may facilitate future screening and enrollment for research, however further refinements to the algorithm or addition of natural language processing may help better distinguish primary and secondary FSGS.

**Funding:** NIDDK Support, Other U.S. Government Support

**2 x 2 Computable Phenotype Classification Table**

Data from all 3 health systems

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**POI873**

**Family History of Diabetes Is Associated with Progression of Kidney Disease: The CureGN and CRIC studies**

Francesca Zanoni, 1Miguel Verbistsky, 1Maddalena Marasà, 1Joshua D. Bundy, 2Afshin Parsa, 3Krzysztof Kiryluk, 1Harold I. Feldman, 3Ali G. Ghazikian, 1

1Columbia University Irving Medical Center, New York, NY; 2National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD; 3Tulane University, New Orleans, LA; 4University of Pennsylvania, Philadelphia, PA.

**Background:** Family history (FHx) of complex traits may reflect shared genetic/environmental risk. We studied associations of FHx with presentation patterns, comorbidities and renal disease progression in a prospective cohort of primary GN and one of non-GN chronic kidney disease(CKD).

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**

*Underline represents presenting author.*
Methods: The Cure Glomerulopathy Network (CureGN) is a prospective multi-center study of patients (N=2474, median age 29 years) with biopsy-proven GN. Associations of self-reported FHs of diabetes (DM), cancer (C), clotting disorders (CD), and autoimmune diseases (AD) with eGFR and comorbidities prevalence were studied with multivariable regression models. We investigated associations of FHs and end-stage renal disease (ESRD)/50%eGFR decline (ESRD/50%eGFR) with multivariate Cox models. The Chronic Renal Insufficiency Cohort (CRIC) Study, a multi-center prospective study of 3939 adult (median age 59 years) CKD patients, was used for replication.

Results: FHs of DM predicted lower eGFR at diagnosis (p=0.002) in CureGN. Figure 1 summarizes associations of FHs of complex traits with comorbidities in CureGN. FHs of DM was associated with higher odds of DM (OR 1.56, 95%CI 1.16-2.09, p=0.003) in the subgroup of CRIC with no DM at baseline. After adjustment for relevant covariates, FHs of DM was associated with higher risk of the composite outcome of ESRD/50%eGFR reduction in both CureGN (HR 1.43, 95%CI 1.06-1.94, p=0.02) and CRIC (HR 1.15, 95%CI 1.01-1.31, p=0.038).

Conclusions: FHs of complex traits are associated with specific comorbidities. FHs of DM identifies patients with lower eGFR and disease progression. In conclusion, FHs could be an additional parameter for risk stratification and management of CKD.

Funding: NIDDK Support

Figure 1: FHs and comorbidity prevalence in CureGN. CVD: cardiovascular disease.

PO1875
Fractional Excretion of Total Protein in Nephrotic Syndrome
Hideaki Kuno, Go Kanzaki, Takaya Sasaki, Yusuke Okabayashi, Kotaro Haruhara, Kentaro Koike, Nobuo Tsuibo, Takashi Yokoo. The jikei university school of medicine, Minato-ku, Japan.

Background: Lower estimated glomerular filtration rate (eGFR) and higher proteinuria are the most sensitive predictor of the development of progressive renal insufficiency in various glomerular diseases. Fractional excretion of total protein (FETP) calculated by dividing the total protein clearance by the creatinine clearance is tightly associated with both proteinuria and GFR. However, few studies have analyzed in glomerular diseases the FETP to evaluate their relationship with renal function and histologic lesions. This study aimed to evaluate the relationship between FETP and the clinical features and histologic lesions and to assess whether FETP predicts outcome in nephrotic syndrome (NS).

Methods: Subjects who exhibited NS with a histological diagnosis were retrospectively analyzed at the Jikei University School of Medicine Hospital, Tokyo, Japan, during biopsy performed between 2002 and 2018. We analyzed 24-h urinary protein excretion, FETP, and other clinicopathological findings at kidney biopsy. The FETP was determined by the standard clearance technique based on 24-h urine collection: FETP = (urinary total protein / serum total protein) / (urinary creatinine / serum creatinine) × 100.

Results: A total of 113 subjects with NS were identified (Age 53.7 ± 17.3 [mean ± SD] years old; Male 71.7%, eGFR 57.6 ± 27.7 mL/min/1.73m²; urinary protein excretion 7.02 ± 3.67 g/day; minimal change nephrotic syndrome [n = 41]; focal segmental glomerulosclerosis [n = 10]; membranous nephropathy [n = 36]; diabetic nephropathy [n = 26]; FETP was significantly associated with eGFR (p = 0.05), urinary protein excretion (p = 0.58, P < 0.01), interstitial fibrosis and tubular atrophy (p = 0.24, P < 0.05), and glomerulosclerosis (p = 0.24, P < 0.05). Interestingly, patients with diabetic nephropathy showed the highest level of FETP with the poor renal outcome, while membranous nephropathy revealed the lowest level of FETP.

Conclusions: These results suggest that FETP would be a useful marker combining the two predictors of the decline of renal function in NS showing increased glomerular protein permeability and decreased glomerular filtration function.

PO1876
Prediction of Morphological Lesions Using Various Glomerular Filtration Rate Equations in Patients with Primary Glomerulonephritis

Background: Glomerular filtration rate (GFR) is generally accepted best overall index of kidney function. However, it remains controversial to use GFR as a marker of morphological lesions. Aim. To assess GFR equations as a predictor of chronic morphological lesions in patients with glomerulonephritis (GN).

Methods: 100 patients [48 female, age Me 39 (27; 54) years] with biopsy proven primary GN were included in the study (9%− minimal change disease, 28%− focal segmental glomerulosclerosis, 26%− membranous nephropathy, 37%− IgA nephropathy). Serum creatinine was measured by enzymatic, serum cystatin C - immunoturbidimetric methods. GFR was estimated using creatinine clearance (Ccr), MDRD, CKD-EPICr, CKD-EPICysC, full age spectrum (FASsCr) equations. Glomerulosclerosis (GS) was assessed quantitatively, tubulo-interstitial fibrosis (TIF), tubular atrophy (TA) - semi-quantitatively (0-lesions absent; 1-mild focal lesions; 2-moderate lesions; 3-diffuse lesions). All patients were separated consistently in two groups according to the degree of each morphological lesion: "mild" (GS<25% or TIF/TA<1−), “severe” (GS≥25% or TIF/TA≥2−3).

Results: Independently of estimating equation, GFR positively correlated (p<0.001) with GS, TIF, TA and was higher in patients with "mild" GS, TIF and TA (p<0.001). Based on the results of ROC-analysis patients were separated (p=0.001) in two groups using all equations according to the degree of morphological lesions ("mild" or “severe” GS, TIF and TA). Using comparison of AUC we found the significant difference between Ccr and CKD-EPICr, CKD-EPICysC, CKD-EPICrCysC, between MDRD and CKD-EPICr, CKD-EPICysC equations in prediction of TIF, between CKD-EPICrCysC and FASsCr* in prediction of GS and no difference for all equations in prediction of TA (Fig 1).

Conclusions: Independently of estimating equation, GFR is a good marker of morphological lesions in patients with primary GN. Our data shows that CKD-EPI equations, especially CKD-EPICysC, provide the highest diagnostic value in prediction GS and TIF.

Funding: Government Support - Non-U.S.
**PO1877**

**Fluid Overload and Markers of Cardiovascular Damage in Severe Nephrotic Syndrome**

Aleksandra Rymarz, Anna Matyjeck, Stanislaw Niemczyk. **Military Institute of Medicine,** Warsaw, Poland, Warsaw, Poland.

**Background:** The purpose of the study was to evaluate the dimension of body water compartments and markers of cardiovascular damage in patients with severe nephrotic syndrome (SNS) defined as nephrotic range proteinuria and hypalbuminaemia ≤ 2.5 g/dl. Methods: 40 patients with SNS and eGFR >30 ml/min/1.73m² formed the study group (SNSG) and 40 healthy volunteers without SNS matched according to age, sex, height, body mass, kidney function formed the control group (CG). Body water compartments were assessed using Body Composition Monitor, Fresenius Medical Care. For statistical analysis Spearman’s correlation coefficients, chi² or Mann-Whitney U tests were used (Statistica v 13.1).

**Results:** SNSG included 28 males and 12 females, the mean daily proteinuria was 10.5±5.0 g. The groups are described in the table. In SNSG significantly higher fluid retention was associated with the increase in ECW and the decrease in ICW whereas TBW was the same in both groups. Such constellation can indicate intracellular dehydration which was not described so far. OH, which is a derivative of ECW, correlated with markers of cardiovascular damage and can be important for patients with resistant SNS and influence their prognosis.

**Clinical characteristic of the study groups**

<table>
<thead>
<tr>
<th></th>
<th>SNSG (n=40)</th>
<th>Control (n=40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.6±11.3</td>
<td>51.1±9.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171±7.2</td>
<td>173±8.1</td>
<td>0.038</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>26.7±3.4</td>
<td>25.7±3.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>137±2.7</td>
<td>138±2.7</td>
<td>0.006</td>
</tr>
<tr>
<td>Creatinine, µmol/l</td>
<td>117±27.3</td>
<td>67±15.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total proteinuria</td>
<td>10.5±5.0</td>
<td>1.2±0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protein/creatinine</td>
<td>27.2±7.8</td>
<td>11.6±5.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urine albumin/creatinine</td>
<td>7.7±4.4</td>
<td>0.7±0.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** In SNSG fluid retention was associated with the increase in ECW and the decrease in ICW whereas TBW was the same in both groups. Such constellation can indicate intracellular dehydration which was not described so far. OH, which is a derivative of ECW, correlated with markers of cardiovascular damage and can be important for patients with resistant SNS and influence their prognosis.

**PO1878**

**Glomerular Filtration Barrier Dysfunction in an RNA Virus-Induced Glomerulopathy: The Similarities with Findings of Common Nephrotic Syndromes**

Florian Källble, 1 Christoph Eckert, 1 Christian Morath, 1 Jochen Reiser, 1 Martin G. Zeier, 1 Ellen Krautkrämer, 1 Heidelberg University Hospital, Heidelberg, Germany; 2 Rush University Medical Center, Chicago, IL.

**Background:** Virally induced kidney dysfunction is highlighted by the alarming incidence of SARS-CoV-2 associated acute renal disease including nephrotic syndrome (NS). Plasma levels of soluble urinokase plasminogen activator receptor (suPAR) are elevated in COVID patients and provide prognostic insights. SuPAR is also involved in podocyte injury, kidney diseases such as focal segmental glomerulosclerosis (FSGS) in which podocytes effacement/injury is a common feature. Hantavirus-induced hemorrhagic fever with renal syndrome (HFRS) represents another RNA virus-induced disease with acute kidney injury and NS. The exact pathophysiology of proteinuria is, however, unclear. We hypothesized that hantavirus infection results in podocyte injury and a dysfuntional glomerular filtration barrier (GFB), similar to findings in common NS.

**Methods:** Renal biopsy specimens were analyzed by light and electron microscopy. Urinary neprin and suPAR concentrations were measured in 26 patients with HFRS and 18 healthy controls.

**Results:** Hantavirus patients showed significantly increased urinary neprin, immunoglobulin G (IgG), α1-microglobulin (α1-MG) and suPAR concentrations compared to healthy controls. Furthermore, neprin and IgG levels were significantly higher in patients with severe than with mild proteinuria. Differences in α1-MG levels, however, disappeared after normalization to urinary creatinine. Urinary neprin levels as a marker for podocyte damage correlated strongly with biomarkers of non-selective glomerular proteinuria. Interestingly, suPAR correlated significantly with urinary neprin, IgG and α1-MG levels, suggesting suPAR as a potential pathophysiological mediator in GFB dysfunction in response to RNA virus infection. The main finding in microscopy analyses was a focal foot process effacement. Proteinuria and kidney dysfunction recovered autonomously in all patients.

**Conclusion:** Hantavirus infection causes a podocyte injury leading to GFB dysfunction. A better understanding of transient virally induced proteinuria syndromes and their often self-limiting disease character may generate new therapeutic approaches for NS.

**PO1879**

**Nephrotic Syndrome from the Age of 65 Years: Epidemiological, Clinical, and Renal Biopsy Data**

Luanara R. Soares, Jose Mariano S. Pantoja, Lecticia Jorge, Viktoria Woronik, Cristiane B. Dias. **Universidade de Sao Paulo Hospital das Clinicas, Sao Paulo, Brazil.**

**Background:** This study aims to evaluate epidemiological, clinical, and renal biopsy data of patients aged 65 or over with nephrotic syndrome, admitted in a University Hospital.

**Methods:** Retrospective cohort study of renal biopsies performed from 2012 to 2017, considering the age 65 years or over, with diagnosis of nephrotic syndrome, under follow-up at the Nephrology Department of the Hospital das Clinicas of the University of Sao Paulo.

**Results:** In these period 103 renal biopsies were performed in patients aged 65 or over, 45 (43.68%) of them were indicated by the diagnosis of nephrotic syndrome. These 45 patients had mean age of 70.60±5.24 years old, 60% male, laboratory data at diagnosis were median serum creatinine of 2.02±1.53 mg/dl, hemoglobin of 11.34±4.11 g/dl, serum albumin of 2.23±0.83 g/dl and proteinuria of 6.9±4.64 g/day. Only minor complications of renal biopsy were observed and occurred in 6.6% of cases. The most frequent histological lesion was Membranous Nephropathy in 13 cases (28.88%), followed by Membranoproliferative Glomerulonephritis in 9 cases (20%), Focal Segmental Glomerulosclerosis (FSGS) in 8 (17.77%) highlighting that 4 patients had the Collapsing Form, Minimal Change Disease (MCD) occurred in 7 cases (15.55%) and the remaining 8 had others glomerular diseases. In Table 1 has the comparison between patients data according the glomerular disease. [Table]

**Funding:** Private Foundation Support

**PO1880**

**Clinical Characteristics, Treatment Patterns, and Outcomes of Children and Adults with Biopsy-Proven Minimal Change Disease from the Cure Glomerulonephropathy Network Study (CureGN)**

Dhruvit P. Chen, 1 Margaret Helmuth, 2 Rasheed A. Ghabadeseng, 3 Amy K. Mottil, 3 Debbie S. Gipson, 4 Katherine Twombley. 5 The Cure Glomerulonephropathy Network Study (CureGN) University of North Carolina, Chapel Hill, NC; 1 Research Collaborative for Health, Ann Arbor, MI; 2 Duke University Hospital, Durham, NC; 3 University of Michigan Mott Children’s Hospital, Ann Arbor, MI; 4 Medical University of South Carolina, Charleston, SC.

**Background:** The age of Minimal Change Disease (MCD) onset spans all ages. We analyzed the CureGN multi-center observational cohort study to elucidate differences in natural history and treatment patterns by age of MCD onset.

**Methods:** 567 participants enrolled within 5 years from kidney biopsy were available. Continuous variables were described as median [25,75 percentile] [IQR]. Univariate comparisons were performed using chi-square tests and Wilcoxon rank-sum tests for categorical and continuous variables, respectively. eGFR was winsorized to 120 or over, 45 (43.68%) of them were nephrotic syndrome, under follow-up at the Nephrology Department of the Hospital das Clinicas of the University of Sao Paulo.

**Results:** Comparisons of age group are shown in the table. There were modest differences in the racial/ethnic composition and weight. Severity of proteinuria was similar at disease onset [6.1 vs 6.5, p-value=0.5] but higher in adults at biopsy (6.6 vs. 3.4, p-value<0.001). At biopsy, eGFR was higher in children than adults (127.7 vs 88.6, p-value=0.001), and were more likely to have received immunosuppression prior to biopsy (58% vs. 18%, p-value<0.001). Compared to children, adults were more likely to report a history of HTN (29% vs 43%, p-value=0.001). Children were more likely to have frequently relapsing/steroid dependent disease than adults (51% vs. 29%, p-value<0.001) and higher steroid resistant disease than adults (17% vs. 12%, p-value<0.001). Over a median of 29.1 months follow up, ESKD occurred in 13 (2%) participants.

**Conclusion:** Significant sociodemographic and clinical differences exist between adult-onset versus pediatric onset MCD at the time of biopsy. These differences are most apparent in race/ethnic differences in renal and biopsy practices relative to symptom onset.

**Funding:** NIDDK Support
PO1881

Clinical Characteristics of Acute Glomerulonephritis with Presentation of Nephrotic Syndrome at Onset in Children

Huiping Ge, Qiongjing Yuan, Xiangcheng Xiao. Xiangya Hospital Central South University, Changsha, China.

Background: Acute glomerulonephritis (AGN) is a common disease in children, which placed a huge burden on developing countries. Prognosis of it may not always good. However, the clinical characteristics of AGN with nephrotic syndrome (NS) at onset has not fully clarified.

Methods: 113 cases were analyzed retrospectively. Clinical data, pathological results and prognosis between AGN with NS (AGN-NS) and AGN without NS (AGN-no-NS) were compared.

Results: 20 (17.7%) of 113 patients were AGN-NS. The patients with AGN-NS were more likely to have hypertension (55.0% vs. 25.8%) and acute kidney injury (AKI) (50% vs. 17.2%). The AKI was significantly related to the manifestation of AGN-NS in children (OR=3.812, P=0.040). Compared with the AGN-no-NS, the immunosuppressive treatments were more common in AGN-NS. A severer pathological grade was significantly related to the lower C3 fraction, estimated glomerular filtration rate (eGFR) and AKI, but not the performance of AGN-NS. There was no difference in prognosis between two groups.

Conclusions: The AKI was significantly associated with AGN-NS. The prognosis of AGN-NS and AGN-no-NS in our study was almost good. Given the fact that AGN-NS patients more likely to use the immunosuppressive therapy, the long-term outcome of AGN-NS is worth a further research.

PO1882

Estimation of Childhood Nephrotic Syndrome Incidence: Data from the Atlanta Metropolitan Statistical Area and Meta-Analysis of Worldwide Cases

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Background: There is limited epidemiological data on childhood idiopathic nephrotic syndrome (NS) in the United States. We estimated contemporary childhood NS incidence estimates in a racially and ethnically diverse U.S. population, and performed a meta-analysis of published reports to examine differences by race and ethnicity and changes over time.

Methods: Children 1-17 years-old diagnosed with NS in the Atlanta MSA between 1/1/2013 and 12/31/2018 were identified by chart review using practice data from the only pediatric nephrology practice in the region. Annual incidence rates were calculated by dividing the number of cases by population data provided by the Georgia Department of Public Health. We also performed a literature review for published childhood NS incidence and calculated pooled incidence estimates using random-effects regression models. Incidence estimates by race and ethnicity were compared by calculating pooled estimates within each subgroup and testing for significant heterogeneity between subgroup estimates. We also reviewed U.S. incidence over time comparing pooled incidence estimates before and after 1984.

Results: 175 children aged 1-17y were diagnosed with NS between 2013-2018 in the Atlanta MSA. Incidence by race and ethnicity from the Atlanta MSA and meta-analysis demonstrated highest incidence in Asian children, followed by those of African descent, Hispanics and Caucasians (Table 1). Incidence in the U.S. was stable over time.

Conclusions: Risk for childhood NS development differs by race and ethnicity without changes over time. Future studies need to evaluate the underlying genetic and environmental factors associated with NS incidence.

PO1883

Steroid Treatment for the First Episode of Childhood Nephrotic Syndrome

Comparison of the 8- and 12-Week Regimen Using an Individual Patient Data Meta-Analysis

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Background: Steroids are the cornerstone of the treatment of childhood nephrotic syndrome. The optimal duration for the first episode remains a matter of debate. The aim of this study is to determine whether the 8 weeks ISKDC regimen (prednisolone 4 weeks 60mg/m² daily, 4 weeks 40mg/m² on alternate days) is equally effective as the 12 weeks APN regimen (prednisolone 6 weeks 60mg/m² daily, 6 weeks 40mg/m² on alternate days).

Methods: An individual patient data (IPD) meta-analysis of randomized controlled trials reporting on prednisolone treatment for a first episode of childhood nephrotic syndrome was conducted. European trials investigating the ISKDC and/or APN steroid regimen were selected. Statistical models were adjusted for relevant covariates.

Results: Four trials included European patient cohorts treated according to the ISKDC and/or APN steroid regimen. IPD of two trials were available (PREDNOS, UK, 2019, n=109 and Nephrotic Syndrome trial, the Netherlands, 2013, n=62). Baseline characteristics did not significantly differ between the two treatment groups, with the exception of ethnicity. A significant difference was found in the time to first relapse after cessation of steroid treatment between the 8 and 12 weeks treatment group (p=0.04). The incidence of frequent relapsing nephrotic syndrome (FRNS) was similar in the two groups (p=0.75). Importantly, a significant difference was found in the incidence of steroid dependent nephrotic syndrome (44% [8 weeks] vs 24% [12 weeks], p=0.01). Overall, relapse rate ratios were 51% higher in the 8 weeks group compared to the 12 weeks group (p<0.01). Finally, children below 4 years of age seem to have a significantly lower survival time to first relapse and time to FRNS compared to children of 4 years and older (p=0.02 and p=0.003).

Conclusions: The results of this IPD meta-analysis suggest that the 8 weeks regimen for a first episode of nephrotic syndrome is not equally effective as the 12 weeks steroid regimen. Although high less steroids for the first episode would be the most effective method to reduce steroid toxicity in the short term, these results suggest patients treated with a 12 week steroid regimen may have a less complicated disease course.

Funding: Private Foundation Support

PO1884

Targeted B-Cell Depletion with Rituximab in Adult Relapsing Minimal Change Disease


Background: Case series suggest use of rituximab is effective in treating adults with relapsing Minimal Change Disease (MCD). We previously reported rituximab to increase time in remission, however, the majority of patients did have further relapses. We thus studied the efficacy of retreatment with rituximab on B cell repletion 2 years to prevent relapse.

Methods: Adult patients with recurrent MCD relapses were identified and treated with rituximab and monitored for lymphocyte depletion (total B-lymphocyte <10x) with pre-emptive re-dosing after reconstitution was observed.

Results: 16 patients (8 female, 8 male) started B cell targeted maintenance rituximab for 10 years. At start of the maintenance period, 14/16 were on immunosuppression, tacrolimus (7) steroids (3), or both (4), stopped at a mean of 6.4 months (range 2-16 months). 15/16 patients re-dosed after reconstitution was observed. 1/16 received 6 monthly rituximab, without waiting for lymphocyte reconstitution, due to a history of rapidly relapsing disease. 3/16 achieved lymphocyte depletion post rituximab. 3/16 relapsed during the 2 year treatment period, 1/3 was B cell deplete at relapse, 2/3 were B cell replete at relapse having been deplete on their previous blood test. As of May 2020, 10/16, have completed 2 years treatment, with a mean follow up post treatment of 6.6 months (range 1 to 13). Of these 3/10 have subsequently relapsed at mean time of
3.3 months (range 1-5), 2/3 were B cell replete at relapse. Rituximab was generally well tolerated, with no significant hypogammaglobulinemia or hospital admissions observed.

Conclusions: Targeting B cell depletion with rituximab is effective in maintaining remission of MCD. However, relapse can occur rapidly post repletion of lymphocytes, so frequent monitoring of lymphocyte subsets is required to ensure early retreatment upon relapse. An alternative strategy, maybe pre-emptive rituximab dosing at fixed intervals. Even after 2 years of maintenance therapy, B cell repletion is still associated with relapse. Further work is needed to compare maintenance strategies and to determine the optimal length of time of maintenance rituximab.

PO1885
Belimumab for the Treatment of Frequently Relapsing Nephrotic Syndrome: The BELNEPH Study

Background: A pathogenic role of B cells in pediatric idiopathic nephrotic syndrome (INS) has been suggested by the therapeutic efficacy of B-cell depletion, which however can impair immune memory. Belimumab treatment affects B-cell survival and differentiation but preserves the established immune memory. Its efficacy has been proven in other immune-mediated diseases, such as systemic lupus erythematosus and membranous nephropathy.

Methods: In this open-label, prospective, single-arm study, 5 children with frequently-relapsing INS who were on alternate-day prednisone only were enrolled. Belimumab was administered at 10 mg/kg i.v. on day 0, 14, 28 and then every 4 weeks for up to 12 months. Concomitant prednisone treatment was gradually tapered up to recommended dose levels. Safety, efficacy and laboratory blood and urine parameters were monitored for the duration of the study.

Results: Four patients completed the primary endpoint (6 months) and 2 patients completed the study. Infusions were well tolerated. One patient experienced a pulmonary infection which required hospitalization 2.3 months after the first infusion. Four patients experienced a first relapse within 6 months (1.9, 2.5, 2.6, 3.3 months after starting treatment) and 1 patient 8.1 months from first infusion. Three patients discontinued the study due to the frequency of relapses (a2) after 5.2, 9.2, 9.6 months, respectively, and were started on another steroid-sparing agent. The study was discontinued due to apparent lack of effect in 1 child. CDR19 B cells decreased during the follow-up, with a nadir at 6 months (8.6% of lymphocytes vs 19.1% at baseline, p<0.01). Naïve B cells started to significantly decrease after 1 month (7.7% vs 12.4% at baseline, p<0.05) and continued to decline during the follow-up. In contrast, no significant impact was observed on memory B cells, which became the most representative B-cell subset already at month 1 (43.5% of B cells vs 27.3% at baseline, p<0.01), with an initial shift toward a switched memory B cells, which became the most representative B-cell subset already at 1 month.

Conclusions: A reduction in B-cell count in healthy subjects. The objectives were to characterize safety, tolerability, PK profile, and safety in healthy subjects. GFB-887 exhibits dose-dependent reduction in urinary Rac1, with an initial shift toward a switched memory B cells, which became the most representative B-cell subset already at 1 month.

Funding: Private Foundation Support

PO1886
GFB-887, a TRPC5 Inhibitor, Is Safe and Well Tolerated and Engages the TRPC5-Rac1 pathway. The safety and efficacy of GFB-887 is summarized as Ratio of Means (ROM) between baseline and follow-up measurements, or change from baseline in healthy subjects.

Methods: This is a phase 1, double-blinded, randomized, placebo-controlled, study in healthy subjects. Subjects were randomized to either GFB-887 or placebo (8:2) in 5, 20, 40, 80,160, 320, and 900 mg SAC cohorts. Each subject received a single dose, had 24-hour urine collection pre and post-dose, and followed for 28 days post-dose.

Results: 70 healthy subjects (median age 43 years, 86% male, 56% Caucasians, 42% African Americans) were dosed with GFB-887. The most common adverse event (AE) was headache. All AEs were mild and non-serious. There were no clinically significant changes in ECGs, vital signs or laboratory results. Blood pressure was modestly and asymptotically reduced at the highest doses. Cmax and AUC of GFB-887 increased with higher doses in a less than dose proportionally manner through 900mg. Urinary Rac1 was significantly reduced from baseline with increasing doses of GFB-887.

Conclusions: The PK profiles of GFB-887 were well tolerated with a favorable PK profile in healthy subjects. GFB-887 exhibits dose-dependent reduction in urinary Rac1, a regulator of podocyte cytoskeleton structure and motility, indicating that GFB-887 engages and inhibits the TRPC5-Rac1 pathway. The safety and efficacy of GFB-887 is currently being evaluated in patients with FSGS, MCD, and DN (NCT04387448).

Funding: Commercial Support - Goldfinch Bio

PO1887
Phase 1 Study of N-Acetylmannosamine (ManNAc) for Glomerular Disease

Background: ManNAc is an uncharged monosaccharide and precursor of N-acetylgalactosaminic acid (NeuAc, sialic acid). It provides anionic charges to proteins, including those constituting the glomerular filtration barrier. Glomerular hyposialylation is common in nephrotic diseases and may contribute to podocyte foot process effacement and increased protein permeability. ManNAc showed benefit in nephrotic mouse models.

Methods: We performed a phase 1 study to evaluate the safety, tolerability, and pharmacokinetics of single and multiple doses of ManNAc in nephrotic subjects (NCT02639260). Seven subjects were enrolled, 6 with focal segmental glomerulosclerosis and 1 with membranous nephropathy. Urine protein/creatinine ratio was 1.3 to 9.9 g/l g.

Results: We evaluated the safety and efficacy of ManNAc in patients with focal segmental glomerulosclerosis (FSGS) and membranous nephropathy. All patients showed a reduction in proteinuria. Two patients (1 with FSGS and 1 with membranous nephropathy) had a ≥50% reduction in proteinuria. Two patients (1 with FSGS and 1 with membranous nephropathy) had a 24-48% reduction in proteinuria. There were no serious adverse events. The most common AEs were nausea, vomiting, and rash.

Conclusions: Oral ManNAc was safe and well tolerated in nephrotic disease subjects. ManNAc supplementation showed a trend towards proteinuria reduction, possibly linked to the degree of glomerular hyposialylation. A phase 2 study is planned to include assessment of longer-term pharmacokinetics, efficacy and safety.

Funding: NIDDK Support, Other NIH Support - NHGRI, Commercial Support - Escal Therapeutics

PO1888
Efficacy and Safety of ACE Inhibitor and ARB Therapies in Primary FSGS and Nephrotic Syndrome: A Systematic Review and Meta-Analysis
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Background: Use of ACEi and/or ARBs (RASi) as conservative management to control proteinuria in primary and genetic focal segmental glomerulosclerosis (FSGS) following guideline recommendations based on other proteinuria-related kidney diseases. There is lack of consensus about the efficacy and safety of RASi therapies in primary and genetic FSGS, thus this systematic review aims to assess the benefits and risks of RASi therapies on renal outcomes in these patients.

Methods: English-language studies were searched in MEDLINE, Embase and Cochrane Central Register of Controlled Trials, from inception to April 2019. Cohort studies assessing efficacy (response to treatment and indicators of renal function) and safety outcomes in primary and genetic FSGS were selected. Study results were summarized as Ratio of Means (ROM) between baseline and follow-up measurements, or as Hazard Ratio (HR) using random effects models.

Results: We selected 30 studies of which only 5 were controlled trials. Only 8 assessed RASi as monotherapy while the rest studied them in combination with other drugs, mainly immunosuppressants (IS). On average, a 32% reduction on proteinuria (ROM-0.68; 95% CI: 0.47-0.98) and no change on CrCl (ROM=0.95; 95% CI: 0.77-1.16) from baseline to variable follow-up periods was observed in patients treated with RASi therapy alone. A reduction of 72% in proteinuria was observed when RASi were combined with other drugs, mainly IS (ROM-0.24, 95% CI: 0.08-0.55). Published data did not allow to evaluate the eGFR ROM between follow-up and baseline and the

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Efficacy and Safety of Immunosuppressive Therapy in Primary FSGS: A Systematic Review and Meta-Analysis

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Background: Focal segmental glomerulosclerosis (FSGS) is a rare condition which can lead to decline in renal function and progression to ESRD. Immunosuppressants (IS) are often used to treat primary FSGS. However, their efficacy and safety is not clearly established. The aim of this work was to provide evidence on the current knowledge on the clinical effectiveness and safety of IS in the treatment of primary FSGS.

Methods: MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials were searched for English-language studies on primary FSGS from inception to 2019. Clinical outcomes of IS were changes from baseline to follow-up, proteinuria and renal function (eGFR or CrCl) and survival (ESRD, renal failure, doubling of creatinine, or author reported). When possible, study results were summarized using random effects models as Ratio of Means (ROM) between follow-up and baseline measurements as Hazard Ratio (HR).

Results: We included 100 articles. Substantial heterogeneity was observed in patient baseline characteristics and study design. Most studies assessed treatment with corticosteroids alone or combined with other drugs, mainly other IS. On average, patients treated with IS showed a reduction of proteinuria (14 studies, ROM=0.34, 95% CI 0.25-0.46). Pooled studies showed a lower CrCl at the end of the follow-up compared to baseline (ROM=0.77; 95% CI 0.71-0.83). In contrast, eGFR measurements suggested no change from baseline to follow-up (16 studies, ROM=0.92; 95% CI 0.84-1.01). IS treatment had an uncertain effect on reducing the risk of reaching ESRD (HR=0.79; 95% CI 0.45-1.39) and renal endpoint (HR=0.80; 95% CI 0.66-0.96) and moderately reported in <5 studies.

Conclusions: This systematic literature review supports that patients treated with IS have on average, a reduction in proteinuria between baseline and varying follow-up periods. Reported changes from baseline to follow-up in CrCl and eGFR are contrasting and effect of IS on renal survival is uncertain. However, due to lack of properly controlled studies, it is hard to attribute how much of these outcomes are due to IS treatment effect, stressing the low certainty evidence currently available in the literature and the need for better designed studies to reliably assess the effect of IS on primary FSGS patients.

Funding: Commercial Support - Retropin, Inc.

Cellular Senescence Is Associated with Faster Progression of Renal Disease in Adults with Focal Segmental Glomerulosclerosis: A 6-Year Prospective Cohort Study

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Background: Focal Segmental Glomerulosclerosis (FSGS) is a glomerular disease defined by pathognomonic histopathology but is caused by multiple mechanisms of disease, not all of which have been fully elucidated. Therefore, the reported renal prognosis, treatment strategies, and treatment response has varied significantly in previous small case series. We sought to analyze long term renal survival and associated risk factors in the largest cohort over the longest period of follow up described to date.

Methods: We performed a retrospective cohort study on all previous and current active duty military with biopsy proven FSGS. Potential cases were identified through a query of the military electronic medical record for International Classification of Diseases codes 9 and 10 codes (581.1, 582.1, and N04) and then confirmed by comprehensive chart review. Extensive data collection was performed and then analyzed using STATA 16.

Results: We identified 348 patients with biopsy proven FSGS with a mean follow up of 9.5 years. The majority were black, male, and under 40 years old. Progression to end stage kidney disease (ESKD) was 14%, 25%, and 35% at 5 years, 10 years, and 15 years after diagnosis, respectively. More patients with nephrotic range proteinuria progressed to ESKD (20%, 31%, and 49% at 5, 10, and 15 year follow up, respectively) than non-nephrotic range proteinuria (13%, 20%, and 31% at 5, 10, and 15 year follow up, respectively), and no significant proteinuria (6%, 14%, and 23% at 5, 10, and 15 year follow up, respectively) p=0.04. Overall progression to stage 3 chronic kidney disease (CKD3) was 32%, 40% and 50% at 5, 10, and 15 years after diagnosis, respectively. Full renography at initial treatment was associated with a substantial reduction in progression to ESKD (2%, 4%, and 7% at 5, 10, and 15 years follow up, respectively) compared to partial remission (12%, 21%, and 30%) and no remission (27%, 45%, 63%), p<0.001.

Conclusions: We present the largest cohort of biopsy proven FSGS cases over the longest follow up period to date. Approximately one third of all FSGS patients develop ESKD and one half developed CKD3 within 15 years. Proteinuria significantly increased the risk of progression to ESKD. Achieving a full or partial remission after initial treatment significantly decreased the risk of progression to ESKD.

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PO1893
Clinicopathologic Characterization of Focal and Segmental Glomerulosclerosis in a Dominican Republic Sample
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Background: There are limited recent epidemiological and clinicopathological behavior reports on FSGS in the Caribbean population. The aim is to identify clinical characteristic, epidemiological trend and treatment response of patients with diagnosed FSGS and their different variants in a Dominican Republic sample.

Methods: Cross-sectional study of performed transcutaneous native kidney biopsy taken in an interval date from years 2018-2019 of two separate nephrology consult from Dominican Republic. Diagnosed FSGS biopsy reports available and biochemical laboratories (creatinine, BUN, 24h Proteinuria, cholesterol, triglycerides, hematuria) within the date of biopsy were analyzed. Histopathological analysis of foot process effacement (FPE) degree reported and nephrotic syndrome (NS) presentation was correlated to primary or secondary cause of FSGS. Also, description of FSGS variants and response to the different treatments imposed in the time of data collection, overlapping comorbidities and serology were taken in notice.

Results: 49 biopsies were analyzed with FSGS. NS variant was the most common (72%), tip lesion (6%) and collapsing (6%), with no reported perihilar or cellular variants and (4%) reported as unsampled biopsy of FSGS. Biopsy with diffuse FPE (>90%) 24 presented with nephrotic syndrome and 8 did not (p=0.01). Remission in biopsy with described diffuse foot process effacement (DFPE) with unidentified cause 32% had complete remission (CR) (serum albumin >3.5g/dl or <300 mg/24h protein), 16% had partial CR (serum albumin =3.5 to <4.5g/dl) and 52% did not remitted at 6 months period (p=0.92). Steroids and calcineurin inhibitors treatment were significantly associated with CR in FSGS with DFPE with unidentified cause (p=0.029, p=0.014 respectively).

Conclusions: Biopsies analyzed in a 2 year period presented NOS as the most common variant while perihilar or cellular variants were not reported. In the sample studied the degree of FPE was associated to NS presentation. The use of steroids and calcineurin inhibitors in suitable patients is significantly associated with remission of disease. The FPE degree, clinical manifestations of patients and history represent the best tools for correct diagnose and treatment.

PO1894
Differentialiating Focal and Segmental Glomerulosclerosis
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Background: FSGS is a histological pattern of kidney injury associated to broad causes and pathogenesis. FSGS can be primary, genetic or secondary to other conditions. Differentiating these subclasses is crucial for management and prognosis, but there is no general consensus, since the diagnosis is not always straightforward. This study aimed to identify FSGS histological diagnosis and clinical and histological criteria comparing outcomes.

Methods: In a retrospective analysis of 359 kidney biopsies we identified patients with diagnosis of FSGS histological diagnosis and secondary FSGS were identified based on clinical and histological data. Genetic FSGS was considered if they present at least one of the following: a nephrotic syndrome (NS) resistant to corticosteroids;b)NS with normal albuminuria;c)NS with focal foot process effacement or diffuse-nephrotic proteinuria with diffuse foot process effacement. Each group was divided in immunosuppression treatment (IST) or only supportive treatment (ST) groups. Renal and survival outcomes were assessed.

Results: Among 66 FSGS patients, 65% were males, 71% non-black, 74% had HTN, 26% diabetes; median eGFR 26.5mL/min/1.73m2 (IQG 15.3-48.8), 24h-UProtein 4.4g (IQG 2.5-7.6). Globally, 38% (n=25) progressed to ESKD and mean time to RRT was longer in IST group (p=0.37). According to the applied criteria 52% (n=34) were classified as having secondary FSGS, 23% (n=15) primary and 25% (n=17) as genetic FSGS. Among primary FSGS patients 40% received IST. In ST group 25% progressed to ESKD in a median time to RRT of 24 months (SD±21.7) vs 13% in 66mo (SD±33.3) in IST group. Among secondary FSGS, 17.6% received IST. Of them, 50% developed ESKD in 31.7mo (IQQ SD±28.6) vs ST group with 46% progression to ESKD in 12mo (SD±28.7). From the genetic group 59% were in IST group and 30% progressed to ESKD in 12mo (SD±27.1) vs ST group with 29% ESKD in 42mo (SD±27.1).

Conclusions: FSGS etiology is not straightforward in most patients. Since IST can be inappropriate and potentially harmful in some FSGS subclasses, it is crucial to identify patients with these conditions to the different treatments imposed in the time of data collection, overlapping comorbidities and serology were taken in notice.

Results: Among 66 FSGS patients, 65% were males, 71% non-black, 74% had HTN, 26% diabetes; median eGFR 26.5mL/min/1.73m2 (IQG 15.3-48.8), 24h-UProtein 4.4g (IQG 2.5-7.6). Globally, 38% (n=25) progressed to ESKD and mean time to RRT was longer in IST group (p=0.37). According to the applied criteria 52% (n=34) were classified as having secondary FSGS, 23% (n=15) primary and 25% (n=17) as genetic FSGS. Among primary FSGS patients 40% received IST. In ST group 25% progressed to ESKD in a median time to RRT of 24 months (SD±21.7) vs 13% in 66mo (SD±33.3) in IST group. Among secondary FSGS, 17.6% received IST. Of them, 50% developed ESKD in 31.7mo (IQQ SD±28.6) vs ST group with 46% progression to ESKD in 12mo (SD±28.7). From the genetic group 59% were in IST group and 30% progressed to ESKD in 12mo (SD±27.1) vs ST group with 29% ESKD in 42mo (SD±27.1).

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PO1897
The Dual Endothelin/Angiotensin II Receptor (ET, R/AT, R) Antagonist Sarspantien Slows Renal Disease, Improves Lifespan, and Attenuates Hearing Loss in Alport Mice: Comparison with Losartan and Atrasentan

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Background: In Alport syndrome (AS), ET, R activation is important in renal and inner ear pathologies. Previously, sparsentan (SP) was shown to prevent increases in proteinuria, glomerulosclerosis, and glomerular basement membrane dysmorphology in AS mice. Here we compare the effect of SP, the AT R antagonist losartan (LS), and the ET R antagonist atrasentan (ATR) on lifespan and proteinuria, and of SP and LS on hearing loss and inner ear pathology.

Methods: Wild type (WT) and AS mice were gavaged daily with vehicle (V), 60 or 120 mg/kg of SP (SP60, SP120), LS (20 mg/kg; 3-4 W) or LS (10 mg/kg from 4 W), or ATR (7.5 mg/kg females or 10 mg/kg males) in the drinking water. Two studies were conducted: early intervention for hearing from 3-8.75 W (V, SP120 and LS), and for lifespan with treatment from 3 W (V or 4 W, SP60, SP120, LS or ATR). Urinary protein/creatinine ratio (UP/C) was assessed weekly. The auditory brainstem response (ABR) was used to assess hearing ability and sensitivity to noise at 8.75-7.5 W. The cochleae were preserved and strial pathology determined by transmission electron microscopy.

Results: SP120 significantly (P<0.05) increased median lifespan compared to any other group (Figure 1). At 8 W, only SP120 significantly (P<0.05) attenuated the increase in UP/C compared to V (UP/C:mg/ml mean±SD: 47±16 V; 12±18 ATR; 42±18 ATAR; 51±16 SP60; 20±32 SP120). UP/C at 11 W in SP120 mice was significantly attenuated (P<0.05) vs. LS mice. SP120 significantly improved post-noise ABR thresholds at 16 kHz vs. V mice (P<0.05). LS had no effect. Dysmorphology of the stria vascularis was noted in LS treated mice, but not in SP120 mice.

Conclusions: SP120 in AS mice extended lifespan beyond that of mice treated with SP60, LS, or ATR and attenuated noise-induced hearing loss compared to LS. Sarspantien may therefore offer a novel, dual-therapeutic approach in AS by reducing both renal injury and hearing loss.

Funding: Commercial Support - Retrophin, Inc.

PO1898
Long-Term Outcomes of Tacrolimus Treatment for Idiopathic Membranous Nephropathy

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Background: Tacrolimus (TAC) is effective for the treatment of membranous nephropathy (MN). Methods: Retrospective study of longterm outcomes of 111 patients (pts) with MN treated with TAC from January 2000 to June 2018. Results: Demographics/table 1. Treatment: 91/111 TAC monotherapy, 20/111 dual therapy with mycophenolate + TAC. All pretreated with ACEi/ARB. Median follow up (FU) 68 months (IQR 33-115). 93/111 pts (84%) reached Partial Remission (pCR) reduction by 50% and <300mg/mmol at 5.1 months (median, IQR 2-11), 76/111 (69%) also reached Complete Remission (cPCR). 3/111 pts (6%) had proteinuria, 3/111 pts (6%) had no proteinuria, 1/111 pts (1%) had a rapid reduction of immunosuppression. 28/48 were retreated with TAC and all achieved remission, 15/84 treated with RTX, remission in 11/15. 3/84 treated with TAC and steroids. Only 4 achieved remission, all in the RTX group. 2 lost to FU. 48/83 (51%) of pts that achieved remission relapsed after 22 months (14-34) (Figure 1) following withdrawal of TAC. cPCR rate (37 patients) had urinary protein excretion less than 3.5 grams per day, and one (3%) had no proteinuria. To evaluate renal biopsy specimens, light microscopy was performed in all cases, fluorescence microscopy in 36 cases and electron microscopy (EM) in 28 cases. 14 patients (38%) were diagnosed with primary MN, 22 patients (59%) with secondary MN, and one patient (3%) with de novo MN post-transplantation. Secondary MN were due to lupus erythematosus (27%), mixed connective tissue disease (14%), Sjögren’s syndrome (3%), hepatitis B (11%), b-cellulitis use (3%), and grafted versus host disease (GHVD) after peripheral blood stem cell transplantation (3%). Mean and median follow-up period was 14.9 and 12.0 years, respectively. At the end of follow-up, only two patients out of the 37 patients reached end-stage renal disease, and 33 patients (89%) observed serum creatinine level lower than 1.5 mg/dL. 21 patients achieved complete remission (CR). Among 27 cases who underwent EM, cases with subendothelial deposits had smaller CR rate (3/11 cases) than those without subendothelial deposits (12/16 cases), which was statistically significant (χ²=6.01, p=0.014). The CR rates of cases with mesangial deposits (12/21 cases) and those without mesangial deposits (3/6) was not significantly different (χ²=0.096, p=0.76).

Conclusions: The diagnosis of renal function was fairly good in patients with MN in the age under 50 years old. Cases with coexisting subendothelial deposits showed lower CR rate than the rest.

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PO1900
A Target Antibody-Based Approach to the Classification of Membranous Nephropathy

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Background: Primary membranous nephropathy (MN) is caused by circulating auto-antibodies against podocyte surface antigens, identified as M-type-phospholipase–A2-receptor (PLA2R) in 70-80% and thrombospondin-type-1-domain-containing-7A (THSD7A) in 2-5% of patients. Secondary MN occurs in the context of malignancy, autoimmune disease, infection, paraproteinemia or medication. Some patients with PLA2R-associated MN have a current or previously diagnosed associated condition, but it remains statistically significant (χ²=6.01, p=0.014). A few THSD7A-associated MN cases have a strong etiologic link with active malignancy, while in others malignancy appears coincidental. Exostosin 1/exostosin 2 (EXT1/EXT2) are recently discovered target antigens in patients with MN, the majority of whom have autoimmune disease. These recent findings blur the traditional distinction between primary and secondary-containing MN.

Methods: To describe the phenotypes of PLA2R-, THSD7A- and EXT1/EXT2-associated MN, 201 adult patients with biopsy-proven MN were classified using serology, immunostaining and mass spectrometry. Clinical, biochemical and follow-up data were examined for associated disease and its relationship with MN.

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Results: PL-2R-associated MN (n=161) occurred predominantly in middle-aged women, with a peak at 40-50 years. Only 1 case of PL-2R-associated MN was identified, with a concomitant malignancy. EX1/EX2-associated MN (n=8) was identified in younger females and was strongly linked with active autoimmunity. The majority of patients who were negative for all three target antigens (n=70) presented with associated disease, mainly malignancy and autoimmunity.

Conclusions: In conclusion, the historical primary-secondary dichotomy has substantial limitations when applied to MN. We propose a terminology combining the target antigen involved in pathogenesis and the associated clinical diseases in order to classify MN and guide clinical decision making.

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PO1902
Non-invasive Diagnosis of Primary Membranous Nephropathy Using Anti-PLA2R A2 Receptor (PLA2R) Antibodies: A Validation Study
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Background: Kidney biopsy is the current gold standard to diagnose membranous nephropathy (MN). Approximately 70-80% of patients with primary MN have circulating anti-PLA2R antibodies, which could provide an alternative diagnostic test to kidney biopsy. We performed a multi-center validation study of two ELISA tests to establish its value as a diagnostic test in MN.

Methods: We retrospectively analyzed 1112 unique Mayo Clinic patients with positive serum anti-PLA2R antibody tests by both ELISA and IFA between July 2018 and April 2020. The test results were compared with the histopathological diagnosis of MN.

Results: A total of 1522 anti-PLA2R antibody tests were ordered in 1112 unique patients, yielding 128 positive results. We excluded previously reported patients (n=33), renal transplant recipients (n=5), no biopsy available (n=18), and pediatric cases (n=2). In all 70 remaining patients, the primary biopsy diagnosis was MN. Associated disease was identified in 28 cases (autoimmunity = 10, malignancy = 6, NSAID = 4, Hepatitis = 3, and unknown = 9). A total of 28 patients were classified into the anti-PLA2R antibody positive group by both ELISA and IFA.

Conclusions: We established that anti-PLA2R antibodies are predictive of membranous nephropathy (MN) and may be used as a non-invasive alternative to kidney biopsy.

PO1903
Concurrent Anti-Glomerular Basement Membrane Nephritis and Membranous Nephropathy
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Background: Anti-GBM nephritis is an uncommon entity with a rapidly progressive course. The concurrent occurrence of anti-GBM nephritis with membranous nephropathy (MN) is rare and poorly understood. We report a single center case series of this dual glomerulopathy with emphasis on presenting features, course, and outcome.

Methods: A total of 12 cases of combined anti-GBM nephritis and MN were identified from the archives of the Columbia Renal Pathology Laboratory over the past 18 years. Presenting clinical, histopathologic and laboratory data with follow up were obtained by chart review.

Results: The cohort of 12 cases included 7 men and 5 women with age range 18-81 years. The most common presenting feature was AKI (mean creatinine 9.3 mg/dl), with one patient having pulmonary symptoms. Positive anti-GBM serology was available at presentation for 11 cases, 5 with titters >100 AU/mL, and all were ANCA negative. Of those tested the majority were PL-2R negative. Patients were predominantly Caucasian (N = 9). All patients required hemodialysis (HD) at presentation, and two patients, a 19-year-old woman and an 81-year-old woman had renal recovery with the later having a stable creatinine of 2.0 mg/dl 11 months later. Treatment regimens included the following: cyclophosphamide, plasmapheresis, and prednisone (N=9); cyclophosphamide and granulocyte colony stimulating factor (N=2) and corticosteroids alone (N=1). The mean follow up time was 36 months after presentation from sepsis. Analysis of the 12 renal biopsies showed combined linear and granular staining of GBMs for IgG, with crescents involving 23-100% of glomeruli, and fibrinoid necrosis involving 15-100%. The two patients who recovered renal function had total crescents (82% crescents, and 23%, respectively) and less fibrinoid necrosis (15% and 31%) compared to the subgroup without recovery respectively, on kidney biopsy.

Conclusions: Combined anti-GBM and MN is a rare entity presenting with severe AKI and HD. Renal recovery is uncommon. High percentage of crescents are consistent with poor outcomes. Treatment and course are dominated by anti-GBM nephritis. The MN component is predominantly PL-2R negative, and further studies into pathogenesis are needed.

PO1904
Recurrent Membranous Post Transplantation: Histopathology, Treatment, and Outcomes
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Background: Membranous nephropathy(MN) recurs in 30-45% of transplants. Reported recurrence rates are higher in centres that perform surveillance biopsies. Optimal treatment is unknown. We examined recurrent MN in our cohort in terms of their histopathology, treatment and outcomes.

Methods: Patients with MN as the cause of their ESRF who were later transplanted were identified from an in-house database. Further data was collected from the electronic health record.

Results: 36 patients with a diagnosis of MN were transplanted. Mean follow up was 6.4 ± 4.2 years. 41.6% had a rejection episode (mean time from transplant 0.42 ± 0.15 years). Overall there was 22% graft loss (mean time 6.5 ± 3.7 years), 11% deaths (8.6 ± 2.3 years from transplant) and 6% deaths with functioning grafts (mean time 6.9 ± 2.3 years). Mean eGFR at 3 months and 1 year were 48.1 ± 18.5 and 48.1±14.5 ml/min. 30/36 patients had at least one biopsy following transplantation. Of those whose biopsies did not show recurrence, the mean time to the most recent biopsy was 2.9 ± 2.7 years (range 0.02-9.3) 8/36 patients (22%) had recurrent MN, 7 detected on indication biopsy and 1 on surveillance biopsy. The mean time to recurrence was 1.9 ± 1.1 years (range 0.09-4.46 years). Granular C4d staining of the capillary wall was detected in 6/8 biopsies prompting immunofluorescence and electron microscopy, leading to the diagnosis of recurrent MN. Histological anti-PLA2R staining was positive in 3/8 biopsies. 2/8 patients had donor specific antibodies. In the 4 patients with clinically significant proteinuria rituximab was used to treat with a complete or partial response in all patients (mean time 22.5±16 months (range 4-43.8 months). There are no significant differences in rejection, graft loss, death or death with functioning graft between those with recurrence and those without recurrence in our cohort.

Conclusions: Recurrent MN was frequent but not associated with increased alloagraft failure in our programme, with the use of rituximab in selected cases. Granular C4d in the glomeruli in transplant patients with MN could prompt further investigation with immunofluorescence and electron microscopy to look for recurrent disease.
Secondary Polycythemia Associated with Membranous Nephropathy
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Introduction: Polycythemia has been recognized as a common occurrence in certain renal diseases such as cystic diseases of the kidney, renal cancer, tuberous sclerosis and hydropnephrosis. However, polycythemia in association with membranous nephropathy has rarely been reported. Here we report a case of secondary polycythemia from membranous nephropathy. Although the mechanism of this phenomenon is unclear, decreased effective circulating volume leading to hypoxemia and thereby polycythemia seems to be the most likely explanation.

Case Description: 37-year old white male with Hypertension, OSA using CPAP, tobacco use was admitted with 40-lb weight gain and anasarca. 24-hour urine collection revealed 17-gram protein excretion with serum albumin of 1.1 and marked hyperlipidemia. Kidney biopsy revealed membranous nephropathy. Staining for PLA2R and THSD7a were negative within the glomerular deposits. Evaluation for secondary causes of membranous nephropathy was negative for ANA, RPR/ rhythm antibodies, Hepatitis, HIV, ANCA, Anti-GBM Ab and normal C3,C4 levels. CT of thorax was negative for overt malignancy or hepatoplenomegaly. Patient’s hemoglobin ranged between 16.5 – 18.5 g/dl (hct 52-60%). Serum erythropoietin level was 12.3 IU/L (Normal 5-30 IU/L) with corresponding hemoglobin of 18.2 g/dl. JAK2 exon12, V617F mutations were negative. Hematology evaluation concluded that primary polycythemia is unlikely. Patient received 2 doses of 1 Gm Rituximab given 4 weeks apart. Patient was placed on Apixaban for prophylactic anticoagulation. Follow up labs to evaluate response to therapy are currently pending. It is yet to be seen if polycythemia resolves with remission of membranous nephropathy.

Discussion: Polycythemia is seldom seen in patients with membranous nephropathy. We postulated that hypoxia induced by decreased renal perfusion is the main trigger for polycythemia. However, it is puzzling as to why more patients with membranous nephropathy are not polycythemic. This leads us to believe that there might be some unique processes leading to polycythemia in membranous nephropathy, as in this patient, which probably contribute to these polycythemic patients. Certainly, further enhancements to this research need to be considered in these patients.

Membranous Nephropathy Preceding the Recurrence of Thymoma
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Introduction: Membranous nephropathy secondary to neoplastic processes is a recognized phenomenon, and it may be the first finding that leads to the diagnosis of the underlying malignancy. Here we describe a case of secondary MN in a patient with a history of recurrent thymoma that led to a prompt evaluation for malignancy, which did not appear on PET imaging until a few months later.

Case Description: We describe the case of a 62 year old man with myasthenia gravis (on IVIG), history of thymoma with recurrence in 2017 and March 2019 requiring multiple surgeries and adjuvant chemoradiation. There was no evidence of disease in 2018. In November 2019, he presented with worsening anasarca and a myasthenic flare, for which he was treated with steroids, Rituximab and plasma exchange. A kidney biopsy was performed and consistent with recurrent thymoma. He was then referred to Metabolic Stone Center. In February 2020, he presented with marked oedema and heavy proteinuria a kidney biopsy was performed for the possibility of membranous nephropathy. Kidney biopsy revealed a mixed membranous and membranoproliferative glomerulopathy. Investigations: creatinine 44umol/L (55-110), albumin 7g/L (35-50), urine PCR 1456mg/mmol (Normal <50mg/mmol), renal biopsy demonstrated MCD. He was treated with steroids. In order to search for possible secondary causes of membranous nephropathy, this case presentation suggests that hypoxemia and immunosuppression may be the optimal imaging for undiagnosed malignancy or recurrent malignancy in this setting.

Discussion: There have only been 4 previous reports of de novo MCD in pregnancy all of whom were treated with steroids. In our patient who presented early in pregnancy with marked oedema and heavy proteinuria a kidney biopsy was performed. Kidney biopsy should be performed when the benefit of obtaining a diagnosis outweighs the risks of the procedure. In pregnancy the risks are increased (7% versus 1% outside pregnancy). Polycythemia during the 1st trimester is safest. Corticosteroids are often used to treat MCD outside pregnancy. Prednisone is safe in pregnancy as the fetal dose is minimal. However, there were maternal complications including gestational diabetes and weight gain. The recent MinTac trial of prednisone and tacrolimus in patients with MCD found no difference in remission rates at 8, 16 or 26 weeks and no difference in relapse rates. We achieved partial remission in this heavily nephrotic patient with use of tacrolimus alone and rituximab. Anticoagulation, which was started in the first trimester, was maintained on rivaroxaban which was compatible with the GI bleed. We believe tacrolimus is a valuable option for treatment of MCD in pregnancy.

A New Approach to De Novo Minimal Change Disease in Pregnancy
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Introduction: Although proteinuria in pregnancy is common and usually due to preeclampsia, nephrotic range proteinuria especially in early pregnancy, warrants investigation and treatment. We present the first case of minimal change disease (MCD) presenting in pregnancy, treated successfully with tacrolimus.

Case Description: A previously well 20 year old G1P0, presented at 9 weeks gestation with 3 weeks of oedema and shortness of breath. Examination revealed marked oedema. Investigations: creatinine 44umol/L (55-110), albumin 1g/L (35-50), urine PCR 1456mg/mmol (Normal <50mg/mmol). A PET scan confirmed a via renal malignancy. A renal biopsy was performed which demonstrated MCD. She was started on tacrolimus in addition to enoxaparin, furosemide and aspirin. At 12 weeks she had melena with a haematoglobin drop. There was no active bleeding on endoscopy and she had no further episodes in pregnancy. She was managed by serial transfusions and joint renal-obstetric management. The patient subsequently delivered a healthy baby, which was born at term. She was then maintained on tacrolimus alone (levels 5-8ug/L). Her albumin rose and PCR fell throughout pregnancy. By 34 weeks her albumin was 28g/L and uPCR was 128 mg/mmol. Fetal growth was normal on serial growth scans. She did not develop preeclampsia. Labour was induced at 39 weeks and she had a normal vaginal delivery of a 3194g healthy baby.

Discussion: There have only been 4 previous reports of de novo MCD in pregnancy all of whom were treated with steroids. In our patient who presented early in pregnancy with marked oedema and heavy proteinuria a kidney biopsy was performed. Kidney biopsy should be performed when the benefit of obtaining a diagnosis outweighs the risks of the procedure. In pregnancy the risks are increased (7% versus 1% outside pregnancy). Polycythemia is seldom seen in patients with membranous nephropathy. Although the mechanism of this phenomenon is unclear, decreased effective circulating volume leading to hypoxemia and thereby polycythemia seems to be the most likely explanation.

Prevention of TP-Induced Nephrotic Syndrome (NS) in Pregnancy
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Introduction: Cystinuria, a rare inherited metabolic disorder characterized by defective proximal tubule cysteine transport, manifests predominantly in childhood or young adulthood with renal colic and recurrent nephrolithiasis, often requiring urologic intervention. Insoluble cystine in the urine precipitates into hexagonal crystals that can coalesce into larger, recurrent calculi, with associated higher risk of chronic kidney disease. Prevention of stone formation is the primary goal, using conservative non-pharmacologic approaches and if unsuccessful then pharmacologic. Since its approval in 1986, thiazide (TP), a thiol compound that forms a soluble mixed disulfide, has been used to increase urine cystine solubility. Adverse effects of TP include hypokalemia, cutaneous and mucosal. Reports of TP-induced nephrotic syndrome (NS) are rare, especially due to minimal change disease (MCD).

Case Description: A 19-year-old male with cystinuria and bilateral nephrolithiasis requiring extensive urologic interventions was on TP 300 mg bid for 6 months, when he presented to the Emergency Department with foamy urine, decreased urine output and anasarca. Labs showed elevated urine protein/creatinine ratio 9.2 (uPCR), low serum albumin 1.6 mg/dl and elevated cholesterol. ANA, ANCA, anti-GBM, HBV, HCV, HIV, C3, C4, and cryoglobulins were negative. Renal biopsy demonstrated MCD. He was not treated with steroids. TP was discontinued and uPCR 2 months later was 0.21 and albumin 2.3, with complete resolution of symptoms. He was referred to Metabolic Stone Center to discuss alternative treatment options.

Discussion: Only 31 cases of TP-induced NS have been reported to date, the majority membranous glomerulonephritis (GN), fewer cases of mesangiproliferative or membranoproliferative GN and only two cases of MCD. Although the exact mechanism is unclear, TP is speculated to play an antigenic role interfering with podocyte function. TP induced NS is not necessarily dose-dependent, with no relationship between mean daily dose and prevalence. The highest prevalence occurs in the first six months and is self-limiting. However, treatment with TP should be limited upon cessation of TP, without need for immunosuppressives. Clinicians should be aware of the rare but severe occurrence of NS due to TP. A weekly dipstick for protein may help in early detection.

Recent Nephrotic Syndrome in Podocyte Infolding Glomerulopathy: Remission with Rituximab
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Introduction: Podocyte infolding glomerulopathy (PIG) is a recently recognized entity. The seminal paper showed that it is associated with autoimmune disorders and is often responsive to corticosteroids (CS). We present a case of PIG with recurrent nephrotic syndrome (NS) who is maintaining remission on Rituximab off of CS.
Case Description: A 61-year-old woman with type II diabetes mellitus, inflammatory bowel disease (IBD), and uveitis presented in 2009 with proteinuria. Kidney biopsy was read as focal segmental glomerulosclerosis (FSGS). She was treated with angiotensin converting enzyme inhibitor (ACE-I) and prednisone, and proteinuria remitted. In 2012, an increase in proteinuria prompted repeat biopsy resulting in a diagnosis of membranous glomerulonephritis. Anti-PLA2R was negative. ACE-I and prednisone were continued and proteinuria remitted. In 2014, she developed nephrotic syndrome (NS). Repeat biopsy was read as showing FSGS. Prednisone 1 mg/kg/day induced remission. When prednisone was tapered, NS flared. She did not remit with high dose prednisone and at 8 weeks developed acute kidney injury (AKI). Tacrolimus was added and proteinuria and creatinine (Cr) improved. Steroids were tapered over several months. On Humira for IBD and tacrolimus (level 11 µg/dL), NS and AKI flared 1 year later with urine protein:creatinine (UP/C) of 2 and Cr 2.1 mg/dL. Prednisone was restarted. Intravenous cyclophosphamide was started, steroids were tapered, and Humira was discontinued. Within 5 weeks, proteinuria worsened (UP/C 29) and cr rose to 4 mg/dL. Renal biopsy demonstrated foot process invagination yielding a diagnosis of PIG. At trial of cyclosporine was stopped at 1 week due to drug intolerance. Mycophenolate mofetil (MMF) in combination with prednisone and tacrolimus was started. MMF caused severe diarrhea. In September of 2019, 4 weekly treatments of rituximab were administered. Proteinuria remitted and creatinine improved to 1 mg/dL. She remains in remission off of steroids and on lower dose tacrolimus now for 11 months.

Discussion: This case is the first to describe the effectiveness of Rituxan as rescue and maintenance therapy following failure of other IS regimens in a patient with recurrent NS due to PIG. Rituxan should be considered in refractory cases of PIG to induce and maintain remission and allow for steroid sparing.

PO1910 Glomerular Tip Lesion FSGS: A Rare Case of Nephrotic Syndrome in African Americans

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Introduction: Nephrotic syndrome caused by focal segmental glomerular sclerosis (FSGS) in African Americans is known to have a poor prognosis and frequent treatment failure. Tip variant FSGS connotes good prognosis, usually responsive to calcineurin inhibitor (CNI) and steroid. We present a case of CNI resistant tip lesion FSGS requiring plasma exchange (PLEX) and rituximab.

Case Description: A 25-year-old African-American male, initially presenting to our outpatient clinic for edema associated with proteinuria. He had a past medical history of seizure disorder controlled with zonisamide. He trialed hydrochlorothiazide and furosemide without success. His urine showed nephrotic range proteinuria with 6g/g creatinine on spot urine. Outpatient workup was unremarkable, and was managed with enalapril and torsemide. He eventually had worsening edema and shortness of breath, prompting ED visit. Biopsy was performed which showed FSGS, tip variant. He was discharged on cyclosporine and increased diuretics. Cyclosporine caused gastrointestinal upset, and so patient switched to tacrolimus. He again had increasing swelling, and was admitted to hospital. He was found to have acute kidney injury, and 10g/g creatinine despite therapeutic tacrolimus levels. Patient trialed stress dose steroids but serum creatinine rose to 4.44. He started PLEX for 10 treatments, and then transitioned to rituximab. During treatment with PLEX patient creatinine quickly downtrended, and after second dose of rituximab as an outpatient he was back to baseline. He lost 30 kg with resolution of his edema. Patient then tapered off steroids, and will continue on rituximab alone.

Discussion: Glomerular tip lesion is more common in European Americans and associated with a favorable outcome compared to other subtypes of FSGS. Resistance to one immunosuppressive treatment is not always associated with resistance to other treatment modalities. PLEX and rituximab should be considered in glomerular tip lesion in African Americans.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO1911 Utility of Immunofluorescent Intensity of IgG3 and Phospholipase A2 Receptor-to-IgG4 Ratio to Presume the Prognosis of Patients with Membranous Nephropathy

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Background: Membranous nephropathy (MN) is likely to show the long-term course and is a frequent glomerulonephritis in the elderly. For this reason, effective use of immunosuppressive drugs in a short period of time is desirable. In this study, we aimed to investigate the factors that could predict treatment responsiveness, using the treatment outcome in a short period of time, and retrospectively analyzed patients with MN in our hospital.

Methods: We included 66 patients who underwent renal biopsy and were diagnosed with MN in our hospital between April 2009 and December 2017. The percentage reduction in proteinuria one month after initiation of steroids, immunosuppressants, and ARBs was set to the endpoint. Intensity of immunofluorescent staining (IF) was scored according to the criteria of Japanese Society of Nephrology. Hematuria was quantified by 7-grade scoring of RBC numbers in high powered microscopic field.

Results: The intensity of IF (IgG subclass, PLA2R, THSD7A) was numerically evaluated and used for the analysis. The mean age of the patients included in the analysis was 66.4±11.7 years and baseline cGFR 63.9±18.7 ml/min, baseline urine protein was 7.05±5.45 g/gCr. Multiple parameters in high responder (HR, n=39) that resulted in less than 50% of urine protein after one month and low responder (LR, n=27) that remained proteinuria more than 50% were compared. Baseline urine protein and scored baseline hematuria were both higher in HR group (urine protein: 6.95 in HR vs 3.86 g/gCr in LR, p=0.003; hematuria: 1.0 in HR vs 0.0 in LR, p=0.036), but there was no difference in baseline cGFR (70.5 in HR vs 60.4 ml/min in LR, p=0.087). The mean dose of prednisone was also not different between the two groups (18.6 in HR vs 14.0 mg/day in LR, p=0.451). In IF, significant differences were observed between the two groups in the scored staining intensity of IgG3 and the staining intensity ratio of PLA2R to IgG4 (PLA2R-to-IgG4 intensity ratio;PGIR) were both lower in HR group (IgG3: 0.9 in HR vs 0.0 in LR, p=0.049; PIGR: 0.58 in HR vs 1.00 in LR, p=0.029).

Conclusions: From the result of the present examination, staining intensity of IgG3 and intensity ratio of PLA2R to IgG4 might be helpful to predict better therapeutic responsiveness in addition to the baseline proteinuria and hematuria.

PO1912 Graves Disease and Nephrotic Syndrome

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Introduction: Disorders of the thyroid and kidney may co-exist. Isolated case reports of Graves’ disease associated with various glomerular diseases, including membranous nephropathy, membranoproliferative GN, fibrillary GN, and minimal change disease have been published. A patient with membranous nephropathy and Graves’ disease who had improvement but not resolution of proteinuria after treatment with radioactive iodine has been described (Sasaki et al. CEN Case Rep. 2014; 3(1): 90-93). We report a case of nephrotic syndrome associated with Graves’ disease which completely resolved after treatment with radioactive iodine.

Case Description: A 33-year-old healthy female was seen for evaluation of proteinuria discovered during a routine life insurance evaluation. BP was normal, and she had trace-1+ lower extremity edema. Urinalysis showed 3+ protein, 1 red blood cell and 1 white blood cell per high power field. Urinary albumin/creatinine ratio was 4010 mg/g. Serum albumin was 2.7 g/dL. Renal function was normal. Tests for histoplasmin B and C, HIV, RPR, ANA, C3, C4, cryoglobulins, immunofixation, and free light chains were normal. Renal biopsy was planned but the patient missed the biopsy date. Subsequently she returned to clinic complaining of neck swelling. Exam revealed tachycardia, palpable goiter, 1+ pedal edema, no tremor. She reported heat intolerance, occasional diarrhea, insomnia, diaphoresis, and weight loss for the past month. A thyroid panel showed TSH <0.01 UU/mL (0.40-4.60 UU/mL), free T3 <2000 pg/dL (230-420), and free T4 10.6 ng/dL (8.5-1.7). TSH receptor and thyroid peroxidase antibodies were present. The patient was treated with methimazole and tapering steroids. She refused thyroid surgery and ultimately underwent two sessions of radioactive iodine treatment. After this treatment, nephrotic syndrome went into complete remission (Figure).

Discussion: Although relatively uncommon, Graves’ disease needs to be considered as a reversible cause of nephrotic syndrome.
TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS WITH OR WITHOUT NEPHRITIS WITH THE IMMUNOPROTEASOME INHIBITOR KZR-616: INITIAL RESULTS OF THE MISSION STUDY

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Background: Immunoproteasome inhibition demonstrated therapeutic potential in preclinical models of systemic lupus erythematosus (SLE) and lupus nephritis (LN). KZR-616 is a first-in-class selective immunoproteasome inhibitor, which has been safe and well tolerated in early clinical trials. One hundred subjects across 2 healthy volunteer studies, with dosing of KZR-616 up to 75mg SC, achieved target levels of immunoproteasome inhibition at doses ≥30mg. Here we report safety, tolerability and exploratory efficacy data from the Phase 1b portion of MISSION (KZR-616-002; NCT: NCT03393013), a clinical trial in which KZR-616 was administered to patients with active SLE with or without LN.

Methods: In this open-label dose-escalation study, SLE patients (per SLICC classification criteria) with SLEDAI ≥4 despite stable background therapy received KZR-616 at doses of 45mg (Cohort 1), 60mg (Cohort 2), or 60mg following a step-up dose (Cohort 2a, 2b, 2c) SC weekly through Week 13 (W13) with 12 weeks of follow-up.

Results: To date, 39 patients with SLE, including 2 patients with active proliferative LN, have enrolled in MISSION. The majority of TEAEs have been mild or moderate with injection site reactions the most common TEAE. Tolerability has improved with an initial step-up dosing regime, subsequent doses and the introduction of a lyophilized formulation. To date, no patients have discontinued from cohorts after implementation of these protocol modifications. Multiple measures of disease activity improved from Baseline to W13 and persisted through W25; no patients worsened over 13 weeks. KZR-616 administration resulted in improvements in multiple serologic markers as well as reduced expression of inflammatory gene expression modules. Both patients with biopsy-proven active proliferative LN had reductions in proteinuria.

Conclusions: KZR-616 has been safe and tolerated at a target dose of 60mg weekly. Step-up dosing, use of select pre-medications, and/or introduction of a lyophilized preparation have increased its tolerability. The administration of KZR-616 resulted in improvements across multiple disease activity measures as well as serologic markers, including improvement in proteinuria in patients with active proliferative LN. MISSION is an on-going study now focused on patients with LN.

Funding: Commercial Support - Kezar Life Sciences, Inc

RITUXIMAB AS MAINTENANCE THERAPY IN LUPUS NEPHRITIS

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Background: Rituximab (RTX) has been shown to be effective in refractory lupus nephritis (LN) in some studies. Minimal literature exists on using RTX as maintenance therapy for LN.

Methods: We performed a retrospective review of 21 patients (pts) with biopsy-proven LN who received RTX. We analyzed clinical data at baseline (pre-RTX) and up to 36 months (mo) of follow-up.

Results: Of 21 pts, 7 received RTX as part of first-line treatment, 7 for refractory LN and 7 for relapsing LN. All continued RTX (1gm q4-6 mo) as maintenance therapy, 15/21 (71%) pts were on RTX monotherapy (excluding prednisone and plaquenil) at 12 mo, 14/16 (88%) at 24 mo, and 13/13 (100%) at 36 mo. At 12 mo, 16/21 (76%) achieved complete or partial remission. Median UPCR (g/g) decreased from 2.95 at baseline to 0.61 at 12 mo, 0.42 at 24 mo and 0.21 at 36 mo. 16/21 (76%) pts were on prednisone ≤5mg/day at 12 mo, 13/16 (81%) at 24 mo, and 10/13 (77%) at 36 mo. Over 36 mo, 2 pts had LN relapses while on RTX alone, and later progressed to ESRD. 2 pts developed hypogammaglobulinemia.

Conclusions: RTX monotherapy appears promising as maintenance therapy in LN. Given favorable renal outcomes and steroid-sparing effect, larger studies studying this effect may be warranted.
POI196

A Multicenter Double-Blinded Preclinical Randomized Controlled Trial (pRCT) on Jak1/2 Inhibition in Lupus Nephritis

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Background: We conducted the first multicenter double-blinded pRCT in the field of nephrology and tested the Jak1/2 inhibitor baricitinib in experimental lupus nephritis.

Methods: We conducted a pRCT at two Spanish and two German academic sites. One site included MRL/lpr mice from their own breeding colony and the other sites included an intent to treat (ITT) population of 266 control and 268 VCS 23.7 mg/BID patients. Here we report key integrated data of interest including renal response, defined as: ● UPCR ≤ 0.5 mg/g Cr ● eGFR ≥ 60 mL/min ● No decline > 20% from baseline ● ≤ 10 mg prednisone 8 weeks prior to endpoint measurement ● No rescue medications

Results: RR at one year was 43.7% for VCS vs 23.3% for control (OR 2.67, 95% CI: 1.21, 5.45; p < 0.011), in a phase II analysis, we noted a 57% increase in RR for VCS compared to control patients. In the phase III clinical trial in patients with active lupus nephritis (LN), patients treated with 23.7 mg voclosporin bid in combination with MMF, achieved renal response rates of 40.8% vs. 22.5% for the control arm (OR 2.65; p < 0.001). The dose of voclosporin (VCS) was adjusted in response to decreases in eGFR. The objective of the present analysis was to evaluate the potential added value for therapeutic drug monitoring (TDM) in the LN patient population.

Methods: Pharmacokinetic (PK) data was analyzed from patients with LN treated with VCS. Based on a population PK model, the influence of various covariates on the disposition of voclosporin was evaluated. Calcineurin inhibition (CNI) was estimated using concentration data in the LN population and previously measured inhibition. Obtained exposure were put into perspective of renal response and the established safety margin.

Results: Sex, body weight, race, age, serum albumin, total bilirubin and eGFR demonstrated no significant or clinically relevant effect on the PK parameters. VCS has linear PK, and the goodness-of-fit plots (Figure 1 a–b) indicate that the model adequately describes observed and predicted concentrations of VCS. A strong correlation between VCS concentration and calcineurin inhibition is observed. VCS inhibits calcineurin in a dose-dependent manner up to maximum of 64 mg bid. In healthy subjects, a 96 mg bid dose was considered to be the upper limit of tolerability though did not present any safety concerns. At the 4-fold lower therapeutic dose of 23.7 mg bid, CNI was estimated to be 15.7% at Cmax and 58.1% at Cinf. In a quartile exposure analysis, no relationship with the odds ratio for renal response was observed and favored VCS in all quartiles.

Conclusions: At a therapeutic dose of 23.7 mg bid, sex, body weight, race, age, serum albumin, total bilirubin and eGFR demonstrated no clinically relevant effect on VCS PK parameters. The linear PK profile of VCS allows the use of a pharmacodynamic approach instead of a pharmacokinetic approach, in which the dose of VCS is adjusted in response to decreases in eGFR. These data suggest that TDM is unlikely to be of added benefit to patient management.

POI197

Management of Lupus Nephritis (LN) with Voclosporin: An Update from a Pooled Analysis of 534 Patients

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Background: Voclosporin (VCS) is a novel calcineurin inhibitor (CNI) with a favorable metabolic profile and a consistent, predictable dose response potentially eliminating the need for therapeutic drug monitoring. VCS significantly improved renal response (RR) in patients with LN in two pivotal trials. Compared to MMF (target dose 2g/day) and prednisone (rapid taper), the addition of VCS 23.7 mg bid increased renal response by 25% in the Phase 2 AURA-LV (OR: 3.21; 95% CI: 1.68, 6.13; p < 0.001) and 18% in the Phase 3 AURA (OR: 2.65; 95% CI: 1.64, 4.27; p < 0.001) studies at one year. To provide more information on VCS treatment effect we analyzed an integrated data set from AURA-LV and AURA.

Methods: The two pivotal trials were of similar design, conducted in comparable patient populations and defined similar key outcome measures. The integrated data set included an intent to treat (ITT) population of 266 control and 268 VCS 23.7 mg/BID patients. Here we report key integrated data of interest including renal response, defined as: ● UPCR ≤ 0.5 mg/g Cr ● eGFR ≥ 60 mL/min ● No decline > 20% from baseline ● ≤ 10 mg prednisone 8 weeks prior to endpoint measurement ● No rescue medications.

Results: RR at one year was 43.7% for VCS vs 23.3% for control (OR 2.76, 95% CI: 1.88, 4.05; p < 0.0001), and at 6 months (VCS 31%; control 20%); (OR: 2.01; 95% CI: 1.34, 3.01; p = 0.0008). In addition, 1-year RR for Hispanic patients was 37.9% in VCS vs 22.5% in control (OR 2.65; p < 0.001). In the phase III clinical trial in patients with active lupus nephritis (LN), patients treated with 23.7 mg voclosporin bid in combination with MMF, achieved renal response rates of 40.8% vs. 22.5% for the control arm (OR 2.65; p < 0.001).

Conclusions: This integrated analysis provides further support to the efficacy of VCS seen in both AURA-LV and AURA including in Hispanic patients, a high-risk LN patient population. Furthermore, VCS’ expected impact on mean eGFR as a CNI was mild over the course of one year.

Funding: Commercial Support - Aurinia Pharmaceuticals, Inc.
**PO1919**
Clinical Outcomes in Lupus Nephritis by Renal Response Status: A Retrospective Analysis of the Hopkins Lupus Cohort

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Background: A retrospective analysis of the Hopkins Lupus Cohort (a prospective, longitudinal study of patients [pts] with systemic lupus erythematosus) reported that renal response (complete/partial/none) at 24 months post-diagnosis of lupus nephritis (LN) predicts long-term renal survival.1 Here, we compare long-term renal survival and chronic renal insufficiency-free survival in pts with and without a renal response (RR) to standard LN therapy, as defined by primary endpoint in the Phase 3 BLISS-LN study (GSK Study BEL114054; NCT01639339).

Methods: This retrospective analysis (GSK Study 213039) of the Hopkins Lupus Cohort included pts with biopsy-proven class III, IV, or V LN. Endpoints were: long-term renal survival (no end-stage renal disease [ESRD] and/or mortality) and long-term chronic renal insufficiency-free survival by RR status at 24 months post-biopsy, both assessed by Kaplan–Meier plots with log-rank test and Cox proportional hazards regression.

Results: 173 pts with LN were included, 91.3% were female and mean (SD) age at biopsy was 36.2 (11.8) years. At 24 months post-biopsy, 114 (65.9%) pts achieved RR. Pts with RR at 24 months were less likely to experience an ESRD/mortality event and chronic renal insufficiency (Figure), even after adjusting for covariates (HR [95% CI] 0.33 [0.13, 0.87], p=0.0255; and HR [95% CI] 0.26 [0.14, 0.47], p<0.0001, respectively).


**Funding:** Other NIH Support - The Hopkins Lupus Cohort is funded by NIH grant R01-AR069752, Commercial Support - GSK.

**Figure:** Survival analysis of renal survival and chronic renal insufficiency-free survival by renal response at 24 months.

**PO1920**
Predictors of Doubling of Serum Creatinine at the Time of Biopsy in a Lupus Nephritis Cohort

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Background: Lupus nephritis is associated with significant morbidity and it is imperative to study the factors associated with renal survival. We study the determinants of doubling of serum creatinine in a predominantly Hispanic cohort.

Methods: We identified patients with biopsy-proven lupus nephritis from the biopsy registry that comprises of biopsies performed between 2002-2016. Demographic, clinical, and biochemical variables were obtained from the registry and electronic medical records. We studied the factors associated with the doubling of creatinine by performing univariate and multivariate proportional hazard analysis. All significant associations (p <0.05) were studied in a multivariate Cox regression model. Patients were censored upon death or the last follow-up.

Results: Out of 62 patients with biopsy-proven lupus nephritis, 53 (85.5%) were female. Whites, Hispanics, and Native Americans comprised 35.5, 30.6, and 16.1% of the cohort, respectively while 56% of the participants identified ethnically as Hispanic. Mean biopsy age, serum creatinine, and spot urine Protein/Creatinine were 34.5 (SD 15.3) years, 1.34 (SD 0.83) mg/dl, and 4.2 (SD 4.3) g/g, respectively. Class IV (48.4%) and III (16.1%) were the most prevalent lupus classes. Median (IQR) follow-up was 474.5 (1170) days. On multivariable analysis, higher age at biopsy was associated with decreased risk of doubling of serum creatinine (Figure 1). A higher spot urine Protein/Creatinine and C4 level at the time of biopsy were associated with increased risk of doubling of serum Cr.5

Conclusions: Previous studies have shown that biochemical markers at the time of kidney biopsy are a poor prognostic marker of renal outcomes in lupus nephritis. In this study, demographic, biochemical, and histological markers failed to predict doubling of serum creatinine. The age and the level of proteinuria at the time of kidney biopsy were associated with doubling of serum creatinine.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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**PO1921**
Lupus-Related Renal Disease Increases Inpatient Mortality: Analysis of the National Inpatient Sample

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Background: The aim of this study is to analyze the difference in outcomes of Systemic Lupus Erythematosus (SLE) with and without lupus-related renal disease. The primary outcome was inpatient mortality, while secondary outcomes were hospital length of stay (LOS) and total hospital charges.

Methods: Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 Database. NIS is the largest inpatient admission database in the USA. The NIS was searched for adult SLE hospitalizations with and without lupus-related renal disease as principal or secondary diagnosis using ICD-10 codes. Multivariate logistic and linear regression analysis was used to test for confounders for the primary and secondary outcomes respectively. STATA software was used to analyze the data.

Results: There were over 71 million discharges included in the combined 2016 and 2017 NIS database. 355,740 hospitalizations were for adult patients, who had either a principal or secondary ICD-10 code for SLE: 51,875 (14.6%) and 303,865 (85.4%) of these hospitalizations were for SLE with and without lupus-related renal disease respectively. 7,060 adult SLE hospitalizations (2%) resulted in inpatient mortality. 1,110 (2.14%) of the deaths occurred in SLE with lupus-related renal disease vs 5950 (1.96%) without lupus-related renal disease (P=0.228). The adjusted odds ratio (AOR) for inpatient mortality for SLE with lupus-related renal disease compared to those without lupus-related renal disease was 1.38 (95% CI 1.17-1.63, P<0.0001). SLE with lupus-related renal disease hospitalizations had a mean increase in adjusted LOS of 1.14 days (95% CI 0.95-1.34, P<0.0001) compared to SLE without lupus-related renal disease.

Conclusions: Hospitalizations for SLE with lupus-related renal disease have increased inpatient mortality, LOS, and total hospital charges compared to those without lupus-related renal disease. SLE patients with lupus-related renal disease require a multidisciplinary approach involving the rheumatologist and nephrologist to optimize outcomes.

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1922

Analysis of Characteristics and Risk Factors of Sepsis in Patients with Lupus Nephritis

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Background: Patients with lupus nephritis are at high risk of infection due to intrinsic immune dysregulation and treatment with glucocorticoids and immunosuppressants. Infection is a common complication in patients with lupus nephritis and is a major determinant of in-hospital mortality. Sepsis are the most frequent causes of infection-related mortality. In this research, we study the clinical characteristics and related risk factors of sepsis in patients with lupus nephritis according to a retrospective analysis.

Methods: A retrospective study was carried out for 322 hospitalized patients with lupus nephritis in Sun Yat-Sen Memorial Hospital from 2010 to 2019. The infected group consisted of 140 patients (The infected patients were subdivided into septic group and non-septic group according to the sepsis criteria) while the non-infected group consisted of 182 patients without infection. Baseline data including sex, age, disease duration, hospitalization duration, associated organ involvement, use of glucocorticoid and immunosuppressants.

Results: Compared to the non-infected group, longer hospitalization duration (14 vs. 30 days, P<0.05), pulsed methylprednisolone treatment within 1 month (29.7% vs. 15.5%, P<0.05), cyclophosphamide (22.9% vs. 14.3%, P<0.05), and calcineurin inhibitors (18.6% vs. 10.4%, P<0.05), and higher dose of oral corticosteroid (15 vs. 10mg, P<0.05)can be seen in the infected group (P<0.05). Compared to the non-septic group, higher proportion of patients with elevation of blood pressure (84% vs. 78%, P=0.05), while higher level of serum creatinine (134.0 vs. 88.0μmol/L, P<0.05), C reactive protein (43.8 vs. 32.3mg/L, P<0.05)and erythrocyte sedimentation rate (60.0 vs. 45.5mm/h, P<0.05) can be seen in the septic group. Multivariate Logistic regression analysis revealed that male and pulsed methylprednisolone treatment within 1 month were independent risk factors of sepsis in patients with lupus nephritis (P<0.05).

Conclusions: Male and pulse methylprednisolone treatment within 1 month were independently associated with sepsis in patients with lupus nephritis.

PO1923

An Evaluation of Costs Associated with Overall and Renal-Specific Organ Damage in Patients with Systemic Lupus Erythematosus in the United States

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Background: Systemic lupus erythematosus (SLE) is a chronic, multisystem, inflammatory, autoimmune disease affecting multiple organ systems, and characterized by fluctuating disease activity (flares). The combination of flares and SLE treatment can lead to progression of end-organ damage and death. The costs associated with SLE are substantial and are driven by frequent hospitalizations, use of glucocorticoids and immunosuppressants.

Methods: This retrospective analysis (GSK Study 208380) used the IQVIA PharMetrics Plus Database to identify patients with SLE and OD during 01/01/09–06/30/18. Patients with OD were identified using International Classification of Diseases (ICD)-9/10 codes derived from the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Inclusion criteria: ICHD II classification; >18 years of age; continuous enrollment 12 months both pre and post index (index: date of first observed OD medical claim; a1 inpatient IP or a3 outpatient OP claims within 6 months for an OD diagnosis code a1 IP or a2 OP claims separated by ≥30 days for SLE (ICD-9: 710.0 or ICD-10: M32.X) prior to the index date. Patients with renal-specific OD at index were noted. Patient characteristics were identified in the 12-month pre-index period and all-cause healthcare costs (2018 US$) were reported in the 12-month pre- and post-index periods. Results were analyzed with descriptive statistics.

Results: A total of 8952 patients met OD criteria and 486 (5.4%) had renal-specific OD. Patients were 92% female, mean (standard deviation [SD]) age was 46.4 (12.2) years, and mean (SD) Charlson Comorbidity Index was 2.0 (1.1). Mean (SD) all-cause healthcare costs increased from $15,746 ($20,637) to $26,998 ($57,082) in pre- versus post-index periods, respectively. In patients with renal-specific OD, mean (SD) all-cause healthcare costs increased from $16,131 ($22,914) to $36,905 ($72,188) in pre- versus post-index periods, respectively.

Conclusions: In patients with SLE and OD, annual costs increased after OD diagnosis. A similar increase in annual costs was observed for patients with renal-specific OD at index. Greenwood DM and Urowitz MB. Lupus. 1999;8:632–7.

Funding: Commercial Support - GSK

PO1924

Characteristics of Lupus Nephritis in a Cross-Sectional Study of Hispanic and Native American Patients in New Mexico

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Background: In patients with lupus, nephritis develops in ~50% of patients, and is associated with significant morbidity. Therefore, it is important to characterize the demographic and biochemical variables associated with lupus nephritis. In this cross-sectional study comprised of many Hispanics and Native Americans, we investigate the demographic and biochemical variables at the time of lupus nephritis diagnosis.

Methods: We identified 62 patients with lupus nephritis from the University of New Mexico kidney biopsy registry that contains biopsies from 2002-2016. Demographics, comorbidities, outcomes, therapies, and laboratory data typically followed in lupus patients (complements, spot urine protein/creatinine (Pr/Cr) ratio, urine RBCs, serologies, etc) were collected from the registry and medical charts.

Results: 62 patients were included, 53 females and 9 males. White, Hispanic, and Native American races accounted for 35.5%, 30.6%, and 16.1% of the cohort, while 56.6% of patients identified ethnically as Hispanic. 3 patients had no labs. Overall mean age at the time of renal biopsy was 34.5 (SD 15.3) years old. Laboratory data among ethnicities is shown in Figure 1. Class IV was the most common classification in the whole cohort (48.5%), for Hispanics (56.7%), and Non-Hispanics (30%). Antibody status was similar among all ethnicities: ANA positive (95%, 80% titer >1,800), anti-dsDNA positivity (73%), anti-Smith positive (52%), and SS-A positive (50%). The most common comorbidities were hypertension (n=46) and depression (n=16). For induction therapy, Hispanics patients received lower dose cyclophosphamide (24.5% vs. 75.5%, P=0.02) and mycophenolate mofetil (MMP) (38% vs. 61%), Non-Hispanics received mycophenolate mofetil (MMP) (38% vs. 61%). For maintenance therapy, both Hispanics (37%) and Non-Hispanics (35%) most often received MMP. 7 patients progressed to ESKD, by ethnicity: Hispanic and 2 Unavailable (1 African American).

Conclusions: We found similar baseline characteristics and lupus nephritis outcomes among Hispanic and Native American patients in New Mexico. Conditions (e.g. hypertension and depression) were more common among Hispanic patients.

PO1925

The ISN/RPS 2016 Classification Predicts Renal Prognosis in Patients with First-Onset Class III/IV Lupus Nephritis

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Background: Lupus nephritis (LN) is a life-threatening complication of systemic lupus erythematosus. The 2003 pathological classification of LN by the International Society of Nephrology/Renal Pathology Society (ISN/RPS) was revised in 2016; it quantitatively evaluates the interstitium in addition to the glomeruli. To date, the clinical usefulness of the 2016 classification has not been fully evaluated.

Methods: We performed a prospective multicenter cohort study and investigated the utility of the 2016 classification—including the activity index (AI), chronicity index (CI), and each pathological component to predict CR or renal function decline defined as >10 ml/min/1.73m2 in estimated glomerular filtration rate (eGFR) decline in serum creatinine and urine protein at 2 years from the time of diagnosis. The primary endpoint was renal failure to achieve CR (adjusted hazard ratios (HR) [95% confident interval (CI)]: 0.75 [0.64–0.88], 0.39 [0.25–0.61], respectively). Similarly, higher CI and higher interstitial fibrosis and lower hyaline deposit scores were associated with failure to achieve CR (adjusted hazard ratios (HR) [95% confidence interval (CI)]: 0.75 [0.64–0.88], 0.39 [0.25–0.61], respectively). Higher CI and higher interstitial fibrosis and lower hyaline deposit scores were associated with renal function decline (adjusted HR [95%CI]: 1.24 [1.01–1.53], 2.66 [1.43–4.93], 0.45 [0.21–0.97], respectively).

Conclusions: We demonstrated the utility of CI and AI of assessing interstitial regions in predicting renal prognosis. The 2016 classification can predict the clinical outcomes more precisely than the 2003 classification.

Funding: Commercial Support - Chugai Pharmaceutical Co
Resolution of Immune Deposits in the Glomeruli of Patients with Lupus Nephritis (LN)

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Background: Patients with proliferative LN have severe glomerular immune injury that resolves over time with treatment. The extent of resolution has been assessed by the histologic activity index (AI) but patients who have had a repeat kidney biopsy during maintenance immunosuppression, and many patients do achieve an AI=0, so-called histologic remission. The fate of glomerular immune complexes in treated LN patients has not yet been characterized. This study examined the immunofluorescence (IF) patterns in biopsies obtained during LN therapy.

Methods: A cohort of Hispanic LN patients (n=89) was studied. All patients had biopsy-proven (Bx1) proliferative (Class III, IVaV) LN, and were treated with corticosteroids plus cyclophosphamide or MMF for 6 months and then switched to MMF for maintenance therapy. After a median of 42 (range 30-52) months patients had a second protocol biopsy (Bx2) to determine if they had achieved histologic remission (AI=0) or had persistent histologic activity (AI>0). Kidney biopsies were evaluated by standard IF microscopy (IgG, IgA, IgM, C3, C4q), and semi-quantitatively graded on a scale of 0-3 (not present;bright).

Results: cyclophosphamide (48%). These patients had a median serum creatinine of 0.7 mg/dl (0.5-2.2) and proteinuria of 0.2 g/dl (0.0-8.0). The 26 patients who had persistent histologic activity at Bx2 had a median AI of 2 (1-6), serum creatinine of 0.75 mg/dl (0.6-1.1), and proteinuria of 0.2 g/dl (0.1-0.9) and about half had been treated with MMF. No residual AI was present in 30% of patients with an AI of 0, but was present in all patients who had an AI>1. IF for IgG became negative in 46% of patients with an AI=0 between Bx1 and Bx2, but in only 7.7% of patients with AI>1 (P=0.005). Similarly, IF for C3 became negative in 84% of patients with AI=0, compared to 31% of patients with AI>1(P=0.0001). After a median of 23 months (11-39) 7 patients who had been in histologic remission suffered an LN flare. None of these patients had complete resolution of IF on Bx2. In contrast, no patient with an AI=0 and an absence of IF on Bx has had an LN flare during a follow-up of 3.5 years.

Conclusions: About one third of patients with LN can achieve histologic and immunologic kidney remission. These patients appear to have an outstanding long-term kidney prognosis.

Funding: Clinical Revenue Support

Vasculopathy Associated with Lupus Nephritis (Severity and Outcomes)

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Background: Lupus nephritis (LN) is common in patients with systemic lupus erythematosus. Classification, prognosis, and treatment considerations of LN relies mainly on kidney biopsy features. Although few observational studies showed LN with vasculopathy has more severe course, literature reviews are scarce and mostly from Asian populations. The goal of the study was to shed more light on severity and response to Immunosuppression (IS) therapy in this subgroup of LN.

Methods: This was a single center retrospective chart review of LN patients from 2010-2019. Inclusion criteria were adults with native kidney biopsy proven LN documented in chart. Patients with systemic thrombocytic microangiopathy (TMA) or possible secondary cause of renal TMA (other than SLE) were excluded. Two groups were identified for comparison, LN without vasculopathy (WV) and LN with vasculopathy (WV). Vasculopathy was defined from kidney biopsy as vascular sclerosis (at least moderate), vascular immunoglobulins deposits, vasculitis, or TMA. Creatinine (Cr), albumin (Alb), urine protein-creatinine ratio (UPCR), stage-end renal disease (ESRD) and treatment regimens were compared, p-values are calculated by Mann Whitney, chi square and ANOVA of repeated measures.

Results: There were 431 patients with LN, 65 patients qualified for the study, patients with LN-WOV (n=38), and LN-WV (n=27). Racial demographics: 49=black (75%), 14=white (21%), 1=Hispanic, 1=Asian. Females 57 (88%). Median age 37 years. Average follow-up 3.5 years. Induction IS regimen for LN-WOV was mycophenolate (75%),14=white (21%), 1=Hispanic, 1=Asian. Females 57 (88%). Median age 37 years. Average follow-up 3.5 years. Induction IS regimen for LN-WOV was mycophenolate mofetil (MMF) in 52%, Cyclophosphamide (CYC) in 11%, and Rituximab (RTX) in 15%. In LN-WV induction IS regimen was MMF in 52%, and CYC in 23%. At baseline, mean values of serum creatinine (Cr), uric acid (UA), and UPCR were similar in LN-WOV and LN-WV were similar (p = 0.38, 0.53, 0.53, respectively). At 6 and 12 months of follow-up, mean values of Cr, Alb, and UPCR remained similar (p = 0.59, 0.49, and 0.64 for 6 months, and 0.34, 0.41, 0.53 for 12 months). No difference was found in ESRD events (7% (18%) in LN-WOV and 10% in LN-WV, p=0.86.

Conclusions: In our cohort, both groups of LN-WOv and LN-WV showed no statistical difference in the severity of presentation, nor in response to IS therapy assessed at 6 and 12 months follow-up of Cr, Alb, and UPCR, and ESRD. Hence, LN-WV was not associated with ominous outcomes or more resistance to IS.
known to rarely occur in lupus. This phenomenon has not been previously described. We speculate that this hypocytic holocellulosis is the result of a novel target of autoimmunity in lupus affecting renal tubular transport.

**Funding:** Other NIH Support - University of Texas Southwestern O’Brien Grant 5P30DK07928-13

**POI1930**

Outcomes of Lupus-Related Glomerular and Tubulointerstitial Disease: Analysis of the National Inpatient Sample

**Funding:** Emory University W Eugene EHIZOGIE Analysis of the National Inpatient Sample

**Background:** The study aims to compare the differences in outcomes of hospitalizations for Systemic Lupus Erythematosus (SLE) with glomerular and tubulointerstitial disease as principal or secondary diagnosis using ICD-10 codes. The analysis was done using STATA. Multivariable logistic and linear regression analysis was used accordingly to adjust for confounders for the outcomes.

**Results:** There were combined 71 million discharges included in the 2016 and 2017 NIS database. 51,875 hospitalizations were for adult patients, who had either a principal or secondary ICD-10 code for SLE with lupus-related renal disease. 51,525 (99.3%) and 350 (0.7%) of these hospitalizations were for SLE with lupus-related glomerular and tubulointerstitial disease respectively. The mean age for SLE with lupus-related glomerular disease was 40.6 vs 44.2 years for lupus-related tubulointerstitial disease (P=0.084). 7,060 adult SLE hospitalizations resulted in inpatient mortality, 1,110 (2.14%) of the deaths occurred in SLE with lupus-related glomerular disease. The number of deaths for lupus-related tubulointerstitial disease was less than 10, hence it was omitted during the analysis by STATA. SLE with lupus-related glomerular disease had similar LOS (6.8 vs 6.7 days, p=0.865) and total hospital charges ($79,718 vs $83,006, p=0.961) compared to those with tubulointerstitial disease.

**Conclusions:** SLE with glomerular disease makes up the vast majority of SLE with lupus-related renal hospitalization. Almost all the in-hospital deaths of SLE patients with lupus-related renal disease occurred in SLE with glomerular disease. LOS and total hospital charges were similar between hospitalizations for SLE with lupus-related glomerular and tubulointerstitial diseases.

**POI1931**

Lupus Podocytopathy Systematic Review

**Funding:** Other NIH Support - University of Texas Southwestern O’Brien Grant 5P30DK07928-13

**Background:** Patients with lupus, can present with a renal lesion distinct from the ones described by the ISN/RPS classification of lupus nephritis called lupus podocytopathy. Lupus podocytopathy has been described as minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) in patients with SLE with or without membranous involvement but without proliferative or membranous lupus nephritis features. We have gathered the available data on lupus podocytopathy and analyzed it to provide a comprehensive report in this review.

**Methods:** We searched electronic databases including pubmed and google scholar, using keywords related to lupus podocytopathy and synonyms and treatment from inception to December 2019. Articles retrieved were screened for relevance, including reference list of retrieved. We included cohort studies, case series, and retrospective studies. Individual case reports were excluded.

**Results:** The search identified 8 studies, of which 6 were included with a total of 107 patients. The patients were predominantly female (88%). The average age was 35 years. Studies done outside of China had predominantly African-American patients 72.5%. The average serum creatinine was 2.06 mg/dl. The average proteinuria was 6.5 g/day. Four studies reported monotherapy corticosteroids, and three studies reported varied treatments. The average follow up was 3.7 years. Complete remission was reported to be 67% from 3 studies. Four studies reported relapse rate of patients, and it accounted to 72.5% of patients.

**Conclusions:** Our study is the first systematic review of lupus podocytopathy. The strength of this study is the merger of data from known studies in lupus podocytopathy. Lupus podocytopathy has been described as minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) in patients with SLE with or without membranous involvement but without proliferative or membranous lupus nephritis features. We have gathered the available data on lupus podocytopathy and analyzed it to provide a comprehensive report in this review.
PO1934
Cost-Effectiveness of Maintenance Therapy with Azathioprine vs. Rituximab (Tailored or Fixed-Schedule) in Adults with Generalized ANCA Vasculitis in Colombia
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Background: Azathioprine has been the drug of choice for maintenance therapy in patients with generalized ANCA vasculitis. However, recent studies show that rituximab, a high-cost biological agent, which can be administered in two different schedules, might be more effective, so it is necessary to know the cost-effectiveness. Our goal was to compare the cost-effectiveness of the 3 maintenance schemes: standard therapy with azathioprine; fixed-dose rituximab and rituximab tailored according to CD19 lymphocyte level and ANCA titres, from the perspective of the Colombian healthcare system.

Methods: We designed a 5-year annual cycle Markov model with the following stages: remission, minor relapse, major relapse and death. Transition probabilities were obtained from a systematic review of the literature (Scopus and Pubmed). Following national guidelines for economic studies, costs, in 2018, USD = 2.956 Colombian pesos (COP), were estimated based on national drug registries, and official tariff manuals for procedures and other resources. Main outcome was quality-adjusted life years (QALY), using lupus nephropathy as a proxy; values were obtained from Tufts CEA Registry and validated by local expert panel through a modified Delphi technique. Cost-effectiveness threshold was three-times per capita GDP (USD 17253). Discount rate was 5%. Univariate and probabilistic sensitivity analyses were performed.

Results: Overall discounted 5-years costs were USD 1356 for azathioprine; USD 4750 for tailored rituximab and USD 6162 for fixed rituximab. QALY gains were 2.94, 3.63 and 3.64, respectively. Both tailored and fixed rituximab were cost-effective (cost per QALY gained: USD 4.919 and USD 6.865 respectively), but tailored dosing was preferable due to its lower cost. Sensitivity analyses did not modify these results significantly.

Conclusions: To our knowledge this is the first economic evaluation that compares azathioprine with tailored and fixed rituximab regimens as a vasculitis maintenance treatment in adults with ANCA generalized. Due to its lower effectiveness azathioprine should not be the first line of treatment. Tailored rituximab should be a better option than fixed schedule due to its lower cost with similar effectiveness.

PO1935
Use of Subcutaneous IgG to Treat Hypogammaglobulinemia in ANCA-Associated Vasculitis
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Background: Intravenous immunoglobulin (IVIG) has been used to treat ANCA vasculitis (AAV) patients with recurrent infections as a result of hypogammaglobulinemia induced by glucocorticoid treatments such as immunoglobulin (SCIG) has a better safety and tolerability profile. We characterized the clinical features, treatment and outcomes of AAV patients treated with SCIG).

Methods: We conducted a retrospective chart analysis of 187 patients in our AAV database to identify patients with recurrent infections and hypogammaglobulinemia subsequently treated with SCIG. Patient demographics, clinical characteristics, treatment and immunological parameters were assessed.

Results: Of the 187 patients identified with AAV, 6 were treated with SCIG. All were Caucasian, PR3 positive and majority (n=4) were females. All patients had pulmonary involvement, and regimens of cyclophosphamide (CYC) and/or rituximab (RTX) were employed for induction and remission. Ig levels (IgG, IgM, IgA) were reduced in all patients. CD19/CD20 B cells were depleted, and CD3/CD4 and NK cells were preserved in all patients. The majority of patients (n=4) experienced recurrent URIs. 3 had shingles in addition to other infections(table 1). All patients had no discernible IgG antibody response to pneumococcal vaccine. Mean duration between first rituximab administration and initiation of SCIG was 6.4 years. Four patients continued to receive RTX every 6 to 12 months while 2 patients remained in remission off RTX for over 2 yrs. IgG levels normalized and none of the patients had recurrence of infections after initiation of SCIG.

PO1936
Glucocorticoid Maintenance Therapy and Severe Infectious Complications in ANCA-Associated Vasculitis
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Background: Although treatment and outcomes in anti-neutrophil cytoplasmic autoantibody associated vasculitis (AAV) have been improved over the last decades, intensified immunosuppressive burden is concurrently associated with life-threatening adverse effects which are the main cause of death during the first year after disease onset. Our study evaluates the impact of cyclophosphamide (CYC) induction dose and glucocorticoid maintenance dose and duration on patient outcomes with an emphasis on infectious complications.

Methods: A total of 130 AAV patients from two different German Vasculitis Centers diagnosed between 2004 and 2019 treated with CYC for induction therapy and glucocorticoids a mycophenolate mofetil or azathioprine for maintenance therapy were included in this study. We evaluated the impact of CYC dose for induction therapy and glucocorticoid dose and treatment duration for maintenance therapy on time to relapse, kidney function, infectious complications, irreversible physical damage and mortality. Patients were separated into four groups: <3g versus ≥3g cumulative CYC dose and <7.5mg after 6 months versus ≥7.5mg glucocorticoids after 6 months.

Results: The baseline demographic and disease characteristics were comparable between groups. Cumulative CYC dose had no impact on relapse rate, kidney function, infectious complications or mortality. Patients receiving ≥7.5mg glucocorticoids after 6 months had an increased rate of infectious episodes per patient (0.6 vs. 1.7; p=0.001). Urinary tract infection (p=0.007), pneumonia (p=0.003) as well as opportunistic pneumonia (p=0.022) and sepsis (p=0.008) appeared more frequently. Especially pneumonia during the first 24 months after disease onset (hazard ratio, 3.0 [95% confidence interval (CI), 1.5–6.1]) led to more death by infections (p=0.034). Patients ≥65 years with ≥7.5mg glucocorticoids after 6 months were at particular risk for infectious complications. Glucocorticoid maintenance therapy had no impact on relapse rate or kidney function after the last follow-up.

Conclusions: An extended glucocorticoid maintenance therapy may induce severe infectious complications leading to an increased frequency of death by infection, has no effect on time to relapse and should therefore be critically revised throughout the aftercare of AAV patients.

PO1937
Country Differences Exist in the Treatment of ANCA-Associated Vasculitis (AAV), but High-Dose and Prolonged Glucocorticoid Use Is Observed Across Europe
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Background: European AAV guidelines recommend remission induction therapy with combination of high dose glucocorticoids (GC) and rituximab (RTX) or cyclophosphamide (CYC) and maintenance therapy with either RTX or azathioprine (AZA). This retrospective study examined the pattern of prescribing, including the use of GCs, across Europe in AAV patients managed in routine clinical practice.

Methods: 1478 AAV patients managed by 493 physicians in France, Germany, Italy, Spain and UK who completed induction therapy for organ or life threatening AAV (49%
incidence and 51% relapsing) and initiated maintenance therapy between 2014-16 were studied. Data were collected at the time maintenance was determined to begin by the physician and then after 6, 12, 18 and 36 months.

**Results:** AAV type varied with more GPA in Germany (52%) and UK (56%) compared to France (47%), Italy (47%) and Spain (40%). Proportion of patients with severe progressive disease varied – 41% in Italy to 48% France. Induction therapy varied with lowest use of IV GC and rituximab (RTX) and highest cyclophosphamide (CYC) use in the UK. Maintenance was defined by clinicians as approximately 6 months following treatment start and GCs were used similarly across all countries with less RTX and less GC use in UK and more AZA in Germany and UK. At 36 months prescribing patterns were similar and a variable proportion of patients (13% Germany to 30% France) stopped therapy but with approximately 25% patients not in full remission.

**Conclusions:** AAV treatment prescribing patterns vary across Europe particularly RTX, driven by economic as well as case mix differences. GC use is high across all countries with high GC use (including IV at induction) and prolonged use over 36 months being common. Sustained remission rates could be improved and there is need for more targeted therapies to reduce reliance on GCs.

**Funding:** Commercial Support - Vifor Pharma

**AAV prescribing (\(p<0.05\) vs respective highest/lowest country)

**PO1938**

**Validation of a Clinical-Pathologic Renal Risk Score in ANCA-Associated Glomerulonephritis: The US Experience**

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**Background:** The prognostication of renal disease in the setting of ANCA associated vasculitis (AAV) continues to pose a significant clinical challenge given lack of validated clinical and pathologic correlates. A risk score has been developed by a German consortium (Brix et al Kidney International 2018), to stratify risk of AAV related renal disease progression to ESKD. We applied this risk score in our cohort of AAV patients to ascertain its reproducibility.

**Methods:** A single center retrospective cohort study was performed reviewing 148 renal biopsies of patients with AAV GN. Data for score calculation was available of 119 patients with a median follow up of 58 months (IQR 28 – 97 months). Three parameters were used in the risk prediction score: (1) # of normal glomeruli (N0 >25%, N1 10-25%, N2 <10%), (2) tubular atrophy and interstitial fibrosis (T0 <25%, T1 >25%) and (3) eGFR at the time of diagnosis (G0 >15, G1 <15). A weighted assignment of points to each parameter was as follows: N1 [4], N2 [6], T1 [2], G1[3], and the resulting aggregate risk score used to classify predicted ESRD risk was low (0), intermediate (2 to 7), or high (8 to 11 points).

**Results:** In the cohort of 148 patients, median age was 67 years and mean eGFR at diagnosis was 27.7. Seventy-six were MPO, 57 were PR3 positive and 15 were ANCA negative. With regards to risk stratification, 34 were in low risk category, 59 in the medium risk category and 26 patients in the high-risk category. Overall, 23 patients (15.3%) progressed to ESKD with 2 (5.9%), 11 (18.6%), 10 (38.5%) in low, medium and high risk groups, respectively. A Kaplan-Meier survival curve (Figure1) demonstrates worsening of renal survival across the risk groups (p=0.0035).

**Conclusions:** This AAV renal risk score was able to reliably predict risk for progression to ESKD. A further analysis revalidating cut-offs and risk score points would likely refine the score improving its prediction accuracy.

**PO1939**

**Clinical Features and Outcomes of Anti-Neutrophil Cytoplasmic Autoantibody-Associated Vasculitis in Chinese Elderly and Very Elderly Patients**

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**Background:** Anti-neutrophil cytoplasmic autoantibody-associated vasculitis (AAV) is predominantly a disease of the elderly, and the incidence increases with age. However, there are few data focusing on the clinical features in elderly-onset AAV, especially in very elderly-onset AAV in China. The aim of this study was to explore whether elderly-onset AAV shows any specific clinical features and outcomes in Chinese patients.

**Methods:** We performed a retrospective study in Xiangya Hospital, a mixed tertiary medical center in south China. A total of 177 patients presenting with AAV were included between January 1, 2010 and December 31, 2017. Patients were divided into younger group (age<65 years) and older group (age65 years) which was sub-divided into elderly group (age 65-74 years) and very elderly group (age75 years).

**Results:** We found patients in the very elderly group had more chest and cardiovascular involvement (P=0.033 and P=0.017). Older AAV patients had less renal involvement and lower serum C4 level (P<0.013 and P<0.003). Very elderly AAV patients had lower platelet counts. Patients in the younger group had a higher level of BVAS among three groups (P<0.05 younger group vs. very elderly group; P<0.05 younger group vs. elderly group). There were no significantly difference in the proportion of ISRD patients among the three groups (P=0.473). Patients in the very elderly group had the poorest patient survival (P=0.002).

**Conclusions:** Older AAV patients had less renal involvement, lower serum C4 level and BVAS. The very elderly group got the most chest and cardiovascular involvement and had lower platelet counts. Older age is associated with higher mortality in AAV patients.

**Funding:** Government Support - Non-U.S.
Validation of the Renal Risk Score for ANCA-Associated Glomerulonephritis in a National Irish Cohort
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Background: Histopathological examination is currently the gold standard for diagnosis of ANCA-associated glomerulonephritis (AAV GN). However, the commonly used Benedir score is inconsistent at predicting renal outcomes across different cohorts. Furthermore, treatment related morbidity remains a major problem. Brix et al. recently published a clinicopathologic score to predict End-Stage Disease Kidney (ESKD), using 3 parameters to stratify patients into 3 risk groups. Parameters include: percentage normal glomeruli (N0 >25% = 0, N1 10% – 4, N2 >10% = 6), percentage tubular atrophy and interstitial fibrosis (TO ≤25% = 0, T1 >25% = 2), and estimated glomerular filtration rate at the time of diagnosis (G0 >15 ml/min/1.73 m2 = 0, G1 ≤15 ml/min/1.73 m2 = 3). The ultimate aim is to use this to personalise treatment, enabling the optimal balance of toxic immunosuppression for every patient.

Methods: The Rare Kidney Disease (R KD) registry is an Irish national longitudinal, multi-centre, cohort study which includes 567 AAV patients, to date, diagnosed using the European Medicines Agency Algorithm (1990-2019). Patients with Granulomatosis with polyangiitis (Wegener’s) (n=13), microscopic polyangiitis (n=1), with biopsy proven AAV GN and positive PR3 or MPO serology were included in our validation of the renal risk score.

Results: 248 patients, of whom 43 (17.3%) developed ESKD and 35 (14.1%) died, over a median follow up of 32 months (interquartile range, IQR 5.9-99 months), were identified. Outcome data and histology were available for 205 patients. Forty-five patients were in the lowest risk group (group 1) - (2.4%) of which developed ESKD. Eight (8.6%) of the 93 patients in the middle risk group (group 2) reached ESKD. Sixty-seven patients were in the highest risk group (group 3) and 44 (66%) of these patients reached ESKD. Kaplan Meier survival analysis demonstrated a difference in renal outcome between the 3 risk groups (p <0.0001).

Conclusions: The proposed renal risk score accurately predicts ESKD in patients with AAV GN, in our national Irish cohort. The next step is to further refine the predictive cut-off values for the 3 clinicopathologic parameters using a regression tree analysis.

Hypocomplementemia Is Associated with More Severe Renal Disease and Worse Renal Outcomes in Patients with ANCA-Associated Vasculitis: A Retrospective Cohort Study
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Background: The complement system has been recently proposed to play an important role in the pathogenesis of ANCA associated vasculitides (AAV). Real life data assessing its predictive role in renal outcomes is limited. In this study, we evaluated the value of serum and kidney deposited C3 in predicting renal outcomes in patients with AAV.

Methods: In this retrospective study, patients with AAV were categorized according to their baseline serum C3 levels as hypo- or normo-complementemic and to those with positive or negative kidney biopsy immunofluorescence (IF) for C3. Clinical, serologic, treatment and histopathologic characteristics, as well as prognosis between the 2 groups were compared.

Results: Forty-seven patients (51% men) were enrolled with a mean age at diagnosis of 65 years and were followed up for a median period of 56 months. At baseline, 23% (11/47) of the patients were hypocomplementemic (C3 <75 mg/dL). These patients were older (74 vs. 65 years, p=0.013), had higher creatinine levels (4.9 vs. 2.2 mg/dL, p=0.006), were more often hemodialysis dependent (64% vs. 19%, p<0.009) and progressed more often to ESRD (55% vs. 11%, p=0.01) compared to normo-complementemic patients (n=36). On multivariate analysis, serum Cr at diagnosis (HR=16.8, 95%CI: 1.354-208.62, p=0.028) and low serum C3 (HR=2.492; 95% CI: 0.537-11.567, p=0.044) were independent predictors for ESRD. Among 25 patients with kidney biopsy data, those with positive IF staining for C3 (56%, n=14) had more often a mixed histological pattern (72% vs. 27%, p=0.033), low serum C3 levels (42% vs. 18%, p=0.001) and serious infections during follow-up (57% vs. 18%, p=0.047) compared to those with negative (n=11) IF staining.

Conclusions: The subgroup of patients with AAV and low C3 levels at diagnosis (23%) have more severe renal disease and outcomes (ESRD) compared to patients with normal C3 levels. This should be taken into account in therapeutic and monitoring strategies.

Clinical Features and Treatment Outcomes of Patients with Paucl- Immune Vasculitis with and Without a Medical History of Autoimmune Disease
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Background: A proportion of patients with pauci-immune vasculitis (PIV) report a past medical history (PMH) of other autoimmune disorder prior to the diagnosis of vasculitis. The purpose of this study was to identify the differences, if any, between patients with PIV with or without a PMH of other autoimmune disease prior to the onset of vasculitis.

Methods: Among 304 patients with biopsy proven PIV at any site, detailed information regarding their PMH was available in 235 patients (77.3%). Of these, 60 (25.5%) reported a PMH of other autoimmune disorder including Sjogren syndrome, Crohn’s disease, autoimmune thyroiditis, psoriasis, rheumatoid arthritis, and scleroderm. Results: The clinical characteristics and outcomes of the two groups are displayed in [table 1].

Conclusions: Patients with a PMH of other autoimmune disorder prior to the diagnosis of PIV were predominantly PMPO-ANCA positive, had less impaired kidney function at presentation and a low lower probability of relapse after achieving remission, compared to patients without a PMH of autoimmunity.

Low Serum C3 at Diagnosis of Paucl-Immune Glomerulonephritis Is Associated with More Advanced Kidney Impairment and Worst Renal Prognosis
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Background: Recent evidence supports the notion that complement activation plays a critical role in puacl-immune (PI) vasculitits pathogenesis. The aim of this study was to investigate if the clinical, serological and laboratory characteristics and treatment outcomes of patients with PI glomerulonephritis (GN) with low serum complement levels at diagnosis differ from those of patients with complement values within the normal range.

Methods: In a retrospective design we studied patients with biopsy proven PIGN with available serum complement measurements at diagnosis, or during a relapse, prior to initiation of immunosuppressive therapy. All patients were tested for antineutrophil cytoplasmic antibodies (ANCA) at presentation. Fisher’s exact tests and Wilcoxon rank sum tests were used to compare the characteristics by serum C3.

Results: Of 96 patients included in the study, 22 (23.9%) had low serum C3 at diagnosis. Comparison of clinical, serological and laboratory characteristics and outcomes between the two groups is shown in [table 1].

Conclusions: Almost one quarter of patients with biopsy proven PIGN had low serum C3 at diagnosis in this cohort. These patients had more advanced renal impairment, required acute dialysis more frequently and were more likely to end up in end-stage kidney disease compared to patients with serum C3 within the normal range.
PO1944

Serum and Urinary Metabolites Discriminate Disease Activity in ANCA-Associated Glomerulonephritis
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Background: Relapse of disease and treatment related morbidity due to lack of a reliable biomarker for disease activity continue to be a significant issue in patients with ANCA associated vasculitis (AAV). Renal biopsy is currently gold standard for reliable detection of active disease. Metabolomics have been used to successfully discern disease activity in a number of autoimmune diseases. We sought to investigate the use of serum and urinary metabolomics to discriminate disease activity in ANCA associated GN.

Methods: Ten patients with AAV renal disease had serum and urine supernatant sample collections during active and remission phases of disease. Active renal disease was defined by presence of hematuria >5 RBC/hpf, urinary RBC casts or an increase in serum creatinine >30% or < in eGFR by 25% or biopsy proven GN. The samples were then subjected to targeted metabolomics data acquisition using a Thermo scientific Q Exactive Plus Orbitrap Mass Spectrometer Plus with a Vanquish UPLC at our metabolomics facility.

Results: The mean age in this cohort was 61 years, with 6 patients each being male and Caucasian. Nine patients had biopsy proven renal disease, with clinical diagnosis in one. Mean BVAS and mean GFR was 17 and 28 respectively. Intensities of urinary citrate and iso-citrate are significantly higher in the remission group compared to the active group (Fig 1A). Similar trend of higher citrate and iso-citrate intensities present in serum of patients in remission versus active disease (Fig 1B). There was a disproportionately high intensity difference in citrate and iso-citrate levels in serum and urine samples compared to other metabolites of the TCA cycle implying involvement of additional metabolic pathways.

Conclusions: This study indicates that serum and urinary citrate and iso-citrate may be utilized to monitor disease activity in AAV and emerge as an alternative to kidney biopsy.

PO1945

Renal Involvement in Granulomatosis with Polyangiitis Does Not Increase Inpatient Mortality Compared with No Renal Involvement
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Background: The aim of this study was to analyze the difference in outcomes of Granulomatosis with polyangiitis (GPA) with and without renal involvement. The primary outcome was inpatient mortality, while secondary outcomes were hospital length of stay (LOS) and total hospital charges.

Methods: Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 Database. NIS is the largest inpatient admission database in the United States. The NIS was searched for adult GPA hospitalizations with and without renal involvement as the principal or secondary diagnosis using ICD-10 codes. Multivariate logistic and linear regression analysis was used to adjust for confounders for the primary and secondary outcomes respectively. STATA software was used to analyze the data.

Results: There were 71 million discharges included in the combined 2016 and 2017 NIS database. 23,670 hospitalizations were for adult patients, who had either a principal or secondary ICD-10 code for GPA. 8,265 (34.92%) and 15,405 (65.08%) of these hospitalizations were for GPA with renal and without renal involvement respectively. Inpatient mortality occurred in 3,104 (5.10%) GPA patients (5.14% ± 0.25) vs 558 (3.8%) without renal involvement (p=0.0287). The adjusted odds ratio (AOR) of inpatient mortality for GPA with renal compared to without renal involvement was 1.14 (95% CI 0.84-1.56, p=0.406). GPA with renal involvement hospitalizations had a mean increase in adjusted mean LOS of 1.36 days (95% CI 0.82-1.91, p=0.0001) compared to GPA without renal involvement. GPA with renal involvement hospitalizations had an increased in adjusted total hospital charges of $18,723 compared to GPA without renal involvement (95% CI 9,595-27,852, p=0.0001).

Conclusions: There is no statistically significant difference in inpatient mortality for hospitalizations of GPA with and without renal involvement. However, LOS and total hospital charges in GPA with renal involvement are greater than those without renal involvement. Hence GPA with renal involvement has a greater burden to the healthcare system compared to without renal involvement.

PO1946

Immunological Indexes Both in Renal and Serum Were Associated with Relapse and Patient Outcome in Chinese Patients with Myeloperoxidase-ANCA-Associated Glomerulonephritis
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Background: Rapidly progressive glomerulonephritis (RPGN) caused by antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are typically characterized by few or no immune deposits in glomerular which was defined as pauci-immune glomerulonephritis (GN). Immune complex (IC) deposits in glomerulus and absence of an immune induced also have been reported and/or by the presence of anti-GBM antibodies with AAV in China are positive for anti-myeloperoxidase (MPO), which more frequently had renal involvement and developed RPGN. Therefore, it is necessary to assess serum immunological indexes and the IC deposits in renal in MPO-ANCA-associated GN.

Methods: Clinical and immunological characteristic of AAV in China are positive for anti-myeloperoxidase (MPO) were retrospectively analyzed. Results: Patients with low sC3 (<790 mU/l) and low sC4 (<100 mU/l) at diagnosis showed poorer renal survival compared to patients with normal value (p=0.003, 0.011). Furthermore, among patients of low sC3 at diagnosis, the cases with persistent low sC3 showed obviously worse renal survival than those whose sC3 recovered to normal after treatment (p<0.001). There are 41%(40/97) patients showed positive IF findings (a2- on a 0 to 4+ scale) for at least one Ig or complement component. In our study, the patients with IC deposits showed higher level of serum creatinine (p=0.01) and lower platelet counts (p=0.009), sC3 level (p=0.013) than patients with pauci-IC deposition at diagnosis. We also found IgG deposits related to worse renal outcome than the negative cases (p=0.047). What’s more, complement C1q deposits displayed significant poorer patient survival than the cases without C1q deposits (p=0.001).

Conclusions: Patients with a persistent low sC3 showed poorer renal prognosis than the patients whose sC3 level return to normal after a period of treatment, which was confirmed that both initial and continuously low sC3 can act as predictive indicators for renal outcome. IgG and complement C1q deposits associated with poorer renal and patient outcome, which can help to judge the prognosis of MPO-ANCA-associated GN to some extent.

PO1947

Rituximab vs. Cyclophosphamide in the Treatment of Anti-GBM Crescentic Glomerulonephritis: An Observational Study
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Background: Anti-glomerular basement membrane (GBM) crescentic glomerulonephritis (CGN) is a rare disease affecting kidneys and/or lungs. At present most of the evidence for its treatment is with use of plasmapheresis (PP), high dose steroids (HDS) and cyclophosphamide (CYC). The use of Rituximab (Rtx) in addition to PP and HDS is only anecdotal. Herein, we are describing our experience with the use of both regimens.

Methods: A retrospective analysis of all the patients with anti GBM CGN admitted in our hospital from September 2018 to November 2019 was done. Anti GBM CGN was diagnosed on the basis of ≥50% crescents on kidney biopsy and immunofluorescence showing ≥1 mg/L IgG deposition along GBM and/or by the presence of anti GBM antibodies.

Results: 11 patients were admitted with anti GBM CGN, during this period (15 months). Kidney biopsy was done in 10 patients and in one anti GBM GN was diagnosed on the basis of raised anti GBM antibody titres. There were 8 females and three males (age range 37-72 years). The mean serum creatinine was 8.69mg/dl. Out of 11 patients 2 refused for treatment and 2 were lost to follow up. 3 out of 7 patients had diffuse alveolar hemorrhage (DAH) and in all it succeeded renal involvement (one had diagnosis of usual interstitial pneumonia for 1 year). 4 out of 11 patients had concomitant urinary tract infection. 5 out of 7 (71.42%) were ANCA positive, 2 out 11 had type 2 diabetes mellitus, 5 out of 11 were oligoanuric and 7/11 (63.6%) were dialysis requiring at presentation. PP was given on alternate days. Both the patients who refused for treatment died on follow up. Among remaining 7 patients 5 had received PP+HDS + CYC and 2 had received PP+HDS+Rtx. In CYC group 4 out (all 4 were dialysis dependent and 3 were oligoanuric) out of 5 patients died whereas in Rtx group both the patients survived (one was dialysis dependent and oligoanuric).
Impact of Race on Hospitalization Outcomes for Goodpasture Syndrome in the United States

Methods: The National Inpatient Sample database was used to identify hospitalized patients with a principal diagnosis of Goodpasture’s syndrome from 2003-2014. Goodpasture’s syndrome patients were grouped based on their race. The differences in hospital treatments and outcomes between Caucasian, African American, and Hispanic Goodpasture’s syndrome patients were assessed using logistic regression analysis.

Results: 964 patients were hospitalized with a primarily diagnosis of Goodpasture’s syndrome. Of these, 786 were included in the analysis: 622 (65%) were Caucasian, 73 (8%) were African American, and 91 (9%) were Hispanic. The need for mechanical ventilation, non-invasive ventilation support, and renal replacement therapy in African Americans was greater than Caucasians. There was no significant difference in organ failure, sepsis, and in-hospital mortality between African Americans and Caucasians. In contrast, Hispanics had higher in-hospital mortality than Caucasians but similar risk of organ failure and sepsis.

Conclusions: African American and Hispanic populations account for 8% and 9% of hospitalizations for Goodpasture’s syndrome, respectively. While there is no significant difference in in-hospital mortality between African Americans and Caucasians, Hispanics with Goodpasture’s syndrome carry a higher in-hospital mortality compared to Caucasians.

Overlap Syndrome of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis and IgG4-Related Disease: Distinct Clinicopathologic Clues for Precise Diagnosis

Methods: A case of a 67-year-old man in our hospital who exhibited the characteristics of both AA V and IgG4-RD was performed on PUBMED database from 1976 until January 2020.

Results: Mild hematuria with rapid progressive renal failure of the patient was observed while renal biopsy revealed pauci-immune crescentic glomerulonephritis, the overlap syndrome of AA V and IgG4-RD was performed on PUBMED database from 1976 until January 2020.

Conclusions: Both antineutrophil cytoplasmatic antibody (ANCA)-associated vasculitis (AAV) and IgG4-related disease (IgG4-RD) are multi-system inflammatory disorders. The coexistence of both diseases presents the possibility of a new overlap syndrome which leads to different treatment and outcome. In this study, the symptomatic and pathological concurrence of AAV and IgG4-RD is investigated to explore the possibility and clinicopathologic clues to the diagnosis of this overlapped syndrome.

PO1950

Anti-IL-5 Therapy in Eosinophilic Granulomatosis with Polyangiitis (EGPA): An 18-Month Follow-Up Study of a Steroid-Sparing Therapeutic Approach

Methods: The aim of our study was to analyze the outcome for EGPA patients who received 100mg s/c of MEPO monthly for 18 months and beyond. This retrospective, descriptive study analyzed 13 patients with EGPA, who received 100mg s/c of MEPO therapy monthly. Time points of assessment included MEPO commencement [M0] and ≥ 18 months [M18].

Results: This study demonstrates that anti-IL-5 therapy serves as a favorable model for steroid minimization in EGPA, with an overall 50% reduction in steroid dosage. Additional reduction in conventional immunosuppressants was also observed in 3 patients. ANCA positive serology normalized in all four patients. Well tolerated, it demonstrated considerable clinical benefit, with 12 patients [92.3%] continuing anti-IL5 therapy beyond 18 months. Renal function was preserved. One patient had MEPO switched to Rituximab to treat both EGPA and new onset rheumatoid arthritis. Three patients were switched to alternative anti-IL5 therapies, benralizumab (3x2) and Reslizumab (x1).

Conclusions: The relapsing nature of EGPA places a potential dependency of therapy on steroids, underscoring the importance of targeted pathway specific biologics to minimize steroid exposure, prevent tissue damage and ensure early response to therapy. This was a 50% reduction in steroid dosage in this study, with preserved renal function.

Glomerular Diseases: Clinical, Outcomes, and Trials - 3

PO1951

Pauic-Immune Lupus Nephritis: A Case Report

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease with multisystem involvement, and Lupus nephritis (LN) typically shows immune deposits on biopsy. Pauic-immune LN is a rare entity.

Case Description: A 35 year old female presented with pedal edema, reduced urine output & yellowish discoloration of eyes since 20 days. No vomiting, dyspnea, joint pains, rashes, or hematuria. She had similar episodes in 2011 and 2013 & was given blood transfusion and oral steroids. She is a hypertensive for 10 years and diabetic for 2 years. She had 2 normal vaginal deliveries with no obstetric complications. On examination was normal. She had severe anemia, renal failure, positive ANA, dsDNA and direct Coombs test, with normal complements. There was no evidence of antiphospholipid syndrome, SLE with Antinuclear hemolytic anemia (AHLA) and probable lupus nephritis (LN) was diagnosed. Steroid pulse was started with stabilization of renal function and hemoglobin. Renal biopsy showed necroinflammatory crescentic glomerulonephritis with no endocapillary proliferation. Immunofluorescence did not show any immune deposits. A diagnosis of pauci immune LN was made, and was started on cyclophosphamide. She had partial renal recovery with creatinine of 1.5 mg/dl, no hematuria, no hemoysis.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underlines represents presenting author.

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PO1952

Pulmonary Renal Connection: A Case of ANCA Vasculitis and Atypical Anti-GBM Antibody Associated with Vaping
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Introduction: The use of e cigarettes and vaping is linked to the development of lung injury (EVAI). We present a case of ANCA (antineutrophil cytoplasmic antibody) vasculitis with atypical Anti GBM (glomerular basement membrane antibody) in a patient with EVAI.

Case Description: A 17 year old male with a history of vaping presented with acute respiratory failure requiring mechanical ventilation. CT chest revealed diffuse bilateral consolidation. Evaluation for infection was negative. Nephrology was consulted for acute renal failure. Urine analysis was notable for hematuria and proteinuria. Urine microscopy identified dysmorphic erythrocytes. Renal biopsy showed pauci immune crescentic glomerulonephritis (panel A). ANCA with MPO (myeloperoxidase) specificity and Anti GBM antibody were positive. He was treated with methylprednisolone, therapeutic plasma exchange and oral cyclophosphamide initially and subsequently Rituximab. Four months later his creatinine was 1.2 mg/dL, improved from a peak level of 7.5mg/dL with plasma exchange and oral cyclophosphamide.

Discussion: Anti GBM disease had been associated with alveolar injury from exposure to hydrocarbons or smoking. The presence of the erythrocyte casts and positive anti GBM antibody in patients with vaping associated lung injury raises the possibility exposure to hydrocarbons or smoking. The presence of the erythrocyte casts and positive anti GBM antibody in patients with vaping associated lung injury raises the possibility exposure to hydrocarbons or smoking. The presence of the erythrocyte casts and positive anti GBM antibody in patients with vaping associated lung injury raises the possibility exposure to hydrocarbons or smoking.

PO1954

Isolated ANCA Renal Arteritis
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Introduction: Vasculitis associated with antineutrophil cytoplasmic antibodies (ANCA) usually causes acute kidney injury (AKI) through crescentic glomerulonephritis (GN). Renal ANCA arteritis without GN is often accompanied by prominent interstitial nephritis (IN). We present a case of AKI due to ANCA renal arteritis without significant GN or IN.

Case Description: An 84-year-old woman with hypertension, chronic kidney disease [baseline creatinine (Cr) 1.6 mg/dL], and prior right nephrectomy for renal cell carcinoma presented with nausea and anorexia. She was admitted the prior month for pyleonephritis and AKI and discharged to a rehab facility. On return, her serum Cr was 4.9. She was readmitted and started on hemodialysis. Urine microscopy was consistent with acute tubular injury (ATI), but also showed non-glomerular hematuria which persisted on several UAs. Urine protein was 2.1 mg/dL. Both p-ANCA (1:1280) and MPO (>8 AU) were strongly positive. She was given IV corticosteroids and renal biopsy was obtained [Figure]. She was evaluated by rheumatology and felt to have renal-limited disease. She was treated with plasma exchange followed by rituximab, but a week later she opted to stop dialysis and transition to comfort measures and she died 2 days later.

Discussion: Most patients with AKI from ANCA-associated vasculitis will have GN, often crescentic. Extraglomerular features on biopsy of ANCA disease are common and include IN and arteritis/arteriolitis, but often parallel the activity of glomerular disease. Prior case reports of ANCA renal disease without GN have featured prominent IN with or without arteritis/arteriolitis. This case of marked necrotizing arteritis, minimal IN, and absent GN represents a rare phenotype of ANCA renal disease.

PO1953

Sabotaged: Hydralazine-Induced ANCA Glomerulonephritis
Larissa Kruger gomes, Esilida Sula Karreci, Krishna A. Agarwal, Ruth Schuman, Jeffrey H. William, Stewart H. Lecker, Isaac E. Stillman. Beth Israel Deaconess Medical Center, Boston, MA.

Introduction: While usually well known to cause SLE-like syndrome, hydralazine (HZ) can also be involved in a different clinical scenario with ANCA vasculitis.

Case Description: 77y/o woman with hypertension and COPD presents with 2 days of hemoptysis and hematuria, requiring urgent intubation. CT scan reveals multifocal infiltrates and bronchoscopy shows diffuse alveolar hemorrhage. Labs showed Hb of 6.8 and Cr of 1.7. Dysmorphic RBCs were seen in the urine sediment and proteinuria at 1.2g/dL. Given concern for anti-GBM, she received IgG methylprednisolone and plasma exchange. ANA 1:1280 with MPO-ANCA levels >8.0 U, along with positive anti-histone and SCL-70 antibodies, but with negative anti-GBM and ds-DNA. Kidney biopsy showed pauci-immune crescentic GN with trace staining for IgA, IgM, C3, kappa and lambda. As she had been on HZ, the diagnosis of HZ-induced ANCA-associated vasculitis was made. Offending agent was held and cyclophosphamide was started. After 2 months, kidney function returned to baseline, with resolution of proteinuria and hematuria.

Discussion: In patients with HAV unusually high titer of MPO are present and can be used to differentiate drug-associated and spontaneous cases. A minority of patients can also present with other positive antibodies, such as ds-DNA, anti-histone, or Scl-70. As HZ can also cause SLE-like pattern of injury, it can be difficult to obtain a diagnosis based on serologies alone; biopsy is essential for diagnosis and prognosis. The treatment of HAV involves not only removing the inciting agent, but also further immunosuppression, as HZ is thought to lead to increased expression of MPO and PR3 breaking neutrophils tolerance and leading to auto-antibody formation. When choosing a treatment strategy, guidelines for spontaneous ANCA should be followed, in this particular case, as she had severe lung involvement, cyclophosphamide was chosen.
PO1955

Rare Case of Silicosis-Induced Pauci-Immune Glomerulonephritis
Sandheep Venkataraman, Matthew Ray, James F. Dylewski. University of Colorado, Denver, CO.

Introduction: Pauci-immune glomerulonephritis(GN) caused by ANCA was first described in 1982. Most cases are idiopathic, however, ANCA vasculitis may induced due to certain exposures. Here we report a case of ANCA vasculitis associated with pulmonary silicosis.

Case Description: A 37-year-old man with no prior history presented with anorexia, weight loss, fatigue, and arthralgias for 6 months. He was employed as a sandblaster, stonecutter, and as a mason. On initial exam he was found to have dactylitis and Raynaud’s phenomenon. His presenting creatinine(Cr) was 2.9 mg/dL with urinalysis showing 3+ blood and 1.2 gm proteinuria. Renal ultrasound demonstrated enlarged kidneys bilaterally. Notable serologies were ANA positive 1:1280, p-ANCA positive 1:2560, C3 77 mg/dL, C4 6 mg/dL, and MPO at 78 AU/ml. CT Chest revealed innumerable pulmonary nodules, extensive fibrosis, and mediastinal lymph nodes with eggshell calcifications. Infectious workup was negative. Transbronchial biopsy demonstrated collection of histiocytes containing black pigment without granulomas. Kidney biopsy showed necrotizing crescentic GN, with marked interstitial inflammation and focal intralobular vessel infiltrates. IF and EM was negative, consistent with pauci-immune ANCA vasculitis. Given his history and presentation, he was diagnosed with silica-induced ANCA vasculitis. He was treated with 3 days of IV methylprednisolone, followed by a rapid prednisone taper. He also received IV Rituximab 1 gm on days 0 and 14, plus IV cyclophosphamide 500 mg every 2 weeks for 6 doses starting on day 0. The patient responded well with Cr improving to 1.0 and decreased proteinuria. Unfortunately he relapsed 3 months after last rituximab dose.

Discussion: Silica exposure is most often associated with pulmonary disease but there have been case reports of RPGN associated with it too. The majority of these patients were MPO positive. T-cell dysregulation and endothelial damage from PMNL have been case reports of RPGN associated with it too. The majority of these patients were MPO positive. T-cell dysregulation and endothelial damage from PMNL.

PO1956

ANCA-Negative Small-Vessel Vasculitis with IgG4-Positive Plasma Cell Infiltration: A Case Report and Literature Review
Hui Peng Ge, Cuifang Li, Qiongjing Yuan. Xiangya Hospital Central South University, Changsha, China.

Introduction: Although the histopathology was critically important for differential diagnosis between AAV and IgG4-RD, overlapping morphologies and clinical manifestations put the clinicians in a dilemma of diagnosis sometimes. Here, we described a case of ANCA negative PICG with IgG4-positive plasma cell infiltration.

Case Description: A 60-year-old man patient presented with cough for 3 months and progressive renal impairment for 8 days. He had elevated serum IgG4 level with absence of anti-neutrophil cytoplasmic antibodies (ANCA). Lung CT as shown in Figure 1. Renal biopsy showed severe tubulointerstitial nephritis (TIN) with extensive infiltration of IgG4-positive plasma cells, suggesting a diagnosis of IgG4-related kidney disease(Figure 2). However, the identification of necrotizing glomerulonephritis and crescents forming and the absence of storiform fibrosis and obliterative phlebitis led to a diagnosis of ANCA negative renal small-vessel vasculitis. The condition was improved by using corticosteroids and cyclophosphamide at beginning.

Discussion: ANCA negative cannot exclude the diagnosis of AAV. The elevated serum IgG4 and/or abundant IgG4-positive cell infiltration can act as one of the manifestations in AAV. ANCA-negative pauci-immune crescentic glomerulonephritis (PICG) might represent an independent disease entity from ANCA positive PICG. Besides, IgG4-related disease (IgG4-RD) is an exclusive diagnosis and needs to be differentiated from vasculitis and other diseases. It is suggested that ANCA-negative PICG with elevated serum IgG4 and/or abundant IgG4-positive cell need to be further studied.

Figure 1. Lung CT in different periods.

Figure 2. Histological findings of the kidney.

PO1957

Adalimumab-Associated Pauci-Immune Glomerulonephritis: Coincidence or Causation Effect?
Nirav N. Patel, Emma Spangler, Pavan Annamuraju. Johnston Memorial Hospital, Abingdon, VA.

Introduction: Adalimumab is a TNF-blocker used in the treatment of hidradenitis suppurativa (HS). Infections, lupus-like syndrome, and lymphoma are known safety concerns with TNF-blockers. We report a rare case of adalimumab associated pauci-immune crescentic GN (PICGN) in a patient with HS.

Case Description: A 19-yr-old male with a history of HS on adalimumab for 6 months was seen on 4/1/20 with a fever of 103°F, cough & epistaxis for 2 weeks. CT sinuses showed polypos and sinusitis. He was treated with antibiotics for sinusitis. CT chest, nasal PCR for COVID-19, blood, and urine cultures were negative. By hospital day 8, he remained febrile and developed AKI [Creatinine (Cr) 9 mg/dl; baseline of 0.8 mg/dl]. Physical exam showed chronic scarred skin lesions on the chest and axilla with no signs of infection or rash. Hematuria and microalbuminuria were noted. Ultrasound showed renomegaly. Inflammatory markers were high (CRP 254 mg/L, Ferritin 1059 ng/mL). PR3-ANCA antibody was positive 530 IU/mL. A renal biopsy confirmed PICGN (Fig 1). Bone marrow biopsy showed no evidence of hemophagocytosis. The patient was treated with pulse doses of steroids and rituximab and plasma exchange (peak cr 6.4 mg/dl). On a 3-week follow up creatinine improved to 1.8 mg/dl suggesting a favorable outcome. The patient never required dialysis.

Discussion: AKI, microscopic hematuria, and proteinuria can be seen in a febrile illness. However, epistaxis and renomegaly prompted us to check for ANCA serology. To our knowledge, this is the first case of adalimumab associated PICGN in a patient with HS. Interestingly, our patient is much younger compared to previously reported cases (mean 51.4 years). It is possible that adalimumab may be unrelated to the vasculitis; however, due to a strong temporal association, it was felt to be the culprit agent. Nephrologists must be aware of the renal side effects of this class of drugs.
A Case of C-ANCA Associated Retropertioneal Fibrosis and Periarthritis
Vinay Srinivasan. Darling Downs Health Service, QLD Australia Darling Downs Hospital and Health Service, Toowoomba, QLD, Australia.

Introduction: Granulomatosis with Polyangiitis (GPA) is a type of small vessel vasculitis that has prevalence rate of 25-160 cases per million population, and a incidence rate of 0.5 cases per 100,000 population per year. Clinical features of the disease involve the respiratory and renal systems. However, large vessels such as the Aorta and retropertioneal tissue are rarely involved.

Case Description: We present the case of a middle-aged male who presented with an obstructive nephropathy in which abdominal CT revealed a soft tissue mass encompassing the Aorta and Inferior Vena Cava causing obstruction of the Left ureter. Despite ursodiol stenting, serum creatinine failed to improve. Furthermore urinary analasyst demonstrated an active urinary sediment; hemoproteinuria. Serum c-ANCA and PR-3 antigen titres were positive. Renal biopsy was performed and confirmed pauci-immune vasculitis. The patient was induced with pulse immunosuppressives and cyclophosphamide and as part of his maintenance treatment received prednisolone and oral cyclophosphamide. On follow up, partial remission has been achieved with his serum creatinine returning to baseline level and proteinuria reduced, though erythrocytes are still evident. Repeat abdominal imaging has revealed a reduction in the size of the soft tissue mass with treatment.

Discussion: Biopsy proven vasculitis has been shown in patients with retropertioneal fibrosis. Few case reports and series have described this association, inferring a pathogenic role of ANCA in the development of retropertioneal fibrosis. Moreover it has been suggested that retro peritoneal fibrosis may be an early clinical manifestation of ANCA associated vasculitides. Consequently, ANCA associated vasculitis should be considered in the differential diagnosis of any patient who has Retropertioneal fibrosis and an active urinary sediment

A Rare Case of ANCA-Negative Pauci-Immune Crescentic Glomerulonephritis in an Elderly Woman
Oscar A. Garcia Valencien, Eduardo Edelman Saul, Yanezy Olivera Arencibia, Marte A. Sosa. University of Miami / Jackson Memorial Hospital, Miami, FL.

Introduction: Acute kidney injury is usually multifactorial with a broad differential diagnosis. Of those, rapidly progressive glomerulonephritis (RPGN) requires special attention as it represents a true diagnostic and therapeutic emergency that can lead to irreversible kidney failure.

Case Description: A 92-year-old female with a history of Chronic Kidney Disease Stage III, Diabetes Mellitus type II, hypertension, and recurrent deep vein thrombosis sent to the ER for evaluation of rapidly worsening kidney function sent on outpatient laboratories for assessment of poor oral intake and fatigue for 2 weeks. On arrival, BP was 133/49mmHg, HR 70bp, temperature 36.9°C, RR 17 rpm and SO2 of 99%. Mental status was at baseline and physical exam was unremarkable. Laboratory data were remarkable for serum creatinine of 10.55 mg/dl from baseline of 1.8 mg/dl, potassium level of 6 mEq/L and bicarbonate of 17 mEq/L. Urinalysis showed proteinuria (3+), hematuria (344 RBCs/hpf) and leukocytosis (68 WBC/hpf). Urine protein creatinine ratio of 2.4. No acute EKG changes. Renal ultrasound demonstrated increased bilateral renal size with an increased medulla from 3.5cm-1.5cm. CT-Abdominal/Pelvis showed bilateral pleural effusions and groundglass nodularity within the right middle and lower lobes. Kidney biopsy showed linear GBM staining for IgG4, with glomerular necrosis, crescents, and unusually prominent endocapillary proliferation (Figure). Treatment included diuretics, antibiotics, IV methylprednisolone, oral cyclophosphamide, and 8 plasma exchanges over 11 days. Serum anti-GBM was undetectable after 2 days. He progressed to dialysis-requiring ESRD over the next 6 weeks: a repeat kidney biopsy showed persistent crescentic GN with endocapillary proliferation and strong linear IgG4 staining, despite repeatedly negative serum anti-GBM.

Discussion: This case highlights complexities in the pathogenesis and diagnosis of anti-GBM disease. RPGN was likely triggered by parainfluenza infection, a rarely associated diagnosis. Low anti-GBM antibody levels were likely explained by the poor sensitivity of ELISA to detect IgG4. Finally, prominent endocapillary proliferation is characteristic of “atypical anti-GBM disease”, yet serum anti-GBM was positive in this case.

Seronegative Anti-GBM: A Spectrum of Disease
Alisa Illescas, Michael B. Kuperman, Sara Combs, J Pedro Teixeira.

Introduction: Glomerulonephritis (GN) due to anti-GBM disease is usually associated with detectable antibodies against the NC1 domain of the type IV collagen α3 chain [NC1-α3 (IV)], but a subset of seronegative atypical GN disease has been described with no lung involvement, non-crescentic GN on biopsy, and indolent course. We present a case of anti-GBM disease that is neither typical nor atypical.

Case Description: A 56-year-old woman with hypertension and obesity underwent renal biopsy after routine labs showed rise in creatinine (Cr) above baseline of 1.5 mg/dl 6 months prior and hemoproteinuria on UA. The results [Figure] prompted transfer to our center. On admit, she noted mild chronic dyspea but denied cough or hemoptysis. She had mild hypertension (146/80) and trace edema. Cr had risen to 4.5, urine protein was 3.4 g/g Cr, and chest x-ray was clear. She was started on IV corticosteroids and plasma exchange (PLEX). Anti-GBM IgG [multiplex bead assay, ARUP], drawn prior to PLEX, was negative (4 AU/mL, upper limit normal 19). She was treated with IV cyclophosphamide and 7 PLEX sessions over 2 weeks and her Cr stabilized at 3.5. She avoided dialysis and was discharged on prednisone with plans to continue monthly cyclophosphamide.

Discussion: Our patient exhibited an intermediate phenotype of anti-GBM disease with crescentic GN, subacute Cr rise, no lung involvement, and negative serology. Modern assays for anti-GBM antibody have a sensitivity of 94-100%. However, negative serology is also seen in rare cases of anti-GBM GN due to antibodies against epitopes of the GBM other than NC1-α3 (IV). Our case illustrates that a negative anti-GBM antibody does not exclude anti-GBM disease which is ultimately a pathologic diagnosis. It also suggests a spectrum exists between classic and atypical anti-GBM disease, but favorable outcome is possible regardless with biopsy-directed therapy.

3) protein by UA; negative/normol C3, C4, ANA, anti-dsDNA, ANCA; viral respiratory PCR positive for parainfluenza; serum anti-GBM 15µ/ml (nl <10µ/ml). CT Thorax showed bilateral pleural effusions and groundglass nodularity within the right middle and lower lobes. Kidney biopsy showed linear GBM staining for IgG4, with glomerular necrosis, crescents, and unusually prominent endocapillary proliferation (Figure).

Treatment included diuretics, antibiotics, IV methylprednisolone, oral cyclophosphamide, and 8 plasma exchanges over 11 days. Serum anti-GBM was undetectable after 2 days.

He progressed to dialysis-requiring ESRD over the next 6 weeks: a repeat kidney biopsy showed persistent crescentic GN with endocapillary proliferation and strong linear IgG4 staining, despite repeatedly negative serum anti-GBM.

Discussion: This case highlights complexities in the pathogenesis and diagnosis of anti-GBM disease. RPGN was likely triggered by parainfluenza infection, a rarely associated diagnosis. Low anti-GBM antibody levels were likely explained by the poor sensitivity of ELISA to detect IgG4. Finally, prominent endocapillary proliferation is characteristic of “atypical anti-GBM disease”, yet serum anti-GBM was positive in this case.

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A Case of Lupus Podocytopathy (LP) with Focal Segmental Glomerulosclerosis (FSGS): Is It Time to Add LP to the Next Revision of the Classification of Lupus Nephritis?


Introduction: Lupus podocytopathy is not included in the commonly used International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification of Lupus Nephritis (LN). It has been reported in literature for the last 20 years. LP can have pathologic transition with variable outcomes. We describe a case of LP with FSGS in a young male patient with subsequent relapse.

Case Description: 25 year old male with past history of lupus without nephritis and chronic immune-mediated thrombocytopenia presented with generalized fatigue. Physical exam revealed diffuse rash and vital signs were within normal limits. Relevant laboratory findings included platelet count of 21000/µl, acute kidney injury with creatinine (Cr) of 1.6 mg/dl (baseline Cr of 0.8 to 1.1 mg/dl), spot urine protein creatinine ratio of 43.3 g, 24 hour urine protein of 4.1 g. Low Cr and C4, hemoglobin of 9.6 g/dl and WBC count of 3.6/µl. Serology was positive for ANA, dsDNA and SAA indicating active lupus flare. Left kidney biopsy showed mild mesangial expansion, no endocapillary proliferation and subtotal (<80%) podocyte foot process effacement. No subendothelial or subepithelial deposits were seen. He was treated with pulse dose steroids followed by oral steroids and serum Cr came back to baseline. Subsequently he was treated with mycophenolate mofetil 2 g/day. At 2 weeks, proteinuria came down to 1.8 g/day and by 12 weeks he achieved remission. However at 6 months, he had urine protein of 8.9 g in 24 hours with increase in Cr to 2.4 from 1.6, suggesting relapse.

Discussion: The presence of minimal or no capillary wall immune deposits with or without mesangial proliferation and effacement of podocyte foot processes in the setting of nephritic range proteinuria is collectively termed as LP. LP must be considered in almost half of all patients diagnosed with Systemic Lupus Erythematosus (SLE). While nephrotic syndrome (NS) in these patients is usually due to type IV/V Lupus Nephritis (LN), it may in rare instances occur secondary to minimal change disease (MCD), a pathologic transition with variable outcomes. We describe a case of LP extending this distinct entity in the classification of lupus nephritis.

Oliglciguat Protects Renal Function and Podocytes in In Vivo and In Vitro Models of Podocytopathies

Emmanuel S. Buys,1 Ehestham Ariz,2 Suzana Marusic,1 Deepak Nihalani,2 1Cyolvern, Cambridge, MA; 2Medical University of South Carolina, Charleston, SC; Hook Laboratories, Lawrence, MA.

Background: The nitric oxide (NO) receptor soluble guanylate cyclase (sGC) is a signal-transduction enzyme producing the secondary messenger cGMP. Impaired NO-cGMP signaling is associated with renal dysfunction. sGC stimulators molecules that enhance NO-mediated cGMP signaling, improve renal function in animal models of cardiac injury.

Methods: We studied the renoprotective effects of oliglciguat, a clinical-stage sGC stimulator, by studying in vitro and in vivo models of glomerular injury.

Results: In an acute focal segmental glomerulosclerosis (FSGS) model of glomerular injury induced by nephrotoxic serum (NTS), treatment with oliglciguat attenuated proteinuria and kidney pathology when compared to vehicle-treated mice. Additionally, oliglciguat treatment prevented NTS-induced mislocalization of the slit diaphragm proteins synaptopodin and nephrin. Ultrastructural analysis by transmission electron microscopy revealed that podocyte foot process morphology was preserved in mice treated with oliglciguat. To further assess the protective effect of sGC stimulation on podocytes, human podocytes injured by exposure to protonsulfate (PS) were treated with oliglciguat. Oliglciguat treatment restored PS-induced damage of podocyte actin cytoskeleton organization and the localization of podocyte cell membrane proteins. The genetic MRL/MpJ-Fas+/+ mouse model of systemic lupus erythematosus (SLE), disease progression, assessed by increased serum creatinine, was reversed in mice treated with the positive control cyclophosphamide or with oliglciguat than in vehicle-treated mice. Fewer kidney lesions (interstitial infiltrates, tubular atrophy, tubular epithelial vacuolation, tubular and interstitial lesions, and glomerular lesions) were observed in mice treated with cyclophosphamide or oliglciguat than in vehicle-treated mice. In contrast to cyclophosphamide, oliglciguat treatment did not result in leukenopins, reduction in spleen weight, or lower anti-dsDNA antibody in serum, suggesting that oliglciguat did not impact the auto-immune aspect of SLE.

Conclusions: In summary, oliglciguat, an orally bioavailable sGC stimulator, exhibits significant renoprotective effects in nonclinical models and warrants further evaluation for the treatment of FSGS, other podocytopathies, or nephropathies associated with diseases such as sickle cell disease.

Funding: Commercial Support - Cyolvern

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Minimal Change Disease in Systemic Lupus Erythematosus: An Infrequent Variant

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Introduction: Lupus Nephritis (LN) is thought to complicate the disease course of almost half of all patients diagnosed with Systemic Lupus Erythematosus (SLE). While nephrotic syndrome (NS) in these patients is usually due to type IV/V Lupus Nephritis (LN), it may in rare instances occur secondary to minimal change disease (MCD), a phenomenon known as Lupus Podocytopathy (LP). We report a case of a young female with LP with concomitant Acute Tubular Necrosis (ATN).

Case Description: 40 year old female, known case of SLE (not on maintenance immunosuppression) and Hypertension presented with bright red blood per rectum and dyspnea for 2 weeks. Review of systems was pertinent for generalized swelling and facial rash. On initial assessment, she was hypertensive and physical exam revealed facial rash and vital signs were within normal limits. Relevant laboratory findings included platelet count of 21000/µl, acute kidney injury with creatinine (Cr) of 1.6 mg/dl, spot urine protein creatinine ratio of 43.3 g, 24 hour urine protein of 4.1 g. Low Cr and C4, hemoglobin of 9.6 g/dl and WBC count of 3.6/µl. Serology was positive for ANA, dsDNA and SSA indicating active lupus flare. Left kidney biopsy showed mild mesangial expansion, no endocapillary proliferation and subtotal (<80%) podocyte foot process effacement. No subendothelial or subepithelial deposits were seen. He was treated with pulse dose steroids followed by oral steroids and serum Cr came back to baseline. Subsequently he was treated with mycophenolate mofetil 2 g/day. At 2 weeks, proteinuria came down to 1.8 g/day and by 12 weeks he achieved remission. However at 6 months, he had urine protein of 8.9 g in 24 hours with increase in Cr to 2.4 from 1.6, suggesting relapse.

Discussion: The presence of minimal or no capillary wall immune deposits with or without mesangial proliferation and effacement of podocyte foot processes in the setting of nephritic range proteinuria is collectively termed as LP. LP must be considered in almost half of all patients diagnosed with Systemic Lupus Erythematosus (SLE). While nephrotic syndrome (NS) in these patients is usually due to type IV/V Lupus Nephritis (LN), it may in rare instances occur secondary to minimal change disease (MCD), a phenomenon known as Lupus Podocytopathy (LP). We report a case of a young female with LP with concomitant Acute Tubular Necrosis (ATN).

Case Description: 40 year old female, known case of SLE (not on maintenance immunosuppression) and Hypertension presented with bright red blood per rectum and dyspnea for 2 weeks. Review of systems was pertinent for generalized swelling and facial rash. On initial assessment, she was hypertensive and physical exam revealed facial swelling, discoid rashes and 2+ lower Extremity edema bilaterally. Workup revealed Normocytic Anemia, Acute Kidney injury, Hyperkalemia and Metabolic Acidosis. Urine studies showed nephrotic-range proteinuria and hematuria but were negative for casts. Free K/L ratio was high at 2.32 and C3 levels low at 42 mg/dl. Ultrasound guided kidney biopsy showed mild thickening of GBM and dilated tubules with diminished brush borders in the absence of crescentic changes. Electron Microscopy noted diffuse fusion of foot processes, along with rare intramembranous deposits. Immunofluorescence revealed a full house staining pattern within the Mesangium and the patient was diagnosed with Lupus Podocytopathy with concurrent LN Type 1. Substantial reduction in proteinuria was noted with a brief course of Prednisone.

Discussion: Our patient with SLE presented with NS and AKI, features typical of membranous/proliferative LN. Interestingly, her biopsy findings provided little evidence of endocapillary proliferation or sub-epithelial IC deposits and were more consistent with MCD as suggestive of Lupus podocytopathy. LP is rare to the extent that it does not form part of the official WHO classification for LN and has only been described a handful of times in prior literature, mostly in the form of case reports. However, given its prognostic implications, LP remains an important consideration in the evaluation of NS in SLE patients. While patients with Type IV/V LN require aggressive immunosuppressive therapy, patients with LP frequently respond well to steroids alone and have a much slower progression of disease.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
PO1966
A Novel In Vivo Approach to Capture the Podocyte Foot Process Proteome
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Background: Podocytes are an extraordinary cell of the kidney filtration system with their tentacle-like foot processes flowing out from each cell body and interdigitating with neighboring processes. Proper kidney function relies on these cells and the complex architecture created by the interdigitating processes. They are the most critical component of the glomerular filter. Podocytes are injured and their integrity is compromised in the majority of kidney diseases leading to progressive proteinuria. However, we know little about the full complement of proteins localized to the foot process and how they change with disease.

Methods: We have developed a novel genetic mouse model capable of generating a spatially restricted, real-time, in vivo proteome. Recently, proximity labeling techniques have been developed to provide snapshots of spatially localized proteomes. The BioID method utilizes a promiscuous bacterial biotin ligase flexibly linked to a target protein of interest to biotinylate proteins within the vicinity. We have adapted this approach to identify the podocyte foot process proteome. Using podocin as a handle, we have modified the Nphs2 (podocin) locus to link the mutated, promiscuous BirA biotin ligase to podocin (Nphs2BioID). A flexible, 13x linker allows for a generous proximity around podocin, thereby capturing the broad proteome of the podocyte foot process.

Results: We have obtained viable Nphs2BioID/+ animals. Utilizing immunostaining, we have confirmed the proper expression and localization of the podocin-BioID. The HA-tagged biotin ligase appended to podocin colocализed with podocin and other foot process proteins. To test it’s functionality, we injected biotin dialy for 7 days. This produced an increase of biotinylated proteins in Nphs2BioID/+ podocytes versus wild type biotin injected controls or uninjected Nphs2+/+ mice. We have affinity purified the biotinylated proteins from glomerular isolations and are currently performing proteomic analyses.

Conclusions: We have generated the first of it’s kind in vivo mouse model to specifically identify the spatially localized proteome of the podocyte foot process. Our proteomics results will provide unprecedented insights into the make-up of this highly specialized and critical structure.

Funding: NIDDK Support, Other NIH Support - Vanderbilt O'Brien Kidney Center

PO1967
Soluble RARRES1 Induces Apoptosis of Podocytes to Promote Progression of Kidney Disease
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Background: Podocyte loss is a major event leading to the progression of focal segmental glomerulosclerosis (FSGS) and diabetic nephropathy (DN). Here, we found that retinoic acid receptor responder protein 1 (RARRES1) contributes to the podocyte loss in FSGS and DN.

Methods: We determined the role of RARRES1 in human and mouse with FSGS and DN. We investigated the mechanisms of RARRES1 in cultured human podocytes.

Results: The expression of RARRES1 increased in the glomeruli of patients with FSGS and DN and correlated with eGFR. Single-cell RNA-sequencing of the kidney showed that RARRES1 expressed highly in podocytes. Immunostaining confirmed that podocyte expression of RARRES1 increased in patients with DN and FSGS as compared to MCD. RARRES1 expression was strongly induced by TNF-α in cultured human podocytes. RNA-sequencing of podocytes with RARRES1 overexpression revealed genes enriched in apoptosis. RARRES1 was cleaved into a soluble RARRES1 and the cleavage site was mapped at the aa70. Overexpression of wild RARRES1 or adding soluble RARRES1 in cultured human podocytes induced apoptosis, while overexpression of RARRES1 cleavage mutant lost the apoptotic effect. Further, we showed that soluble RARRES1 underwent endocytosis to interact with intracellular RIOK1, leading to the activation of p53 and apoptosis in podocytes. In vivo, podocyte-specific overexpression of RARRES1 resulted in marked glomerular injury and albuminuria in mice, while the overexpression of RARRES1 cleavage mutant had no renal phenotype. Finally, knockdown of RARRES1 in podocytes ameliorated kidney injury in mice with adriamycin-induced nephropathy.

Conclusions: We demonstrate a new role and mechanism of RARRES1 in regulation of podocyte apoptosis in glomerular disease, as summarized in the Figure. TNFα induces expression of RARRES1, which is cleaved, then undergoes endocytosis to interact with intracellular RIOK1, leading to the activation of p53 and apoptosis. High RARRES1 expression promotes the progression of FSGS and DKD.

Funding: Government Support - Non-U.S.

PO1968
The Glomerulus-on-a-Chip as a System to Unravel Novel Membrane Attack Complex (MAC)-Independent Role of Complement in Membraneous Nephropathy
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Background: Primary membranous nephropathy (MN) is a leading cause of nephrotic syndrome in adults worldwide due to the deposition of anti-podocyte-antibodies against in the glomerular subepithelial space. While complement deposition is thought to play a crucial pathogenic role, the exact effector mechanism of complement in MN is unclear due to the lack of in vitro and in vivo systems that recapitulate human disease. We have developed a novel glomerulus-on-a-chip system (GOAC) using human primary podocytes and human glomerular endothelial cells (GEC) in combination with OrganoPlates and assessed the functional response to human MN serum and the role of MAC deposition and C3a/C3aR1 signaling in MN pathogenesis.

Methods: Glomerulus chips were cultured with serum from anti-PLA2R + MN patients or healthy individuals. Functional response was assessed by albumin permeability assay to evaluate selectivity-permeability. Role of MAC and C3a/C3aR1 signaling pathway in glomerular filtration barrier damage was assessed by immunofluorescence and functional analysis while mechanisms of action were explored by PCR arrays, Western Blotting and immunostaining. Results were confirmed in vitro using podocytes on which C3aR1 was silenced and in vivo using a C3aR1 KO mouse model.

Results: Following exposure to sera from MN patients, we have confirmed deposition of human IgG on podocytes and formation of MAC complex, accompanied by albumin leakage. GOAC supplemented with C3aR1 antagonists as well as GOAC using podocytes in which C3aR1 was silenced were able to prevent glomerular filtration damage on the GOAC kidney confirmed by rescue of permeability efficiency, while inhibition of MAC formation by protein S (an inhibitor of MAC formation) did not significantly reduce GOAC permeability.

Conclusions: We have successfully developed a glomerulus-on-a-chip system that closely mimics the GFB structure and provides a powerful tool for studying renal regenerative and disease mechanisms in proteinuric diseases. Using this model, we showed that C3a/C3aR signaling plays a dominant role in complement-mediated MN pathogenesis.

Funding: Private Foundation Support

PO1969
Dach1 Is Essential for Maintaining Normal Podocytes
Keiko Tanaka, Taiji Matsuoka. Department of Basic Medicine, Tokai University School of Medicine, Isehara, Japan.

Background: Dach1 is a transcription factor, determining cell fates in various organs. Dach1 polymorphism has been reported to be associated with nephrotic syndrome and chronic kidney diseases. We previously found that Dach1 was highly expressed in normal podocytes and rapidly disappeared after induction of podocyte injury, similarly to WT1. We, therefore, aimed to elucidate the function of Dach1 in normal podocytes in vivo.

Methods: Podocyte-specific Dach1-knockout (KO) mice were generated by mating Dach1lox/lox mice with Nphs1-Cre or Nphs2-CreERT2 mice. Podocyte injury was evaluated by urinary analysis (SDS-PAGE) and histology. In addition, we analyzed primary cultured podocytes of Dach1 overexpressing knock-in transgenic (KI) mice (n=9), in which Dach1 is expressed under the control of Rosa26 promoter.

Results: Although the efficiency of Cre-mediated recombination was not high, all of the congenital Dach1/KO mice (n=20, more than 4 weeks old) presented abnormal albuminuria. Seven out of the 11 (63%) mice histologically analyzed showed focal segmental glomerulosclerosis. Injured podocytes lacked Dach1 staining, whereas intact podocytes retained Dach1. When Dach1 KO was induced in adult mice, the mice showed abnormal albuminuria within two weeks. Immunostaining revealed that podocytes lacking Dach1 causes leakage of albumin, while retaining WT1 protein. Since endogenous Dach1

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expression in podocytes is very high compared with transgenic expression of Dach1 driven by the Rosa26 promoter, we analyzed primary cultured podocytes, in which endogenous Dach1 was downregulated. Dach1 mRNA was 3.8-fold higher (p < 0.0007) in Dach1-KI podocytes than in control podocytes. We previously found that Dpp4 is one of the candidate target genes of Dach1 by knockdown experiments. Dpp4 mRNA in Dach1-KI podocytes was found to be increased (1.5-fold, p < 0.0002).

Conclusions: These results indicate that Dach1 is important in maintaining normal podocyte integrity, and Dach1 gene deficiency induces podocyte injury.

PO1970
Dysregulated Dynein-Mediated Vesicle Traffic: Is a New Mechanism of FSGS
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Background: Focal segmental glomerulosclerosis (FSGS) is a deteriorating kidney disease with poor prognosis. The lack of understanding of its mechanism has hindered the development of treatment. Mutations in IN2 cause FSGS characterized by a podocytopathy with mismatched slit diaphragm (SD) protein critical for the integrity of the glomerular filtration barrier (GBF). This feature has been found in FSGS of other etiologies, making IN2 related podocytopathy a good model to dissect the disturbed vesicle trafficking in podocytopenias prone to FSGS. By yeast two hybridization screening we identified the interaction of IN2 with Dynl1, a dynem component. We hypothesized that IN2 regulates dynein mediated vesicle trafficking, which shuttles endocytosed protein to proteolytic system. This interaction could be disrupted by pathogenic mutations in IN2, suggesting dysregulation of dynein mediated trafficking is an underlying mechanism in focal segmental glomerulosclerosis disease.

Methods: The IN2-Dynl1 interaction was confirmed by yeast mating and CO-IP. The dysregulated dynein mediated trafficking of nephrin was investigated in cultured podocytes by fluorescent based and surface biotinylation based assays, and time-lapse imaging in vitro; and was also observed in the purinergic aminonucleotide induced nephrinopathy (PAN) of IN2 transgenic mice with knockin (KI) of R218Q, a pathogenic mutant that disrupts IN2-Dynl1 interaction.

Results: 1. We demonstrated that IN2 limited dynein mediated retrograde trafficking of nephrin by binding to and sequestering Dynl1, a component essential for the integrity of dynein. 2. R218Q KI podocytes illustrated an impaired recycling of nephrin with enhanced recruitment of dynein components, which could be rescued by targeting dynein transport pathway using Cilobrevin D (Dynein inhibitor), dominant negative Dynactin 1, siRNA for Dynl1 or overexpression of wildtype IN2 (to sequester Dynl1). 3. PAN of R218Q KI mice was characterized by increased recruitment of Dynl1 to nephrin, correlated to increased ubiquitination and decreased surface nephrin, suggesting an enhanced dynein trafficking pathway underlies the impaired functional trafficking of nephrin, disintegrity of SDs and malfunction of the GBF.

Conclusions: Recognition of the dysregulated dynein mediated trafficking of SD protein has enlightened a new understanding and therapeutic targets for IN2 related podocytopathy and FSGS.

Funding: NIDDK Support

PO1971
Podocyte Cell Cycle Activation During CKD Progression
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Background: Podocytes, quiescent cells, seem not capable of regeneration to compensate for their loss during CKD progression. Their only adaptive response to injury is their detachment from the basal membrane and cell death. The cell cycle phases modulate this “mitotic catastrophe”. The cell cycle phases are not known. To study the cell cycle in CKD, we used an Alport Syndrome (AS) mouse model characterized by podocyte loss, combined with the Fucci technology which allow the identification of the cell cycle phases using fluorescent reporters: red for G1/S, green for S/G2/M.

Methods: We established a mouse model where Fucci proteins are under the control of Nphs2 gene (podocytes specific) and crossed these mice with AS mice to generate AS-Pod-Fucci mouse. Using flow cytometry, we isolated and evaluated podocytes in different cell cycle phases in WT (wild type and female) and AS-Pod-Fucci mice (hemizygote males; heterozygote, Ht females) and perform proteomics in NPHS2-Cre; Z/EG mice. Using flow cytometry, we isolated and evaluated podocytes in different cell cycle phases (G1, S, G2/M) and performed proteomics in NPHS2-Cre; Z/EG mice.

Results: 1. We demonstrated that INF2 limited dynein mediated retrograde trafficking of nephrin by binding to and sequestering Dynl1, a component essential for the integrity of dynein. 2. R218Q KI podocytes illustrated an impaired recycling of nephrin with enhanced recruitment of dynein components, which could be rescued by targeting dynein transport pathway using Cilobrevin D (Dynein inhibitor), dominant negative Dynactin 1, siRNA for Dynl1 or overexpression of wildtype IN2 (to sequester Dynl1). 3. PAN of R218Q KI mice was characterized by increased recruitment of Dynl1 to nephrin, correlated to increased ubiquitination and decreased surface nephrin, suggesting an enhanced dynein trafficking pathway underlies the impaired functional trafficking of nephrin, disintegrity of SDs and malfunction of the GBF.

Conclusions: Recognition of the dysregulated dynein mediated trafficking of SD protein has enlightened a new understanding and therapeutic targets for IN2 related podocytopathy and FSGS.

Funding: NIDDK Support

PO1973
RNA Sequencing and ATAC-Seq Reveal Gene Profiles in Injured Podocytes in Mice, and Podocyte-Specific Hypoxia Inducible Factor 2a Deletion Protects from Adriamycin-Induced Podocyte Injury
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Background: Roles for hypoxia-inducible factor (HIF) in kidney diseases have been controversial. Upregulation of HIF expression is believed to be protective in kidney from acute injury, while we and others showed that HIF aggravates chronic fibrosis. In podocytes, deletion of VEGFR caused progressive glomerular damage, prevented by overexpression of hypoxia inducible factor 2a. Here, using podocyte-specific HIF-2α deletion mice, we tested effects of HIF-2α deletion on gene profiles in injured podocytes.

Methods: HIF-2αCre or HIF-2αCre mice were crossed with either Nphs1-2 or Z-Cre mice. HIF-2αCre; Nphs1-2 or Z-Cre mice were further crossed with Z/E.G mice that express GFP only in cells where Cre is active. At 8 weeks old, the mice were given Adriamycin (12 mg/kg). After two weeks later, urine and serum were harvested. Creatinine and albumin levels in urine and serum, and blood urea nitrogen levels in serum were measured with ELISA kits. Podocytes were isolated from HIF-2αCre; Z/E.G mice by flow sorting and RNAseq analysis. The sequencing was performed by single cell RNAseq and the sequencing data was analyzed using star algorithm.

Results: HIF-2αCre; Nphs1-2Cre showed preservation of foot process morphologies and functions, and significantly less proteinuria compared to the WT littermates after being subjected to Adriamycin, while HIF-1αCre; Nphs1-2Cre mice developed a similar degree of proteinuria to that of WT. HIF-1 or 2Cre; Nphs1-2Cre mice showed little GFP expression in podocytes, suggesting that weak penetrance of Nphs1-2Cre led to minimal functional effects. This group was therefore not further evaluated. Podocytes isolated from HIF-2αCre; Z/E.G mice were subjected to RNAseq and ATACseq analysis. In RNAseq, Ndufa12 was among the dysregulated genes. In ATACseq, SMPDL3b was among the highly silenced genes. In vivo, podocyte specific induction of SMPDL3b is sufficient to protect from TNF induced podocyte injury.

Conclusions: Our results identify a new role of SMPDL3b in the uptake of fatty acids, the accumulation of TAGs, EEs and the formation of LDs. Further experiments to understand the exact mechanism by which SMPDL3b expression contributes to the progression of podocyte damage in FSGS are underway.

Funding: NIDDK Support

PO1974
Sphingomyelin Phosphodiesterase-like 3B (SMPDL3b) Affects Podocyte Lipid Metabolism and Lipid Droplets Formation
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Background: Lipid droplets (LDs) play an important role in many biological processes and LD size and number have been linked to several diseases such type 2 diabetes, heart disease, and non-alcoholic fatty liver disease. LD are mainly composed of triglycerides and cholesterol. We previously demonstrated that the accumulation of LDs occurs in glomeruli of experimental models of diabetic kidney disease (DKD), focal segmental glomerulosclerosis (FSGS) and Alport syndrome, and that lipid accumulation in podocytes is one of the factors contributing to disease progression and may be linked to glomerulosclerosis expression. We further demonstrated that glomerulosclerosis expression of sphingomyelin phosphodiesterase like 3b (SMPDL3b), a glycosylphosphatidylinositol (GPI) anchored protein primarily localized at plasma membrane (PM), affects the function of podocytes in FSGS and diabetic kidney disease (DKD). With this study, we aimed at exploring the role of SMPDL3b in fatty acid uptake and in the formation of LDs ultimately contributing to podocyte damage.

Methods: Fatty acid uptake assay, Lipid droplets isolation, Western blotting, Mass spectrometry, Lipolysis, TNF IV injections.

Results: We demonstrate that decreased SMPDL3b expression (sSMPDL3b) in podocytes is associated with increased FATP protein expression, fatty acid uptake and an increased number of LDs. The number of LDs was decreased in podocytes with increased SMPDL3b expression (sSMPDL3b OE). Similarly, TAGs and CE contents were increased in sSMPDL3b when compared to control podocytes. Finally, we demonstrated that the first time that SMPDL3b is present in isolated LDs suggesting a possible role for SMPDL3b in the formation of LDs and in lipolysis. In vitro, podocyte specific induction of SMPDL3b is sufficient to protect from TNF induced podocyte injury.

Conclusions: Our results identify a new role of SMPDL3b in the uptake of fatty acids, the accumulation of TAGs, EEs and the formation of LDs. Further experiments to understand the exact mechanism by which SMPDL3b expression contributes to the progression of podocyte damage in FSGS are underway.

Funding: NIDDK Support

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Underlines represent presenting author.
Conclusions: HIF-2α deletion in podocytes protects podocyte from acute adriamycin injury. Novel genes associated with podocyte injury were discovered by RNAseq and ATACseq of podocytes.
Funding: NIDDK Support

PO1974
Shroom3-FYN Regulates Podometrics via LKB1-AMPK Signaling
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Background: Previously, we showed Shroom3–FYN interaction regulated podocyte cytoskeleton via FYN activation. Intriguingly, globally Shroom3 knockdown mice (CAGS-TG/Shr3 Kd) displayed reduction in glomerular volume-VGlom, podocyte & endothelial fraction of VGlom without podocytopenia [1a].
Methods: To examine mechanism of podometrics regulation by Sh3r, we used Shr3 & FYN Kd human podocytes (hPodo) to study cell protein content & growth regulatory pathways; performed unilateral nephrectomy examining VGlom hypertrophy in remnant kidneys.
Results: At day-7, CAGS-TG mice showed restricted VGlom hypertrophy with reduced expansion of PodoVGlom vs NTGs [1b]. We observed reduced hPodo volume (FSC), Protein:DNA ratios (n=3; P<0.01) & inhibited ribosomal biogenesis (18S RNA) in vitro & in vivo suggesting reduced protein synthesis and FYN to be downstream of Shr3 in regulating hPodo size. Notably, we observed increased AMPK activation, increased p-ULK1 & autophagy (high p-ULK1 and LC3II levels) downstream of AMPK, in vivo studies revealed that Shr3 rats chronically treated with BRL53257 exhibited augmented blood pressure (MAP was 179 ± 15 mmHg vs. 151 ± 11 mmHg), nephromia, albuminuria, and elevation in podocyte calcium in BRL53257 treated Dahl SS rats.
Conclusions: Stimulation of kappa-ORs, but not mG-ORs or delta-ORs, mediated calcium influx in podocytes through activation of TRPC6 channels in rat and human kidney. The effect of BRL53257 was completely abolished when we used the 0 mM calcium media or when SAR7334 (a TRPC6 channel inhibitor) was applied. Triggering the kappa-OR/ TRPC6 pathway induced podocyte cell shape changes via actin cytoskeleton remodeling. In vivo studies revealed that SS rats chronically treated with BRL53257 exhibited significant blood pressure increase (MAP was 179 ± 15 mmHg vs. 151 ± 11 mmHg), nephromia, albuminuria, and elevation in podocyte calcium in BRL53257 treated Dahl SS rats.

PO1975
The Role of Opioid Receptor Signaling in Podocyes and Renal Damage in Dahl Salt-Sensitive Rats
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Background: The rise in opioid use underscores the urgent need to better understand the direct and indirect effects of opioids on renal function, especially in patients with chronic kidney disease (CKD) or hypertension. The extensive use of opioids is strongly correlated with poor cardiovascular outcomes. We hypothesize that stimulation of opioid receptors (ORs) elevates increased cardiac level in podocytes leading to kidney damage and progression of hypertension.
Methods: Freshly isolated glomeruli from Dahl salt-sensitive (SS) rats, human kidneys and immortalized human podocytes were used to elucidate the contribution of specific ORs to podocyte calcium flux. Calcium response in the podocytes was analyzed via ratiometric confocal fluorescent microscopy. For chronic studies Dahl SS rats were on a 0.4% (LS) or 8% (HS) NaCl diet for 14 days with or without a daily intravenous bolus infusion of BRL53257, a potent and selective kappa-OR agonist.
Results: Stimulation of kappa-ORs, but not mG-ORs or delta-ORs, mediated calcium influx in podocytes through activation of TRPC6 channels in rat and human kidney. The effect of BRL53257 was completely abolished when we used the 0 mM calcium media or when SAR7334 (a TRPC6 channel inhibitor) was applied. Triggering the kappa-OR/TRPC6 pathway induced podocyte cell shape changes via actin cytoskeleton remodeling. In vivo studies revealed that SS rats chronically treated with BRL53257 exhibited increased blood pressure (MAP was 179 ± 15 mmHg vs. 151 ± 11 mmHg), nephromia, albuminuria, and elevation in podocyte calcium in BRL53257 treated Dahl SS rats.
Conclusions: Stimulation of kappa-ORs modulates calcium influx in podocytes via TRPC6 channels. The opiate-induced increase in the calcium flux in podocytes is expected to contribute to podocytopathy, proteinuria, kidney injury and progression of salt-induced hypertension. These findings are important to advance our knowledge of the pathogenesis of the development of CKD and hypertension in the context of pain management.

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PO1976
Knockout of the Neonatal Fc Receptor (FcRn) Alters Lysosomal Function in Podocytes
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Background: FcRn is a trafficking protein that diverts monomeric IgG from the lysosome but sorts multimeric IgG and immune complexes (ICs) to the lysosome for processing. FcRn is required in dendritic cells to traffic ICs to the lysosome for proteolytic processing and presentation on MHC II. Podocytes express FcRn and previous work had proposed that podocytes can act as antigen presenting cells. Here we show that cultured podocytes are weak antigen presenting cells (APCs) and that knockout (KO) of FcRn in podocytes does not alter podocyte response to an immune stimulus but does result in significant downregulation of lysosomal function.

Methods: Cultured wild type (WT) and FcRn KO podocytes were treated with interferon gamma (IFNγ) to simulate proinflammatory conditions. MHC II and costimulatory marker expression was assessed by flow cytometry. Antigen presentation was evaluated by examining T cells response when WT or FcRn KO podocytes were treated with ICs and used as APCs. Lysosomal size and cellular location in WT and FcRn KO podocytes were examined using confocal microscopy. WT or FcRn KO podocytes were treated with ICs and colocalization of lysosomes and ICs was quantitated. RNA-seq was used to examine lysosomal pathways.

Results: Both WT and FcRn KO podocytes upregulated MHC II after treatment with IFNγ but there was no difference in expression levels between WT and KO. There was no change in CD80 expression between WT and KO after treatment with IFNγ. CD86 and ICOSL expression levels in WT and FcRn KO were minimal at baseline and after treatment with IFNγ. When used as APCs, WT podocytes induced a very modest amount of IL-2 production by T cells (a marker of T cell activation) whereas KO podocytes induced no response. After treatment with ICs, lysosomes in WT podocytes were significantly larger and were more clustered around the nucleus, indicative of lysosomal activation. In contrast, after IC treatment lysosomes in the KO were smaller and more peripherally located. Treatment with ICs also resulted in significantly greater colocalization between lysosomes and ICs in WT versus FcRn KO podocytes, demonstrating that ICs were not directed to the lysosome in the KO. RNA-seq showed significant downregulation of lysosomal pathways in KO podocytes compared to WT after treatment with ICs.

Conclusions: FcRn KO in podocytes alters lysosomal trafficking and function.
Funding: NIDDK Support

PO1977
Apolipoprotein M as a Biomarker of Glomerular Lipotoxicity in Nephrotic Syndrome
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Background: Dysregulation of intrarenal metabolic pathways involved in cholesterol efflux is implicated in lipid-induced podocyte injury in glomerular diseases. Among several genes that are involved in cholesterol efflux, we recently reported a significant downregulation of glomerular apolipoprotein M (APOM) expression in patients with FSGS. HDL-associated APOM facilitates reverse cholesterol transport and is the carrier for the bioactive sphingolipid sphingosine-1-phosphate (S1P). Mutations in S1P lyase, the enzyme responsible for S1P degradation, cause a familial form of FSGS. We hypothesize that glomerular APOM deficiency is a surrogate biomarker for lipid-induced kidney injury in NS.

Methods: Patients with FSGS, MN, and MCD enrolled in NEPTUNE, a multi-center international cohort study of children and adults with NS, who received 1 g/g at baseline were selected for analysis. RNA expression data were obtained from the

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glomerular compartment isolated from kidney biopsies and compared with living kidney donor controls. Plasma and urinary APOM levels were measured by ELISA using baseline samples. Linear regression analysis was used to correlate glomerular APOM expression with plasma and urinary levels of APOM and to correlate glomerular APOM expression and plasma and urinary APOM levels with eGFR at baseline.

Results: Among 84 patients, 68% were male, mean age was 40 years, mean baseline eGFR was 80.6 mL/min/1.73m², and mean uPCR was 4.9 g/g. Glomerular APOM expression was decreased in patients with NS compared to healthy controls (p <0.001), irrespective of histologic diagnosis. APOM expression was positively correlated with plasma and urinary APOM levels in the NS cohort (R² = 0.089, p = 0.003) and in the FSGS subgroup (R² = 0.189, p = 0.0218). Decreased APOM expression (p = 0.005) and decreased plasma APOM (p = 0.031) were associated with a lower eGFR at baseline. After adjustment for age, sex, and race, each unit decrease in APOM expression was associated with a 9.83 mL/min/1.73m² (95% CI, 3.72 to 15.93, p = 0.002) lower eGFR at baseline.

Conclusions: Glomerular APOM deficiency and decreased plasma APOM levels were associated with decreased kidney function at baseline in the NS cohort. These findings identify APOM as a potential biomarker of lipid-induced kidney injury in NS.

Funding: NIDDK Support

PO1978

The Sensitivity of Podocytes to ATP in Vivo Is Distinctly Lower than the Sensitivity of Glomerular Endothelial and Proximal Tubular Cells

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Background: ATP signaling is involved in a plethora of pathways, involving damage signaling. Cell culture models as well as experiments on isolated glomeruli indicate that podocytes respond to ATP with a calcium transient. To date a direct effect of ATP on podocyte calcium signaling has not been described.

Methods: In this study mice expressing GCaMP3 in podocytes (Pod.cre), proximal tubular cells (Pax8.cre) or endothelial cells (Tie2.cre) underwent multiphoton in vivo imaging of the kidney. Mice were anesthetized, an arterial catheter was placed into the right common carotid artery and the aorta and the left kidney was exteriorized. The vasculature was labelled with a 70-kDa dextrane. Different doses of ATP were injected as a bolus via the catheter and dose-dependent calcium transients were monitored.

Results: Our data indicates that even doses of 5 mg/kg ATP did not induce calcium transients in podocytes. ATP transients were observed via a carotid artery catheter, while robust activation of calcium signaling was induced in endothelial and proximal tubular cells with 0.5 mg/kg ATP. Further increasing the ATP dose by injection via an abdominal aortic catheter resulted in a calcium transient in podocytes.

Conclusions: In contrast to endothelial cells and proximal tubular cells, podocytes show a low sensitivity to ATP-mediated calcium signaling. We therefore hypothesize, that the low sensitivity ATP of podocytes is a protection mechanism to avoid calcium signals from filtered ATP.

Funding: Government Support - Non-U.S.

PO1979

Cytomegalovirus Viremia-Associated Collapsing FSGS in an Immunosuppressed Systemic Lupus Erythematosus Patient

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Introduction: Maintaining a broad differential in evaluating AKI in SLE patients with a history of lupus nephritis (LN) is important. We describe a patient with SLE and AKI progressing to dialysis dependence due to collapsing FSGS in the setting of CMV infection. The high CMV viral load and robust response to antiviral therapy argue that the lesion was not representing a high risk APLD. The development of collapsing FSGS is commonly due to a “second hit” on a high risk APLD genetic background, in our case from elevated interferon levels in the setting of CMV viremia. APLD has been implicated in collapsing FSGS due to CMV viremia in African American DDRT recipients, demonstrating the role of genetic testing in African American patients. Our case demonstrates an infectious trigger rather than autoimmune cause of renal failure in an immunosuppressed patient with SLE.

PO1980

Transcriptional Reprogramming by WT1 Mediates a Repair Response During Podocyte Injury in Mice and Human Kidney Organoids

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Background: We previously identified WT1 as one of the most upstream transcription factors regulating gene expression in podocytes, binding nearly all genes known to be crucial for maintenance of the glomerular filtration barrier. Here, we focus on understanding WT1 transcriptional mechanism in response to injury.

Methods: We used Adriaycin (ADR)-induced podocyte injury as a model for human Focal Segmental Glomerulosclerosis in mice and human kidney organoids, and a conditional WT1 inactivated mouse model to decipher the transcriptional mechanism through which WT1 regulates podocyte gene expression during injury, using transcriptomic approaches.

Results: After injury, we observed a transient increased expression of podocyte genes in mice and human kidney organoids. Transcriptomics analyses of podocytes isolated from mTeto-Nphs2cre mice during the course of injury revealed a transient increase in the expression of crucial podocyte genes, including Nphs2. Synpo and many others, reflecting a reparative response during the early stages of injury. ChIP-seq analyses demonstrated that WT1 binds nearly 50% of known genes in podocytes, and the vast majority of genes whose expression changes during the response to injury. We identified de novo binding of WT1 that were only bound during the course of injury, and the expression of novel WT1 target genes. It appears that WT1 increases gene expression during injury through both the acquisition of novel binding sites, and increasing its binding intensity at sites already occupied by WT1. Mechanistically, motifs present in the promoters of other podocyte-specific transcription factors were highly enriched at sites where WT1 binding increased after injury. Since the DNA binding transition of transcription factors is modulated by chromatin accessibility, we used FACS-isolated podocytes to study epigenetic reprogramming. Both ADR-mediated podocyte injury or inducible podocyte specific inactivation of WT1 resulted in the conversion of active to repressive histone marks at WT1-bound sites.

Conclusions: These results demonstrate that target gene binding of WT1 is highly dynamic in response to injury. WT1 directs the epigenetic regulation of gene expression, maintaining active chromatin marks at bound genes, that change to repressive marks in the absence of WT1.

Funding: NIDDK Support

PO1981

Atypical Cyscapse 3-Dependent Death Process in Podocytes

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Background: Apatosis of podocytes has been widely reported in many in vitro studies, however, definitive apoptosis has been rarely documented in vivo podocytes. To elucidate this discrepancy, we analyzed dying process in podocytes in vitro and in vivo. We previously demonstrated that, in vivo, podocytes can die through a classical apoptosis pathway, while in vitro both classical and necroptosis pathways are involved in podocyte death. Here we report the first in vivo evidence that podocytes can die dependently on caspase 3.

Results: In in vitro studies, administration of LMB2 caused leakage of co-introduced ECFP in podocytes. To elucidate this discrepancy, we analyzed dying process in podocytes in vitro and in vivo. We previously demonstrated that, in vivo, podocytes can die through a classical apoptosis pathway, while in vitro both classical and necroptosis pathways are involved in podocyte death. Here we report the first in vivo evidence that podocytes can die dependently on caspase 3.

Conclusions: In vivo studies, administration of LMB2 caused leakage of co-introduced ECFP in podocytes. To elucidate this discrepancy, we analyzed dying process in podocytes in vitro and in vivo. We previously demonstrated that, in vivo, podocytes can die through a classical apoptosis pathway, while in vitro both classical and necroptosis pathways are involved in podocyte death. Here we report the first in vivo evidence that podocytes can die dependently on caspase 3.
Systematic In Silico Exploration of the Kidney Rho-GTPase System Regulation in CKD

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**Background:** It has become evident that dysregulation of the Rho-GTPase system would result in rearrangement of the actin cytoskeleton in the podocyte with resulting foot process effacement, a hallmark for glomerular diseases. To build further understanding how this dysregulation in disease states occurs in CKD, we performed a systematic mining of kidney transcriptomics data to generate a full-face picture and insights on complex interplay between the members of the large family of Rho-GTPases and their regulatory proteins, the Guanine Nucleotide Exchange Factors (GEFs) and the GTPase-activating proteins (GAPs).

**Methods:** A comprehensive list of 143 genes was compiled including the members of the three gene families according to HUGO Gene Nomenclature Committee (HGNIC). Publicly available human transcriptomics data from healthy and CKD kidneys (microarray and RNA-seq, bulk-tissue and single-cell) were used for interrogation of gene expression patterns, including presence of detectable expression, its abundance, cell type specificity, modulation in disease, and co-expression structure. WGCNA and Cytoscape were used to correspondingly generate and visualize the gene co-expression network.

**Results:** All but one (142/143) genes were detectable in the human kidney, with 121 having robust levels >1TPM. The majority of genes were broadly expressed across the different tissues outside the kidney, however expression of several GEF and GAP members showed specific kidney enrichment. A number of GEFs and GAPs were modulated in CKD patient kidneys as compared to controls, predominantly with tendency for up-regulation and negative correlation with renal function, reflecting first time activation in potentially pathophysiological or compensatory disease mechanisms. Hierarchical clustering of pairwise correlation values and WGCNA module analyses identified clusters of closely express genes that may implicate functional similarities.

**Conclusions:** To our knowledge, this is the first systematic evaluation of the Rho-GTPase, GEFs and GAPs kidney expression in the CKD context. Elucidation of the molecular interplay provides systems-level understanding and mechanistic insights that can lead to new biological hypotheses and therapeutic targets.

**Funding:** Commercial Support - Both authors are AstraZeneca employees

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Bag as a Potential Mechanoprotector in Podocytes

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**Background:** Podocyte loss is a hallmark of glomerular diseases leading to glomerulosclerosis and progression of kidney disease. Sitting on the outside of the glomerular tuft podocytes have to withstand extensive mechanical stress due to perfusion and filtration. Hyperfiltration and hyperperfusion e.g. in disease states cause podocyte detachment when overwhelming their mechanoprotective capacity, which start a vicious cycle of mounting strain on the remaining podocytes. Bag3 is an important mechanoprotector in many mechanical strained tissues and by inducing chaperone-assisted autophagy (CASA) maintains the proteostasis of e.g. Filamin and Synaptopodin indispensable for podocyte biology. Additionally Bag3 insufficiency renders susceptibility to diabetic nephropathy in a mouse model. These findings point toward Bag3 as a candidate for mechanical stress protection in podocytes.

**Methods:** Using immunofluorescence, super-resolution-microscopy and mass-spectrometry we examined glomeruli and podocytes for Bag3/CASA expression and characterized the CASA-complex composition in podocytes by immunoprecipitation. The influence of mechanical clues was examined by stiff matrices and cyclic stretch. The role of Bag3 in vivo is being evaluated in different mouse lines (Bag3.F209L mutation, a conditional knockout, fusion-protein).

**Results:** In the glomerulus the Bag3 and the entire CASA-complex is enriched in podocytes in mass-spectrometry. Bag3 staining localizes to the slit diaphragm protein nephrin in superresolution microscopy. Importantly the co-chaperone Bag3 shows interactions with essential actin cytoskeleton regulators like RhoA, Arpc2 and Dynamin2 as effectors for Bag3 in co-immunoprecipitation. The expression of Bag3 and the CASA-complex in podocytes is regulated by mechanical clues. Knockdown of the Bag3 homologue starvin in drosophila nephrocytes displays a mild filtration disturbance. The dominant-negative Bag3.F209L mutation causes a mild proteinuria in a whole-body overexpression model.

**Conclusions:** The data further emphasize the role of Bag3 and chaperone-assisted-selective-autophagy in podocyte mechanoprotection and maintenance of podocyte cytoskeleton architecture. Currently undergoing characterization of podocyte specific Bag3/CASA models and the influence of disease models will further help to understand the role of Bag3 at the kidney filtration barrier.

**Funding:** Government Support - Non-U.S.

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Hepatocyte Growth Factor-Factor-Activated Induction of NEPHRIN and NEPH1 Serves as a Novel Mechanism for Recovery of Podocytes from Injury


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**Background:** Podocytes (podo.) and their slit diaphragm(SD) are critical components of glomerular filtration barrier, whose dysfunction leads to ESRD (end stage renal disease). Treating ESRD remains a global challenge due to our poor understanding of the mechanisms that participate in recovery of podo. from injury. Glomerular injuries commonly induce podo. cell death and loss of SD, which is a modified tight junction and is formed through a trans-interaction between the extracellular domains of NEPHRIN and NEPH1 that maintain its structural integrity. Here, we present a novel concept showing that apart from structural organization, NEPHRIN and NEPH1 constitute a receptor-based function, and can be activated in a ligand-induced fashion.

**Methods:** Proteomics, SPR, Immunofluorescence

**Results:** The ability of NEPHRIN and NEPH1 to interact with tyrosine phosphatase SHP-2 in a phosphorylation (phos.) dependent manner prompted us to investigate whether ligands that induce PTPN11 stimulation also induced activation of NEPHRIN and NEPH1. Ligands screening identified HGF as a prominent inducer of both NEPHRIN and NEPH1 phos. To further establish HGF as a ligand, we used baculovirus system to generate validated NEPHRIN and NEPH1 proteins and confirmed not only a direct interaction between HGF and the extracellular domains of NEPHRIN and NEPH1, but also, the ligand-induced phos. of these proteins. In addition to their ligand-induced activation, we demonstrate that SHP-2 can directly dephos. these proteins, thus presenting for the first time evidence of SHP-2 in co-immunoprecipitation. The expression of Bag3 and the CASA-complex in podocytes is regulated by mechanical clues. Knockdown of the Bag3 homologue starvin in drosophila nephrocytes displays a mild filtration disturbance. The dominant-negative Bag3.F209L mutation causes a mild proteinuria in a whole-body overexpression model.

**Conclusions:** The data further emphasize the role of Bag3 and chaperone-assisted-selective-autophagy in podocyte mechanoprotection and maintenance of podocyte cytoskeleton architecture. Currently undergoing characterization of podocyte specific Bag3/CASA models and the influence of disease models will further help to understand the role of Bag3 at the kidney filtration barrier.

**Funding:** Government Support - Non-U.S.

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Knockout of the Neonatal Fc Receptor in Podocytes Ameliorates Nephritis by Reducing Glomerular Apoptosis

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**Background:** There are few targeted treatments for immune mediated kidney diseases which can result in progressive renal failure. Podocytes express the neonatal Fc receptor (FcRn), a trafficking receptor that transports immunoglobulin G (IgG) to the lysosome. In dendritic cells FcRn mediated trafficking of ICs to the lysosome is required for antigen processing and presentation on MHC II. We have found that podocyte specific knockout (KO) of FcRn ameliorates nephrotic syndrome (NTS) nephritis but that this protection occurs via a non-immune mediated mechanism. Here we show that KO of FcRn in podocytes results in a significant reduction in apoptosis both in vitro and in vivo after an immune challenge

**Methods:** Wild type (WT) and FcRn KO podocytes were cultured in the presence or absence of ICs. The intrinsic and extrinsic apoptotic pathways were assessed by Western blot and ELISA. RNA-seq was performed to evaluate changes in apoptotic pathways. NTS nephritis was induced in control and podocyte specific FcRn KO (podFcRn KO) mice. Glomerulosclerosis and crescent formation were quantitated on PAS sections. Flow cytometry was used to measure renal CD4+, CD8+ or FoxP3+ T cells. Glomerular apoptosis was assessed using the TUNEL assay.

**Results:** In vitro, after treatment with ICs, FcRn KO podocytes expressed significantly less caspase-3 and caspase-9 (intrinsisc pathway caspases) and caspase-3 activity was significantly decreased in KO podocytes compared to WT. There was no difference in caspase-8 expression (a marker of extrinsic apoptosis) between WT and KO podocytes. RNA-seq analysis demonstrated significant downregulation of intrinsisc apoptotic pathways in FcRn KO podocytes compared to WT. In vivo, after induction of nephrotic serum nephritis, there was no change in renal CD4+, CD8+ or FoxP3+ T cells in WT and KO mice. However, in FcRn KO mice significantly reduced glomerulosclerosis and crescent formation. Podocyte-specific KO of FcRn also resulted in a significant reduction in the number of apoptotic cells within the glomerulus.

**Conclusions:** KO of FcRn reduces apoptosis via the intrinsic pathway in cultured podocytes after an immune challenge and ameliorates immune-mediated nephritis in vivo by reducing glomerular apoptosis.

**Funding:** NIDDK Support

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Funding: NIDDK Support
The African APOL1 E150 SNP and Cell Surface Expression Are Required for Kidney Risk-Variant (G1/G2)-Mediated Cytotoxicity in Podocytes


Background: Apolipoprotein L1 (APOL1) variants G1 and G2 protect against trypanosome infection, but homozygosity greatly increases the risk of chronic kidney diseases, purportedly by acting as surface cation channels in kidney podocytes. “Wild-type” APOL1-G0 exhibits various single nucleotide polymorphisms (SNPs), most commonly haplotype E150K, M228I and R255K (“KIK”, where the Reference Sequence is “EMR”), whereas G1 and G2 are only found in a single African haplotype background (“EIK”), also seen in some G0 Africans. Lannon et al (Kidney Int. 96: 1303) recently documented that differential cytotoxicity of APOL1-G1 and G2 variants versus G0 in HEK-293 cells depended on the haplotype. However, HEK-293 cells are unusually sensitive to APOL1, and podocytes are a more relevant cell type. Furthermore, only the small fraction of APOL1 that is transported to the cell surface (from its major expression in the electron transport chain (ETC)) requires the African (E150) G1 and G2 cytotoxicity required for APOL1 G1 and G2 to exert cytotoxicity. Non-toxic E150 G0 at equal surface expression levels; K150 G0, G1 and G2 were not toxic. E150 APOL1 were measured by FACS and Western blotting at increasing doxycycline levels.

Methods: We generated podocytes stably expressing APOL1 G0, G1 or G2 under a doxycycline-inducible promoter and compared the effect of the African E150 (EIK) vs K150 (KIK) SNPs on cytotoxicity (by the Cyto-Tox Glo assay). Surface and total APOL1 were measured by FACS and Western blotting at increasing doxycycline levels. Blood was used to prevent APOL1 transport to the cell surface.

Results: Cell surface APOL1 levels increased in a doxycycline dose-dependent manner, but only the E150 G1 and G2 variants caused toxicity to podocytes as compared to E150 G0 at equal surface expression levels; K150 G0, G1 and G2 were not toxic. E150 G1 and G2 cytotoxicity was dose-dependent and required exit of APOL1 from the ER.

Conclusions: Using a physiologically relevant podocyte cell line, we confirmed that the African haplotype (EIK) is required for APOL1 G1 and G2 to exert cytotoxicity. Non-natural KIK versions were not toxic. Additionally, APOL1 G0 was not toxic in either the KIK or EIK background. Furthermore, African (E150) G1 and G2 cytotoxicity required ER exit, supporting the surface cation channel hypothesis. Our data thus suggest two potential therapeutic avenues for APOL1 nephropathies.

Funding: Commercial Support - Genentech,Roche

PO1987
Glomerular Heterogeneity and Modulation of miR-93: The Role of Extracellular Vesicles

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Background: Modulation of miRNA in podocytes and glomerular endothelial cells (GEC) has been associated with development of renal diseases. miR-93 is a potent regulator of pathways responsible for glomerular damage, like VEGF, TGFβ and Mek2. We have evidence that miR-93 is altered in the glomeruli of mice with X-linked Alport syndrome (AS), carrying the Col4a5 mutation, and in glomeruli of AS patients. Here, we investigated the role of miR-93 in mesangial cells, podocytes and GEC from WT and AS mice. We also used extracellular vesicles (EVs) derived from human amniotic fluid stem cells (hAFSC) to assess their disease modifying activity in vitro and in vivo by regulation of miR-93.

Methods: miR-93 expression was evaluated by qRT-PCR in mesangial cells, podocytes and GEC sorted from glomeruli of male and female WT (C57BL6/J), and homozygous and heterozygous AS (Col4a5−/−) mice at different stages of disease (2m, 3.5m and 5.5m) and in biopsies of AS patients. Modulation of miR-93 by hEVs was evaluated in vitro and EV therapeutic effect was evaluated in vivo by RNA-seq and survival.

Results: miR-93 expression is different between male and female mice along disease progression. In AS males miR-93 level was significantly lower in GEC, but not in podocytes or mesangial cells vs WT cells. miR-93 expression was downregulated also in AS patients. Expression of WT in panmucin amionucleoside damaged podocytes, and expression of fibronectin and VEGF in damaged GEC was restored by miR-93 hEV cargo transfer. In vivo, hEVs showed therapeutic effect by ameliorating the level of proteinuria and survival.

PO1988
GDC-0879 Rescues Lipid Peroxidation and Podocyte Dysfunction in Coenzyme Q-Deficient Kidney Disease

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Background: Mutations affecting mitochondrial coenzyme Q (CoQ) biosynthesis lead to kidney failure due to selective loss of essential cells of the kidney filtered called podocytes. Curiously, neighboring tubular epithelial cells are spared early in disease, despite their higher mitochondrial content. We therefore sought to illuminate new, cell-specific roles for CoQ, independent of its role in the electron transport chain (ETC).

Methods: Here we use CoQ deficiency caused by a monogenic disorder due to PDS2 mutations as a model system with which to investigate the cell-specific mechanisms of disease. The resolution afforded by single nucleus RNA sequencing revealed podocyte-specific disease pathways in homozygous kid/kid (kidney disease) mice, the result of a spontaneous missense mutation in Pds2 (V117M, Pds2M117V). We combine single nucleus transcriptomics with in vitro metabolomics and transcriptomics analyses to better understand the metabolic perturbations within this disease.

Results: Single nucleus RNA sequencing from kidneys of Pds2M117V mice, characterized by nephric syndrome and CoQ deficiency in all cells, identified a podocyte-specific perturbation of the Braf/Mapk pathway. Treatment with GDC-0879, a Braf/Mapk-targeting compound ameliorated kidney disease in Pds2M117V mice. In vitro, mechanistic studies demonstrated that depleted podocytes revealed a previously unknown perturbation in PUFAPUFA metabolism leading to lipid peroxidation. Ablation PUFAPUFA metabolism was confirmed in vivo, where the abundance of Gpx4, an enzyme that protects cells from lipid peroxidation, was elevated in disease and restored after treatment with GDC-0879. We demonstrate broader human disease relevance of these findings by uncovering patterns of Gpx4 and Braf/Mapk pathway gene expression in tissue from patients with several kidney diseases.

Conclusions: Our studies reveal ETC-independent roles for Coq in podocyte injury and point to Braf/Mapk as a conserved, podocyte-specific pathway for the treatment of kidney diseases.

Funding: NIDDK Support

PO1989
Noncanonical PAR-1 Signalling Leads to Profibrotic Effects in Podocytes in Response to Steroid-Resistant Nephrotic Syndrome Disease Plasma

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Background: Post-transplant recurrence of steroid-resistant nephrotic syndrome (SRNS) is thought to be due to the presence of an unknown “circulating factor”, the identity of which has so far remained elusive. Our previous works suggest a role for protease-activated receptor-1 (PAR-1) involving an unknown circulating protease leading to increased podocyte motility. We have now further elaborated the signalling pathways downstream of PAR-1, which suggests pro-fibrotic activation in podocytes.

Methods: Conditionally immortalised human podocytes (ciPods) were treated with PAR-1 agonist peptide or post-transplant SRNS relapse plasma. Signalling pathways downstream of PAR-1, which promotes pro-fibrotic activation in podocytes were assessed. Furthermore, par-1 knockdown podocytes revealed a previously unknown perturbation in PUFA metabolism leading to lipid peroxidation. Ablation PUFA metabolism was confirmed in vivo, where the abundance of Gpx4, an enzyme that protects cells from lipid peroxidation, was elevated in disease and restored after treatment with GDC-0879. We demonstrate broader human disease relevance of these findings by uncovering patterns of Gpx4 and Braf/Mapk pathway gene expression in tissue from patients with several kidney diseases.

Conclusions: Our studies reveal ETC-independent roles for Coq in podocyte injury and point to Braf/Mapk as a conserved, podocyte-specific pathway for the treatment of kidney diseases.

Funding: NIDDK Support

PO1990
TRPC6 is a Key Mediator of a PAR1 Activation Pathway in Podocytes That Is Responsible for FSGS

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Background: There is good evidence for the role of a circulating factor in the pathogenesis of idiopathic nephrotic syndrome (NS). We have previously presented our work hypothesising the role of circulating plasma proteases. An active form of the protease activated receptor, PAR-1 expressed in the podocytes of SV129 mice (PAR-1acs) led to proteinuria, sclerosis and death at 42 days. It was found that the signalling

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Underline represents presenting author.
response to PAR-1 agonist treatment of podocytes in vitro was also present in the kidney IHC sections from the PAR-1 KO, mouse, and in human podocytes treated with post-transplant recurrence plasma. This response includes the phosphorylation of VASP, JNK and Pakxillin. We hypothesised that the downstream response to PAR-1 signalling involves activation of TRPC6.  

Conclusions: Conditionally immortalised human WT podocytes and TRPC6 KO mouse podocytes were treated with a PAR-1 agonist (15 μM PAR-3931-Pi Peptides International). The PAR-1 KO mouse was crossed with a TRPC6 KO on a C57 Bl6 background to develop the NPHS2 Cre PAR-1 KO, TRPC6 KO mouse. Biopsy tissue was obtained via the UK Nephrotic Syndrome Study, Nephros, housed within the UK Renal Rare Disease Registry, RadDaR.  

Results: We present data confirming activation of the same signalling pathways in vitro in podocytes treated with a PAR-1 agonist, and in vivo in our NPHS2 Cre PAR-1 KO, mouse. TRPC6 activation in human nephropathy biopsies nVASP and JNK signaling is significantly higher in FSGS and Minimal Change Disease biopsies when compared to IgA nephropathy biopsies. TRPC6 is a calcium channel that can be activated at the slit diaphragm and can signal to the actin cytoskeleton. TRPC6 Knock Out (TK6KO) podocytes showed an altered response to PAR-1 agonist treatment. There was no phosphorylation of VASP and only brief phosphorylation of JNK and no phosphorylation of Pakxillin. When we crossed a TK6KO mouse with our NPHS2 Cre PAR-1 Active mouse we saw significantly increased survival from a median of 40 days in the NPHS2 Cre PAR-1 Active mouse to 60 days when TK6KO is knocked out.  

Conclusions: We have identified a common signalling response to PAR-1 activation in podocytes in vitro and in vivo, including in human disease. We identified TRPC6 as being a key player in the response, suggesting a unique role of this ion channel in mediating circulating factor disease, and a direct therapeutic target.  

PO1991  

A Novel Insulin Sensitizer Targeting Nuclear Receptor PPARy Provides Beneficial Effects in a Glomerular Disease Model  

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Background: Thiazolidinediones (TZDs) are nuclear receptor peroxisome proliferator-activated receptor γ (PPARγ) agonists traditionally used to treat type II diabetes由于 their insulin-sensitizing effects. These have recently been demonstrated to be beneficial in protecting podocytes and reducing proteinuria in glomerular disease. Since these FDA-approved drugs are associated with adverse effects such as weight gain, edema, bone loss and increased risk for heart failure, we hypothesized that disparate beneficial vs. adverse molecular activities of PPARγ can be modulated. We determined if GQ-16, a novel insulin sensitizer and partial PPARγ agonist, which de-phosphorylates PPARγ at Ser273 like other TZDs, provides therapeutic advantage in glomerulonephritis mice.  

Methods: The studies were approved by the Institutional Animal Care and Use Committee at Nationwide Children’s Hospital. Proteinuria was induced in male Wistar rats by single intravenous puromycin amino-nucleoside (PAN) injection, while the control group received saline. PAN-injected rats received sham vehicle, pioglitazone (Pio) or GQ-16 by oral gavage daily (n = 7/group). The rats were weighed daily, and urine samples were collected and analyzed for proteinuria. Plasma with sodium citrate and corn trypsin inhibitor was collected from the inferior vena cava. Endogenous thrombin potential was determined by thrombin generation assay.  

Results: PAN induced robust proteinuria (P=0.009) on Day 11 and Pio reduced PAN-induced proteinuria significantly with 63.3% mean reduction (P=0.038). Interestingly, GQ-16 reduced proteinuria even further by 81.2% (P=0.008), and these were comparable to the control (n=7) study. Increased levels of proteinuria was associated with heart failure (P=0.066). Furthermore, proteinuria reduction correlated with correction of disease associated hyper-coagulopathy. GQ-16 improved PAN-induced hyper-coagulopathy as measured by improved endogenous thrombin potential and peak thrombin. No significant differences in body weights were observed in treatment vs. PAN groups.  

Conclusions: GQ-16, a novel insulin sensitizer and partial PPARγ agonist, shows better efficacy profile in an experimental glomerular disease model than Pio, a traditional TZD with full PPARγ agonist activity.  

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PO1992  

Tropomyosin Isomers Play a Role in Healthy and Injured Kidney Podocytes  

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Background: The podocytes are a group of glomerular diseases that affect the kidney’s ability to filter the blood, and often lead to kidney failure. Healthy podocytes cover the glomerular capillaries with thousands of extensions called foot processes that interdigitate with one another and maintain their elaborate cell shape by tightly regulating their actin cytoskeleton. Podocytes respond to insults in a typical fashion by reducing their footprint effacement (PFE), a dramatic shift in podocyte morphology and the disappearance of the intricate foot processes. Tropomyosins (Tpm) are coiled-coil dimers that form co-polymers along actin filaments and change the filaments’ biological properties. Over 40 different Tpm isoforms have been identified as the gene products of 4 genes: Tmga1, Tmga2, Tmga3, Tmga4. Tpm expression varies in different locations and cell types and the change of type of actin cables assembled in those locations. We hypothesize that podocyte shape is controlled by a specific set of Tpm isoforms that regulate actin cytoskeleton than the injured and/or their counterparts, with the most significant changes occurring in Tpm 1.7 & Tpm 3.4. PheBio data also showed an interesting novel Tpm-related gene product only in injured glomeruli. We isolated RNA from WT and AdrN glomeruli and compared them to primary podocytes taken from podocyte-specific translating-ribosome-ribosum-deactivation (TRAP) mice. This study allowed us to purify podocyte mRNA for RNaseq, away from that in other glomerular cell types. Comparing the isolated RNA from WT-TRAP & AdrN-TRAP mice, we are able to identify the podocyte-specific Tpm isoforms that are associated with injury.  

Conclusions: This study suggests roles for tropomyosin isoforms changes in regulating podocyte shape in health and injury conditions.  

Funding: Private Foundation Support  

PO1993  

IRE1α Is Essential for Podocyte Proteinosis and Mitochondrial Health  

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Background: Glomerular epithelial cell (GEC)/podocyte proteinosis is disrupted in glomerular diseases. To maintain proteinosis, the endoplasmic reticulum (ER) orchestrates the unfolded protein response (UPR), which includes upregulation of chaperones and clearance of misfolded proteins via autophagy. Insulin requiring enzyme-α (IRE1α) resides in the ER and is a transducer of the UPR. This study characterizes the mechanisms by which IRE1α regulates proteinosis in GECs.  

Methods: Mice with podocyte-specific deletion of IRE1α (IRE1α KO) were produced by breeding IRE1α flox/flox mice with mice expressing podocy-cre recombinase. Nephrosis was induced with a single injection of adriamycin (ADR). GECs were cultured from glomeruli of IRE1α KO flox/flox mice and IRE1α KO was deleted by transfection of Cre recombinase. Cellular oxygen consumption rate (OCR) was quantified using the Seahorse mitochondrial stress test. Mitochondria were visualized using MitoTracker Red CMXROS or MitoTracker Green FM.  

Results: Podocyte-specific IRE1α KO mice had greater ADR-induced albuminuria compared to control littermates. ADR increased expression of ER chaperones in glomeruli of control mice, but this upregulation was impaired in IRE1α KO mice. Autophagy reduction was blunted in ADR-treated IRE1α KO animals, evidenced by reduced LC3-II and increased p62 levels, compared to treated controls. Electron microscopy showed prominent swelling of the ER and mitochondrial injury in podocytes of ADR-treated IRE1α KO mice. In cultured GECs incubated with tunicamycin (TM), deletion of IRE1α or chemical inhibition of the IRE1α RNase with 4μC8 attenuated upregulation of ER chaperones and LC3 lipidation compared to control. LC3 transcription and total LC3 protein levels were also reduced in TM-treated IRE1α KO GECs. Compared to control, IRE1α KO GECs showed decreased maximal and ATP-linked OCR. Mitochondrial membrane potential was lower in IRE1α KO GECs, which may contribute, while total mitochondrial mass was similar in both groups. Inhibition of IRE1α signaling increased ER stress-induced apoptosis.  

Conclusions: Stress-induced chaperone production, autophagy and mitochondrial function are compromised by IRE1α KO. IRE1α KO is pathogenic in glomerular disease associated with podocyte injury and ER stress.  

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PO1994  

Studying the Pathogenesis of Congenital Nephrotic Syndrome Using NPHS2 Mutant Kidney Organoids  

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Background: Nephrotic syndrome (NS) is one of the most common forms of renal disease in children. NPHS2 mutations are the most common cause of congenital NS with missense NPHS2 mutations reported to result in misfolding and mislocalization of the encoded slit-diaphragm protein, Podocin. Such studies overexpressed mutant protein in cell cultures, with limited podocyte and mouse cell line GECs. This may not capture the consequences of the mutant protein. Here we generated NPHS2 mutant iPSC-derived kidney organoids as a model to dissect the pathogenic process.  

Methods: We have simultaneously reprogrammed and CRISPR/Cas9 gene edited a control human fibroblast line, generating 3 iPSC lines containing mutations of the endogenous NPHS2 locus as well as a control wild type (WT) line. These include the sequence variants c274G>T, c353C>T and c303G>A leading to the protein changes G92C, P118L and R168H respectively. Control and mutant lines were used to generate Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only  

Underline represents presenting author.
kidney organoids containing all nephron segments. Podocin localization was assessed by confocal microscopy and Western blotting.

Results: Podocin protein was evident in the glomeruli of all organoids, however all mutant lines revealed a marked reduction of the Podocin protein. While the G92C mutant protein co-localised with Nphrin at the plasma membrane, the R168H mutant protein failed to show any perinuclear staining suggestive of Golgi retention, together with peripheral co-localisation with the early endosome marker EEA1. Interestingly, the R168H mutant was previously predicted to mislocalise in the endoplasmic reticulum (ER). The P118L mutant was previously predicted to accumulate in the ER and present a trafficking defect from the ER to the Golgi apparatus.

Conclusions: Differences in mutant podocin protein localisation in previous reports and our kidney organoids highlight the need for a more appropriate model to study the pathobiology of NPHS2 mutations. These organoids will allow us to explore approaches to rescue individual Podocin defects, ultimately guiding the development of therapeutic strategies for such patients.

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PO1995

OASIS in Podocytes Promoted Tubular Injury by Suppressing PRKCI Expression

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Background: Old astrocyte specifically induced substance (OASIS), a transcription factor, plays important roles in physiological and pathophysiological processes, such as bone formation. Previously, we found that OASIS is expressed in podocytes in murine kidney. However, the pathophysiological roles of OASIS in podocytes remains unknown. The aim of this study is to investigate the functional roles of OASIS in podocytes in the development of kidney diseases.

Methods: The expression of OASIS protein was investigated in glomeruli of murine kidney and cultured mouse podocytes cell line after lipopolysaccharide (LPS) treatment. To examine the roles of OASIS in podocytes in kidney injury, podocyte-specific OASIS knockout (OASIS CKO) mice were generated and subjected to LPS. Twenty-four hours after LPS treatment, serum creatinine and urinary albumin ratio were measured. Podocytes injury was assessed by electron microscope analysis and tubular injury was analyzed by PAS staining and by measuring LCN2 mRNA expression. To explore the secretory molecules downstream of OASIS, DNA microarray analysis was performed using podocytes with lentiviral overexpression of OASIS. In order to examine the effects of the downstream molecule of OASIS on proximal tubule cells, HK-2 cells were cultured.

Results: LPS treatment increased OASIS expression in glomeruli of murine kidney and in cultured podocytes. Podocyte-specific OASIS deletion suppressed LPS-induced serum creatinine (Cr) level (Cr (mg/dl) : control-LPS=1.0±0.2, OASIS CKO-LPS=0.75±0.16, n=8-10, p<0.05), but did not influence albuminuria and podocyte injury. Surprisingly, on the other hand, OASIS CKO mice were protected from LPS-mediated tubular injury. DNA microarray analysis using OASIS-overexpressed podocytes revealed that PRKCI was negatively regulated by OASIS in podocytes. Finally, we found that recombinant LPS-suppressed LPS-induced LCN2 mRNA expression in HK-2 cells in a dose-dependent manner.

Conclusions: Suppression of OASIS in podocytes attenuated LPS-induced tubular injury in part by increased PRKCI secretion. Targeting OASIS-PRKCI signaling in podocytes could be therapeutic value in kidney diseases.

PO1996

The Renal Risk Variants of Apolipoprotein L-1 Lead to an Influx of Sodium and Calcium That Drive Cytotoxicity

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Background: Apolipoprotein L-1 (APOL1) is an innate immunity gene that protects against protozoan parasites. Recently evolved variants, G1 and G2, provide increased immunity against African trypanosomes while increasing the risk of chronic kidney disease. There is little consensus on how these renal risk variants (RRVs) lead to cell death. We report that the earliest event in RRV-mediated cytotoxicity is localization to the plasma membrane, followed by cation flux driven by Ca2+ and Na+. Because many of the proposed models of RRV cytotoxicity and kidney disease can be activated by an influx of cations Ca2+ and Na+, we propose that the cytosolic cation channels at the cell surface are the upstream even that links them together. Our data suggests that targeting RRV channel activity represents a promising avenue for drug development.

PO1997

Cloning of an IgG Autoantibody Specific for Phospholipase A2 Receptor (PLA2R) Using IgG-Producing Cells from a Patient with Membranous Nephropathy

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Background: Primary membranous nephropathy (MN) is a common autoimmune kidney disease, in which 70% of patients exhibit circulating autoantibodies to one or more conformational epitopes in PLA2R. Anti-B cell therapies have proved effective to decrease autoantibody production and limit further development of the glomerular subepithelial immune deposits of PLA2R and IgG. However, better characterization of anti-PLA2R autoantibodies is needed.

Methods: We used Epstein-Barr virus (EBV)-immortalized B cells isolated from peripheral blood from an anti-PLA2R seropositive MN patient to develop a protocol for the cloning and expression of recombinant IgG (rIgG) specific for PLA2R. A terminally His-tagged fragment consisting of the first 5 domains of human PLA2R was expressed in E. coli. The B cells were transfected with rIgG expression plasmids by transfection or infection and secreted rIgG was isolated from cell supernatant media by incubation with biotin labeled reagents (recombinant PLA2R or IgG-specific antibody) and streptavidin-conjugated magnetic beads. A FITC-conjugated N-terminal PLA2R peptide was used to isolate B cells with antigen-specific B-cell receptor (membrane IgG) by FACS. Variable segments of IgG heavy (VH) and light (VL) chains were cloned through a single-cell workflow that allowed expression of rIgG for follow-up screening using an in-house ELISA to assess IgG binding to human PLA2R. Sera from anti-PLA2R seropositive MN patients and healthy controls served as positive and negative controls, respectively.

Results: Starting with 1.105 EBV-immortalized cells, we first isolated 3.6x106 cells with membrane IgG specifically reactive with non-reduced PLA2R. This subpopulation was next stained with FITC-conjugated PLA2R peptide and the corresponding VH and VL of IgG were cloned using our single-cell workflow. We expressed the cloned VH and VL in Es rIgG in Expi293 cell system. ELISA confirmed that the rIgG bound PLA2R.

Conclusions: This is the first report of cloning a PLA2R-specific IgG autoantibody from a patient with MN. These approaches can be used for further characterization of the molecular mechanisms of autoimmunity and epitope spreading in MN.

Funding: NIDDK Support

PO1998

Pharmacologic Blockade of the Natriuretic Peptide Clearance Receptor Ameliorates Glomerular Disease in an Animal Model of FSGS

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Background: Glomerular podocytes play a key role in glomerular disease processes. Accumulating evidence suggests that cGMP signaling has podocyte protective effects in kidney diseases (J Am Soc Nephrol 28: 260, 2017). cGMP is produced by nitric oxide and by natriuretic peptides (NPs). NPs are the predominant source of cGMP generation in podocytes. NPs stimulate cGMP production by binding to NP receptors (NPRs). NPRA and NPRB stimulate cGMP generation. In contrast, NPRC binds and degrades NPs. Podocytes express all three NPRs (NPRA, NPRB, and NPRC). We hypothesized that blockade of NPRC would enhance local NP levels, promote cGMP signaling in podocytes and ameliorate glomerular injury.

Methods: We blocked clearance of NPs by NPRC using the pharmacologic agent ANP (4-23), which specifically binds NPRC without binding NPRA or NPRB. For the experiments, we used a mouse transgenic (TG) model of focal segmental glomerulosclerosis (FSGS) created in our laboratory (J Clin Invest 125:1913, 2015). These TG mice express constitutively active Gαq-subunit specifically in podocytes. In these animals, treatment with a single dose of the podocyte toxin puromycin aminonucleoside (PAN) causes robust albuminuria in TG mice, but only mild disease in non-TG animals.

Results: PAN induced heavy proteinuria in vehicle-treated TG mice at day 14 (1426 ± 144) vs. 49 ± 19 [baseline] ug/mg creatinine; P = 0.003. The increase in albuminuria at day 14 was significantly reduced by treatment with ANP(4-23) (1426 ± 25 [vehicle] vs. 383 ± 157 [ANP(4-23)]/ug/mg creatinine; P = 0.003). Treatment with ANP(4-23) also tended to reduce the number of mice with glomerular injury (83% [vehicle] vs. 58% [ANP(4-23)]; P = 0.1). ANP(4-23) also reduced proteinuria in TG mice treated with PAN (129 ± 3 [vehicle] vs. 127 ± 3 [ANP(4-23)]) mm Hg; P = NS. Urinary cGMP excretion tended to be higher in ANP(4-23) treated mice (6.7 ± 1.0 ng/mg creatinine) compared to mice treated with vehicle (4.9 ± 1.0 ng/mg creatinine), but this difference was not statistically significant.

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Underline represents presenting author.
Conclusions: These data suggest that: 1. Pharmacologic blockade NPRC may be a useful target for treatment of proteinuric kidney disease, and 2. Treatment outcomes might be improved by optimizing blockade of the NPRC to more effectively inhibit clearance of NPs from the circulation.

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PO1999
Mitochondrial Damage in FSGS due to ANLN Mutation
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Background: We previously identified ANLN R431C as a cause of focal segmental glomerulosclerosis (FSGS). In addition to defects in actin bundling, targeted evaluation of this variant in cultured human podocytes identified disruption of AKT/mTOR signaling as a cause of ER stress and reduced podocyte viability. Creation of the orthologous R431C point mutation in mice confirmed the increased podocyte ER stress and identified mitochondrial damage as another possible feature of disease. To gain an unbiased view of the molecular mechanisms driving ANLN R431C induced disease, we used transcriptomic analysis and automated live cell imaging to interrogate cultured human podocytes.

Methods: Conditionally immortalized human podocytes overexpressing wildtype ANLN or the R431C variant were evaluated by mRNA-Seq and smRNA-Seq analysis to identify differentially expressed genes and microRNAs, as well as the molecular pathways involved. Potential therapeutic strategies were examined by evaluating cultured podocyte cellular and organelle-specific viability using automated live cell imaging.

Results: The top differentially expressed genes encode molecules that interact with previously identified pathological mechanisms including F-actin bundling (SYNP2L) and AKT/mTOR signaling (ANLN R431C), with mTOR signaling identified as a pathway likely to be affected by ANLN R431C. A common feature of the top differentially expressed gene and microRNA candidates is the potential to regulate mitochondrial viability. When evaluated for changes in mitochondrial membrane potential, expressed gene and microRNA candidates is the potential to regulate mitochondrial likely to be affected by

and AKT/mTOR signaling (ANLN R431C). A common feature of the top differentially expressed gene and microRNA candidates is the potential to regulate mitochondrial viability. When evaluated for changes in mitochondrial membrane potential, ANLN R431C podocytes displayed increased susceptibility to mitochondrial damage that could be rescued by treatment with AKT/mTOR pathway inhibitors. Additionally, compounds targeting improved mitochondrial viability through increased bioenergetic function (AP(39), reduced oxidative stress (MitoQ, MitoTEMPO) and prevention of pore opening (Olesoxime) could all rescue the increased susceptibility to apoptosis in ANLN R431C podocytes.

Conclusions: Unbiased transcriptomic analysis confirmed that ANLN R431C disrupts AKT/mTOR signaling and actin cytoskeletal dynamics, resulting in increased ER stress and mitochondrial damage that reduce podocyte viability. Targeting various aspects of mitochondrial regulation may present viable alternative treatment strategies for FSGS due to defects in ANLN gene.

PO2000
Prothrombin Modulates Podocyte Health and Function During Glomerular Proteinuria
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Background: Ongoing podocyte injury is a known critical determinant of glomerular disease progression. Recent research suggests thrombin exerts biotrope podocyte injury, however, pharmacologic manipulation may cause both on- and off-target effects. Thus, the purpose of this study was to directly examine the effects of thrombin on glomerular proteinuria by manipulating its zymogen precursor, prothrombin (PT). We hypothesized that circulating PT would directly modulate both podocyte function and in situ survival in a rat model of nephrotic syndrome.

Methods: Puromycin aminonucleoside (PAN)-induced proteinuria was treated with: 1) PT antisense oligonucleotide to induce hypoprothrombinemia (LoPT), 2) Serial i.v. PT infusions to sustain hyperprothrombinemia (HiPT), or 3) sham (PT only) controls (Con; n=12/group). Group samples and citrated plasma were collected at day 10 post-PAN. PT plasma activity was measured by chromogenic kit. Glomeruli were isolated from the kidneys, dissociated into single-cell suspension and analyzed by flow cytometry following immunofluorescent antibody and TUNEL staining.

Results: Circulating plasma PT levels (Figure A) modulated proteinuria (B) such that it was significantly decreased in LoPT and increased in HiPT, compared to Con. LoPT also decreased in situ podocyte death (C), while HiPT increased in situ podocyte death, and resulted in fewer podocytes per glomerulus (D).

Conclusions: In conclusion, prothrombin modulates podocyte function (proteinuria) and survival (death and numbers) in the PAN model of glomerular proteinuria. Future studies should work to determine the prothrombinase mechanism that enables thrombin formation and signaling in the glomerulus and evaluate its potential as a novel therapy to target slow glomerular disease progression toward chronic kidney disease.

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PO2001
Exosomal Long Non-Coding RNA-G21551 as a Potential Predictive Biomarker for Segmental Sclerosis Change in IgA Nephropathy
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Background: Segmental sclerosis (S) is an independent pathological predictor for renal progression in IgAN patients, and is closely related to proteinuria. However, there is less invasive biomarker for pathological S change. We investigate the difference in expression profiles of exosomal long non-coding RNAs (lncRNAs) in plasma from IgAN patients compared with their healthy first-degree relatives, then explore the possible lncRNA associated with S.

Methods: To isolate exosomes from the plasma of both IgAN patients and their healthy first-degree relatives. High-throughput RNA sequencing and real-time quantitative polymerase chain reaction (qRT-PCR) was used to validate lncRNA expression profiles. Target lncRNAs were selected by bioinformatics analysis. The relationship between target lncRNA and S was analyzed by Spearman correlation. ROC curve evaluated the area under curve (AUC) of the target lncRNA for diagnosis S and its predictive sensitivity and specificity.

Results: 18 pairs of IgAN patients and their healthy first-degree relatives were enrolled in this study. The mean age was 29.7±6.6 years and urinary protein was 1.00±2.00 (g/24h) in these IgAN patients. LncRNA-G21551 was significantly down-regulated in IgAN patients. The predicted target genes of lncRNA-G21551 are FCGRs, which encode family of Fc gamma receptors (FcγRs). S was observed in 12 IgAN patients (66.7%) and was positively correlated with lncRNA-G21551 relative expression (r=0.545, P=0.019), but had no correlation with proteinuria, blood pressure, mesangial hypercellularity(M), endocapillary proliferation(E), tubulointerstitial fibrosis (T) and crescent(C). The relative expression (fold change) of lncRNA-G21551 was significantly higher in S group than in S0 group (11.26(9.79,20.38) vs 7.04(1.39,11.00), P<0.025). The AUC of lncRNA-G21551 to predict S change was 0.81(95% confidence interval, 0.62~1.00) with a sensitivity of 83.3% and a specificity of 83.3% when a cutoff value of 9.58 was used for lncRNA-G21551 relative expression (Fold Change). In addition, patients with higher lncRNA-G21551 relative expression had more severe podocyte injury.

Conclusions: Exosomal lncRNA-G21551 was down-regulated in IgAN patients, but positively correlated with S change. Exosomal lncRNA-G21551 may be a potential independent predictor for S lesion in IgAN patients.

PO2002
Analysis of the Relationship Between Proteasome and Autophagy in Podocytes Using Podocyte-Specific Proteasome Impairment Mice
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Background: Ubiquitin-proteasome system and autophagy-lysosome system are major intracellular protein degradation machinery. The relationship of these systems in podocyte has not well been understood.

Methods: In this study, we generated podocyte-specific proteasome impaired mice (Rpt3pdKO) by deletion of Rpt3, which is essential for construction of 26S proteasome, using Cre-loxP system. Albuminuria and number of sclerotic glomeruli increased in the Rpt3pdKO mice compared with Rpt3control mice. Oxidative stress and podocytes apoptosis were related to podocyte injury. To evaluated autophagic activity, LC3 dots

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Underline represents presenting author.
PO2003
Functionally Resolving WT1 Variants of Uncertain Significance in Nephrotic Syndrome
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Background: Patients with Mendelian forms of nephrotic syndrome (NS) are likely to progress to end stage kidney disease. Because of the increased availability and promise to guide clinical decision, genetic screening among affected patients is proliferating. However, accurate attribution of pathogenicity to rare variants found during genetic screening remains challenging. WT1 is the second most common gene causing Mendelian NS. Therefore, this project aims to develop a model system to test the transcriptional activity of WT1 variants, as a first step towards high-throughput functional analysis to comprehensively classify variants in this key NS gene.

Methods: Wild-type and several bona fide pathogenic WT1 variants were tested for transcriptional activity in a standard dual-luciferase assay. Several cell lines including HeLa, HEK293, and HK2, were co-transfected with variant or wild-type WT1 and an NPHS1 promoter luciferase vector. Furthermore, potential WT1 target genes specific to HEK293 cells were identified by analyzing differential gene expression in RNA-Seq data of WT1 over-expressing HEK293 cells, in order to identify additional WT1-responsive promoters for use as WT1 activity reporters.

Results: Overexpression of wild-type WT1 in HeLa cells and HEK cells increased expression of luciferase under the NPHS1 promoter by ~2-fold relative to trimmed WT1. The luciferase activity of bona fide pathogenic WT1 variants was also significantly lower than the wild-type WT1 and bona fide benign WT1 variants (P<0.05). Overexpression of wild-type WT1 in HEK293 resulted in upregulation (log2 fold change>0.4, adjusted p<0.05) of IGFIR, EGFIR, TGFβ2. These candidates are being developed as WT1-responsive reporters.

Conclusions: Previous reports suggested NPHS1 promoter reporters as a model system to investigate WT1 functionality. However, the transcriptional effect of WT1 was substantially underexposed. Future work is required to establish a robust WT1 reporter in upcoming studies.

PO2004
Sources of Variability in Podocyte Foot Process Width Measurements and Approaches to Mitigation
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Background: Podocyte foot process (FP) morphology is used in the research setting to quantify podocyte injury and has the potential to be leveraged for diagnostic use. However, the impact of pre-analytic and analytic variables on these measurements are not well understood. We sought to identify these sources of variability and develop a robust method for podocyte foot process width (FPW) measurement within different kidney diseases.

Methods: We examined the impact of operator bias and sample size on FPW measurement in electron micrographs from nephropathies (N) and podocytopathy (P) cases, including primary focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD), and other glomerular lesions affecting the podocyte. FPW was measured for each individual FP between the midpoints of flanking filtration slits and the geometric mean of all FPW measurements was reported by image. We found that identification of filtration slits was subjective, but interoperator variability was mitigated through use of standardized morphologic criteria, operator training, adjudication of ambiguous features, and a mapping process that eliminated duplicate measurements in adjacent images. These methods reduced interoperator variability in FPW, averaged by image, from 12% to 7%.

Results: Preliminary analysis suggests that, in addition to the expected larger FPW mean in MCD cases vs. Nx cases, there is also larger FPW variability in MCD cases. Related analysis shows ~125 FPW measurements within each of 2 glomeruli (~250 total) in FSGS as the same precision as ~100 FPW measurements in each of 10 glomeruli (~1,000 total) in a MCD case. We also found that intraglomerular variability among 3 glomeruli in each of 2 cases (1 Nx, 1 MCD) ranged from 29% to 46% (Geometric CV), whereas interglomerular variability was only 12% (Geometric CV). Notably, these results were highly reproducible among the Nephrology data set. The study of a larger sample size and different kidney diseases is needed to confirm these findings.

Conclusions: Sources of variability in FPW measurements include operator variability, analytic variability, and interglomerular variability. Future studies in a larger sample size and different kidney diseases could further refine these findings.

PO2005
Glucomerular Transcriptomic Analysis of Glucocorticoid- and Pioglitazone-Treated Nephrotic Syndrome
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Background: Nephrotic Syndrome (NS) is among the most common glomerular diseases in children. Glucocorticoids (GC) are the primary treatment for NS, but 15-20% of children have or develop steroid resistant NS, creating an unmet need for novel therapeutics. Thiazolidinediones (TZDs) such as pioglitazone (PIO) have been shown to slow diabetic nephropathy progression, and to reduce proteinuria in animal models of NS. Since both GC and PIO act via binding to nuclear receptors we hypothesized that the reported similar degrees of proteinuria reduction by GC and PIO are driven via common molecular pathways.

Methods: We performed transcriptome analyses on glomeruli isolated from GC- and PIO-treated rats 11 days after induction of NS with PAN (n=4/group).

Results: Principal component analyses revealed distinct transcriptional profiles between GC vs. PAN-treated rats, with 319 and 126 differentially up- and down-regulated genes in PAN respectively, which were largely reversed by both GC and PIO. Ingenuity pathway analyses (IPA) combined with drug-target interaction network analyses and gene set enrichment analyses identified 29 glomerular genes that were commonly regulated by GC, PIO, and their respective nuclear receptors (NRECI and PPARγ). Gene ontology annotation revealed these 29 genes to be involved in: ECM modification, plasma membrane dynamics, DNA damage/repair, transcription factor binding, lipid metabolism, and cytoskeletal organization. Gene segregation into their cells of origin using reported high-confidence cell-type transcriptional signatures revealed most dysregulation and restoration of gene expression within podocytes, with moderate changes within mesangial cells and minimal changes within endothelial cells. IPA-based disease and toxicity algorithms developed from these cell-specific data also revealed enhanced cytoskeletal organization and improved cell viability after both GC and PIO vs. PAN.

Conclusions: GC and PIO treatment reduced proteinuria similarly in NS, but by inducing alterations in both distinct and overlapping glomerular gene sets. Notably, informatics analyses of overlapping genes identified ECM proteins, as potential novel targets for future therapies for NS, distinct from current immunosuppressive approaches.

Funding: NIDDK Support

PO2006
Novel Podocyte Protective Compounds Identified Using Ultra-Miniaturized High-Content Screening (HCS) Assays
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Background: Podocytes are specialized epithelial cells which are part of the filtration barrier in the kidney. Podocyte dysfunction is part of kidney pathologies hallmarked by proteinuria. Using a high-content imaging based assay, we have shown that podocytes can be used to identify novel therapeutic compounds.

Methods: Differentiated mouse podocytes were seeded on collagen-I coated multi-well plates. After 10-14 days of differentiation, cells were exposed to puromycin aminonucleoside (PAN, podocyte injury inducing agent), with compounds from the screening library or newly identified targets, or DMSO as control, for 48 hours. After, cells were fixed with 4% paraformaldehyde and permeabilized with 0.1% Triton X-100. Cells were labeled with cytoplasmic stain HCS CellMask Green, and actin fibers were detected by using labeled phalloidin. Cell images were taken with using Opera High-Content Imaging (HCS) System. Columbus software was used to quantify morphology properties such as roundness, as well as the overall F-actin signal. We utilized commercial libraries containing >50k unique compounds to identify podocyte protective hits.

Results: Using PAN as a podocyte damaging agent, we noticed marked reduction in F-actin fiber numbers and intensity, and increased roundness in podocytes. Screening of a library of chemical compounds identified >25 hits which had favorable profiles.

Conclusions: Using our optimized podocytes high-throughput screening assay in 1536-well plates, we have identified a number of highly novel compounds. Further mechanistic studies provide new insights about podocyte pathways that can be therapeutically targeted.

Funding: NIDDK Support
PO2007
The Role for FNBP1L in Podocytes
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Background: Podocytes exhibit a complex cellular morphology characterized by the formation of foot processes. The normal structure of podocytes depends on their unique cytoskeleton, which is composed of subunit components and actin monomers. The rate limiting step in actin polymerization is the interaction between actin monomers and the barbed end of actin filaments. The podocyte may be the rate limiting step in actin polymerization. There are two distinct nucleotides for actin nucleation in podocytes, Arp2/3 complex and formin, which mediate branch and linear actin filament formations, respectively. We previously identified hundreds of genes expressed in every single podocyte, which were potential podocyte essential genes. Of them, FNBP1L is known to be involved in Arp2/3 complex and formin activity in nuclear, supporting FNBP1L’s essentiality for podocytes. Here, we test this hypothesis.

Methods: Cultured podocytes were used for this study. FNBP1L was knocked down by siRNA, and immunostaining, immunoblotting, qPCR, wound healing assay, and immunoprecipitation were performed to test FNBP1L’s essentiality and mechanism.

Results: FNBP1L was specifically expressed in podocytes in glomeruli, and its expression was decreased in purinycin aminonucleosides-treated in podocytes, where FNBP1L was knocked down, we found that the expression of WT1, SYNO and CD2AP was decreased; that the migratory capability was impaired; that F-actin stress fibers were reduced and disorganized; and that focal adhesion number was decreased while their size increased as shown by p-FAK staining. Mechanistically, FNBP1L regulated Arp2/3 complex and IN2 (a formin) actin nucleation activities. Co-IP and IF showed that FNBP1L colocalized and interacted with CDC42 and N-WASP to facilitate interaction of N-WASP with Arp2/3 complex, thereby increasing the activity of Arp2/3 complex in actin nucleation involved with IN2 and affected its localization in cytoplasm and its actin nucleation. Consistently, the reduction of FNBP1L impaired the interaction between N-WASP and Arp2/3 complex and mis-localized IN2 in the cytoplasm.

Conclusions: FNBP1L may regulate branch and linear actin filament podocytes by regulating Arp2/3 complex and IN2 actin nucleation activities in podocytes, thereby maintaining podocyte normal structure and function. Reduction of FNBP1L expression is involved in podocyte injury and targeting FNBP1L may represent a novel therapeutic approach for podocyte injury.

Funding: Government Support - Non-U.S.

PO2008
Role of ATE1 in Radiation-Induced Nephrotoxicity
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Background: Arginylation increases arginine availability for Arg1 and other enzymes. However, the effect of radiation therapy (RT) on arginylation is not known. This study investigated the impact of RT on arginylation in nephrotoxicity.

Methods: Human podocytes were irradiated with 4 Gy, and preced by rituximab mAb (100 μg/mL) or IgG (100 μg/mL) treatment, 30 min before RT. Additionally, 8-6-week-old C57BL/6 male and female mice were submitted to either (i) 1x14Gy bilateral kidney-only RT (ii) unilateral total body irradiation (TBI 10.5Gy) and rescued by strain-donor hematopoietic stem cell transplantation (HSCT) or (iii) left untreated (sham control). Functional, histopathological, and biochemical changes were studied at baseline and 10 weeks post RT.

Results: In podocytes, RT (4Gy) produced time-dependent downregulation of ezrin (30%) and ATE1 (50%) and a significant increase in apoptosis at 4h (p<0.001). Rituximab pretreatment protected against ezrin relocalization and ATE1 downregulation and podocyte apoptosis. In C57BL/6 mice, RT significantly decreased glomerular surface area and increased mesangial expansion scores in 14Gy and TBI animals compared to controls (p<0.05). Similarly, both RT schedules resulted in significant increases in renal fibrosis (p<0.01), serum BUN (p<0.01), and serum creatinine levels (p<0.01). Western blot analysis showed downregulation of ATE1 in the kidney cortex: 67.7±9.6% (14Gy); 69.3±13.3% (TBI) compared to control. Similarly, IHC data showed a decrease in ATE1 expression in glomeruli after 14Gy (30%) and TBI (70%) compared to control. Podocyte nuclei number in the kidney cortex, also decreased significantly after both RT treatments. TEM showed that both RT schedules resulted in significant increases in GBM thickness when compared to control (p<0.001). Foot process width also increased significantly in 14Gy and TBI animals compared to controls (p<0.001).

Conclusions: Our study demonstrates that rituximab pretreatment protects from ATE1 downregulation and confers radioprotective effects in cultured podocytes. ATE1 may be an important therapeutic target for radiation-induced kidney injuries in HSCT patients.

Funding: Other NIH Support - NIH/NCI PQ12 1R01CA227493-01

PO2009
Podocyte Inflowing Glomerulopathy: New Disease or Pattern of Injury?
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Introduction: Occasional podocyte inflowing is reported in membranous nephropathy, but global and diffuse inflowing is rare. Whether this is a new disease entity or a pattern of podocyte inflowing may influence therapy.

Case Description: 52-yr-old female with hypertension developed lower extremity edema, pleuritic chest pain and dyspnea. CT chest showed bilateral pulmonary emboli. Creatinine was 0.92 mg/dL, cholesterol 239 mg/dL, albumin 3.2 g/dL, urine protein:Cr ratio 32.647 mg/gCr. Renal biopsy showed immune complex deposition in a membranous pattern, and subepithelial deposits with targeted microvascular substructures, suggesting a podocyte inflowing glomerulopathy (PIG) [Fig.1 Electron microscopy showing PIG]. Immune deposits were dominantly reactive for IgG4, and also for other IgG subclasses, C3, IgM, and kappa and lambda light chains. Deposits were reactive for PL2AR. Serum PL2AR antibody and other serologies were negative. He was anticoagulated and treated for 6 months with the modified Ponticelli protocol. Creatinine remains normal, but hypoalbuminemia and proteinuria (190mg – 1.2g/p) persist 8 months after starting treatment.

Discussion: In 1985, Dales and Wallace [1] described massive deposits of spherical organelles in the subepithelial space of glomerular capillary walls in a patient with membranous nephropathy. In 2008, Joh et al [2] studied 25 Japanese patients with microspheres and microtubular structures associated with podocyte inflowing, conferring the term “podocyte inflowing glomerulopathy.” Rare cases are reported in India, Latin America and South Africa. It is unclear whether PIG is a subtype of membranous nephropathy or a distinct glomerular lesion. Identification of PIG associated with vesicoureteral reflux, myeloma, and autoimmune diseases, and the absence of immune complexes in many biopsies, suggest a distinct type of podocyte injury. Ultimately, the pathophysiology of PIG is not well understood. Response to therapy and prognosis are not well-defined. This patient was treated with the modified Ponticelli protocol, given findings of membranous nephropathy, with a reduction in proteinuria but not full remission. This may represent a partial response to therapy or may imply that podocyte inflowing glomerulopathy is a separate disease entity not responsive to immunosuppression.

PO2010
CVD Remodels Skeletal Muscle Metabolism Toward Carbohydrate Oxidation
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Background: Skeletal muscle health progressively declines from chronic kidney disease (CKD). To test the hypothesis that exercise mitigates abnormal muscle metabolism in CKD, we utilized high-resolution mitochondrial respiration and metabolomics techniques for indices of skeletal muscle carbohydrate and fat metabolism in a progressive CKD rat model.

Methods: Animals. 1) Cy/+ (CKD) rats, 2) CKD + wheel running, and 3) normal littermates (NL) (N=12/g). Running wheel was accessible 24 h/day 25-35 weeks of age; normal diet, food and water. We used CKD rats, representing CKD, whose chronic kidney disease was maintained by 6/0 Polyethylene glycol-6000 injection to one kidney. Normal mice served as controls. In 1985, Dales and Wallace [1] described massive deposits of spherical organelles in the subepithelial space of glomerular capillary walls in a patient with membranous nephropathy. In 2008, Joh et al [2] studied 25 Japanese patients with microspheres and microtubular structures associated with podocyte inflowing, conferring the term “podocyte inflowing glomerulopathy.” Rare cases are reported in India, Latin America and South Africa. It is unclear whether PIG is a subtype of membranous nephropathy or a distinct glomerular lesion. Identification of PIG associated with vesicoureteral reflux, myeloma, and autoimmune diseases, and the absence of immune complexes in many biopsies, suggest a distinct type of podocyte injury. Ultimately, the pathophysiology of PIG is not well understood. Response to therapy and prognosis are not well-defined. This patient was treated with the modified Ponticelli protocol, given findings of membranous nephropathy, with a reduction in proteinuria but not full remission. This may represent a partial response to therapy or may imply that podocyte inflowing glomerulopathy is a separate disease entity not responsive to immunosuppression.

Conclusions: These intriguing results indicate CKD impairs skeletal muscle mitochondrial oxidative capacity despite increased pyruvate oxidation. In addition, the metabolomics data suggests impaired fatty acid oxidation that worsened with wheel running due to low carnitine levels. These results suggest dual alterations in response to mild exercise in CKD: 1- impaired fatty acid oxidation from deficient carnitine; 2- enhanced pyruvate oxidation consistent with lower lactate production. These cellular metabolic reprogramming events suggests that skeletal muscle may shift away from fatty acid metabolism towards carbohydrates which may explain why patients with CKD do not experience the usual benefit of exercise.

Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2011
Podocyte-Derived Testican 2 Promotes In Vitro Glomerular Angiogenesis
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Background: In addition to their fundamental role in clearance, the kidneys release select molecules into the circulation, but whether any of these anabolic functions provides insight on kidney function is unknown.

Methods: Using aptamer-based proteomics, we characterized arterial (A) to renal venous (V) gradients for >1,300 proteins in 22 human individuals who underwent invasive sampling. To localize testican-2, immunohistochemistry, immunofluorescence, immunogold electron microscopy and single cell RNA sequencing in human kidney tissue were used. Functional effects of testican-2 were tested on cultured primary human glomerular endothelial cells (HGEC).

Results: Although most of the proteins that changed significantly decreased from A to V, consistent with renal clearance, several were found to increase, the most significant of which was testican-2 (V/A = 1.40, P = 1.5 x 10^-9). Imaging and single cell RNA sequencing demonstrated testican-2 expression in human podocytes. Testican-2 promoted angiogenesis and migration in cultured HGEC, but not proliferation. Further, testican-2 upregulated MMP-2/MMP-9 activity in the culture media of HGEC.

Conclusions: Testican-2 is a circulating protein that is synthesized in the human podocyte. Testican-2 promotes angiogenesis in cultured HGEC, which may be mediated by upregulating MMP-2/MMP-9 activity and increased endothelial cell migration.

Funding: NIDDK Support

PO2012
Mitochondrial Quality Control Mechanisms in Renal Cortex During the Normoalbuminuric Stage of Diabetes Mellitus
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Background: Oxidative stress during the normoalbuminuric stage of type 1 diabetes mellitus (DM) damages renal cortical mitochondria. Because accumulation of damaged mitochondria can contribute to renal dysfunction, we aimed to determine if oxidative stress in DM triggered 1) mitochondrial fission or fusion, 2) increased fatty acid metabolism, and 3) mitophagy as quality control mechanisms.

Methods: Rats receiving i.p. injection of streptozotocin (STZ, 65 mg/kg) or vehicle (Sham) were either left untreated or treated with telmisartan (TLM, an angiotensin receptor blocker; 10 mg/kg/d). Two weeks later, blood glucose levels (BG), blood pressure (BP), glomerular filtration rate, and urinary excretion of albumin and N-acetyl-β-D-glucosaminidase (NAG) were measured. The oxidative stress marker, 3-nitrotyrosine (3-NT), was detected by HPLC. Fission-, fusion-, and mitophagy-related proteins were quantified by Western blot. Levels of acylcarnitine, which transports fatty acids into mitochondria via SLC25A10 (3-NT), was detected by HPLC. Fission-, fusion-, and mitophagy-related proteins were quantified by Western blot. Levels of acylcarnitine, which transports fatty acids into mitochondria via SLC25A10, and the expression of muscle atrophy related genes (quantitative-PCR).

Results: In mice treated with vehicle, exercise tolerance was deteriorated and gastrocnemius muscle wet weight was decreased compared to the control group. Intriguingly, IS administration also reduced a cross-sectional area of fast twitch myofiber and protein levels of fast twitch myosin heavy chain. Also, IS treatment tended to upregulated miRNA expression of muscle atrophy related genes (quantitative-PCR).

Conclusions: IS induces direct sarcopenic effect on mouse skeletal muscle and predominantly decreases on fast-twitch muscle fibers. In the future, we will further investigate the molecular mechanism of uremic toxin induced sarcopenia.

PO2013
Indoxyl Sulfate Modulates Expression of Myosin Heavy Chain Isoforms and induces Sarcopenic Phenotype in Mouse
Takaki Higashihara, Hiroshi Nishi, Koji Takemura, Masao Nangaku. Division of Nephrology and Endocrinology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan.

Background: In patients with chronic kidney disease, sarcopenia is frequently associated with decreased renal function and correlates with increased morbidity and mortality. However, the molecular mechanism to underlie uremic sarcopenia is not fully elucidated yet. We hypothesized that the accumulation of uremic toxin might have a direct negative effect on skeletal muscle, and investigated the mechanism of indoxyl sulfate (IS) induced toxicity on mouse skeletal muscle.

Methods: We conducted the in vivo experiments using C57BL/6 mice. After unilateral nephrectomy, vehicle (PBS) or high dose IS was intraperitoneally administered daily for 1 week, and evaluated exercise tolerance (treadmill fatigue test and four limbs grip test), skeletal muscle wet weight, cross-sectional area, and protein levels of myosin heavy chain.

Results: We confirmed the in vivo experiments using C57BL/6 mice. After unilateral nephrectomy, vehicle (PBS) or high dose IS was intraperitoneally administered daily for 1 week, and evaluated exercise tolerance (treadmill fatigue test and four limbs grip test), skeletal muscle wet weight, cross-sectional area, and protein levels of myosin heavy chain.

Conclusions: IS induced sarcopenic effect on mouse skeletal muscle and predominantly decreases on fast-twitch muscle fibers. In the future, we will further investigate the molecular mechanism of uremic toxin induced sarcopenia.

PO2014
Lnc-Gm43360 Regulates TCMK-1 Seneescence by the miR-141/Sirt1 Pathway
Jie Li, Hongli Jiang, Lei Chen. The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China.

Background: Aging is a complex process, which will lead to the gradual decline of physiological functions of all organs. The kidney, which is a metabolically active organ, is extremely susceptible to aging, but the mechanism of kidney aging is not clear. Long-chain non-coding RNA (lncRNA) is an non-coding RNA consisting of 200 nucleotides, which play an important role in kidney fibrosis and diabetic nephropathy, but there is no study on kidney senescence.

Methods: Detection of lnc-Gm43360 expression by qRT-PCR. Transfection with lnc-Gm43360 siRNA and overexpressed plasmid to measure the miR-141 and Sirt1 expression by qRT-PCR, and the p53, p21 and p16 expression by western blot, and SA-β-gal expression. Transfection with miR-141 mimic and inhibitor to measure Sirt1 expression by qRT-PCR, and p53, p21 and p16 expression by western blot, and SA-β-gal expression.

Results: Lnc-Gm43360 expression in 24-month-mouse lower than 3-month-mouse kidney tissue. The induction of Lnc-Gm43360 expression significantly increases miR-141 expression, decrease Sirt1 expression on both the mRNA and protein level, and induces the SA-β-gal expression. miR-141 mimic and inhibitor decrease and increase Sirt1 expression. Lnc-Gm43360 negatively regulates miR-141 expression and positively negatively regulate Sirt1 expression at both the mRNA and protein level. The function of Lnc-Gm43360 in regulating Sirt1 expression depends on modulating miR-141 expression.

Conclusions: Lnc-Gm43360 can induce TCMK-1 seneescence by miR-141-Sirt1 pathway.

PO2015
Modified Lipoproteins Modulate Renal Lymphatic Vessel Vasodynamics via NKCC1 on Lymphatic Endothelial Cells
Jianyong Zhong, Jing Liu, Elaine L. Shelton, Eric J. Delprie, Huiyang Chung, Valentina Kon. Vanderbilt University Medical Center, Nashville, TN.

Background: In addition to its pivotal role in chloride transporting epithelia, the sodium-potassium–chloride cotransporter 1 (NKCC1) is increasingly recognized as a key modulator of vascular tone. We previously documented NKCC1 expression in renal lymphatic endothelial cells (LECs) of rats and cultured human LECs. Ex vivo we showed that blocking NKCC1 by furosemide caused a dose-dependent dilatation in renal lymphatic vessels, decreased amplitude, and decreased frequency of spontaneous contractions. Since lymphatic vessels clear interstitial lipids and kidney injury increases lipid peroxidation products including isolevuglandins (IsoLG) which modify lipoproteins (apoAI), we examined the role of IsoLG-modified apoAI can affect renal lymphatic vessel contractility through NKCC1.

Methods: Purumycin nephrotoxicity (PN) was induced in Sprague Dawley rats, while non-injected rats served as controls (Cont). Renal lymphatic vessels were isolated and mounted in a perfusion chamber to assess vasoreactivity. The effects of apoAI or IsoLG-apoAI on the NKCC1 signaling pathway were assessed in LECs.

Results: PAN rats had significantly higher renal lymph flow which contained significantly more IsoLG vs Cont. Ex vivo studies showed renal collecting lymphatic vessel diameters from PAN were more dilated than Cont. Immunoreactive revealed NKCC1 expression on LECs that was more prominent in PAN renal lymphatic vessels vs Cont.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**PO2016**

**Progranulin Deficiency Exacerbates High-Fat Diet-Induced Inflammation in Kidney**

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**Background:** Progranulin (PGRN) has been reported to bind to tumor necrosis factor (TNF) receptor (TNFR) and inhibit TNFα signals. Conversely, PGRN is a ‘bad’ adipokine that can contribute to insulin resistance in some metabolic diseases. We evaluated the effect of augmentation of TNFα signals by PGRN deficiency on the progression of kidney injury in high-fat diet-induced obesity model mice.

**Methods:** Eight-week-old PGRN knockout (KO) mice and their wild-type (WT) mice were fed a standard diet or high-fat diet (HFD) for 12 weeks. Mouse proximal tubule (mProx24) cells knocked down with PGRN siRNA were treated with TNFα stimulation.

**Results:** The body weight and albuminuria were significantly increased in WT-HFD group compared with WT-standard diet (SD) group. The body weight of KO-HFD group was significantly decreased compared with WT-HFD group. However, albuminuria and the expression of renal inflammatory markers including TNFα in KO-HFD group were increased than those in WT-HFD group. On the other hand, the WT-HFD mice showed vacuolar changes in the proximal tubule, but KO-HFD mice did not. Immuno-histochemical analysis showed that vacuolar membranes were clearly positive for a lysosomal marker, LAMP-1, suggesting impairment in lysosomal function. The expression of mglalin which plays a critical role in the reabsorption of protein in proximal tubules was found to be decreased in KO mice compared with WT mice, and also reduced in mProx24 stimulated with TNFα.

**Conclusions:** PGRN deficient exacerbated renal inflammation caused by high-fat diet, while the results also showed improvement in tubular vacuolation. Anti-inflammatory treatment with PGRN for kidney diseases should be considered based on the opposing function of PGRN.

**Funding:** Private Foundation Support, Government Support - Non-U.S.

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**PO2017**

**Diet Has a Stronger Impact on the Gut Microbiota Than Kidney Function in Rats with Moderate CKD**

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**Background:** Diet and CKD have been shown to alter the gut microbiota. However, whether diet or kidney function plays a stronger role in the gut microbiota in moderate CKD is not well established. We assessed the effects of two diets on the gut microbiota in rats with moderate CKD.

**Methods:** C57BL/10 (C57) and normal (Norm) littermates (NL) consumed an autoclaved grain-based diet containing 7.5% phosphorus (0.3% phytate-bound) and 3.5% crude fiber from birth. At 17-wk-old, half of the animals were maintained on the same diet (Grain) and the other half switched to a semi-purified casein-based diet containing 0.7% phosphorus (0% phytate-bound, 0.6% phosphate additives) and 5% non-fermentable cellulose (Casein) until 28-wk-old (n=10 rats/group). DNA was extracted from cecal and fecal samples collected at euthanasia, the V4 region of the 16S RNA gene was sequenced via Illumina MiSeq, and data were analyzed using QIIME2 and LEfSe.

**Results:** Intestinal microbial α-diversity, or diversity within a sample, was significantly greater in rats fed the grain diet compared to casein diet regardless of kidney function. Diet and kidney function both had significant impacts on microbial β-diversity (diversity between samples), but diet explained a larger portion of the observed variability (27%) than kidney function (11.5%). Consumption of the grain-based diet increased many genera with short-chain fatty acid (SCFA) producing capacity, including *Bifidobacterium, Ruminococcus, Roseburia,* and *Prevotella* than the casein diet. Whereas the casein diet drove greater *Bacteroides* abundance that can metabolize tryptophan to indoles, which may exacerbate the formation of uramic toxins. Notably, the casein diet led to a greater abundance of *Bifidobacterium* in NL rats and greater *Allotriorchis* in CKD. Both of these taxa have been shown to be linked to reduced progression of inflammatory bowel disease. Additionally, CKD rats fed the casein diet had a higher relative abundance of *Akkermansia,* which has been shown to be greater in fiber-free or low fiber interventions, as it may degrade the mucus layer.

**Conclusions:** In rats with moderate CKD, diet had a stronger effect on diversity and gut microbial taxonomic differences than kidney function. Particularly, those fed the grain-based diet had higher bacterial genera known to produce SCFA.

**Funding:** Other NIH Support - T32 DK072922

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**PO2018**

**Effect of High Fiber or Probiotics-Enriched Diets on Kidney Injury in Mice Model of Bilateral Ischemia Reperfusion**

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**Background:** Changes in dietary intake have a significant effect on the incidence and development of chronic kidney disease (CKD). The progressive decline in kidney function during CKD can lead to increased systemic chronic inflammation and worsening of kidney injury. Fibers and probiotics are used by gastrointestinal bacteria to produce metabolites with anti-inflammatory activities. The objective of our study was to investigate the role of fiber and probiotics in ameliorating kidney injury using bilateral ischemia reperfusion (IR) surgery as a CKD model in mice.

**Methods:** Thirty-six C57BL/6J wild type, male mice were purchased from the Jackson Laboratory (Bar Harbor, ME, USA). After co-housing for a week, they were then isolated and randomly assigned to a diet: normal chow (C; control), high fiber (HF; modified AIN-93G with increased Hi-Maize Corn), and probiotics (P; AIN-93G with added *Bifidobacteria* spp.). After 14 days, mice underwent sham surgery (5 per group) or IR surgery (7 per group) and then received assigned diet for 28 days. Blood and fecal samples were collected both before surgery and after surgery. Mice were euthanized after 42 days to collect kidneys, small intestine, colon, fecal, and blood samples. Measurements of plasma creatinine, markers of kidney injury, and tissue staining were performed. Fecal samples were further processed to assess diversity of gut microbiota. Two-way ANOVA with Tukey’s multiple comparisons was used for statistical analysis.

**Results:** On each diet, the IR increased serum creatinine compared to sham (p<0.05). However, both HF and P showed the best protection against kidney injury, compared to C (p<0.05). The histology sections in control group appeared to be more fibrotic compared to the other two groups. The sequencing of 16s rRNA gene was completed and is currently being used to assess the composition and diversity of gut microbiota in each group.

**Conclusions:** Supplementation with fiber or probiotics may reduce kidney injury after ischemia. Additional studies to identify specific changes in metabolites driving this protection are needed.

**Funding:** Other NIH Support - T32 DK072922
PO2020

Dietary Fat Intake and Mortality Across Kidney Function in a Nationally Representative Cohort

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Background: In the general population, lower dietary intake of saturated fatty acids (SFA) and higher intake of polyunsaturated fatty acids (PUFA) are associated with greater survival. However, the optimal amount and type of dietary fat intake in patients with kidney disease is unknown. We assessed the relationship between dietary fat intake and mortality in a cohort of US adults with and without kidney disease.

Methods: In the general population, lower dietary intake of saturated fatty acids (SFA) and higher intake of polyunsaturated fatty acids (PUFA) are associated with greater survival. However, the optimal amount and type of dietary fat intake in patients with kidney disease is unknown. We assessed the relationship between dietary fat intake and mortality in a cohort of US adults with and without kidney disease.

Results: Among 37,155 participants who met eligibility criteria, 7% (N=2,677) had kidney dysfunction. In participants with normal kidney function, those with the highest tertile of SFA intake had higher mortality risk compared to their counterparts (HRs (95%CI) 1.21 (1.04, 1.41) and 1.13 (0.97, 1.31), respectively; however, PUFA was not associated with mortality. In participants with kidney dysfunction, SFA intake was associated with a higher mortality risk and trended towards higher mortality, respectively: HRs (95%CI) 1.21 (1.04, 1.41) and 1.13 (0.97, 1.31), respectively; however, PUFA was not associated with survival. In participants with and without kidney dysfunction, MUFA intake was not associated with mortality.

Conclusions: Higher dietary SFA intake was associated with a higher mortality in US adults with and without kidney dysfunction, whereas higher PUFA intake was associated with greater survival in those with preserved kidney function only. Further studies are needed to elucidate mechanisms behind the association of dietary fat intake with mortality.

PO2021

Predictors of Healthy Behavior Engagement in CKD

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Background: Guidelines for chronic kidney disease (CKD) management recommend healthy behaviors to mitigate disease progression, but behavior engagement is low. Identifying predictors of behavior engagement could inform strategies to increase healthy behaviors.

Methods: Using data from the Chronic Renal Insufficiency Cohort Study, potential predictors of behavior engagement included demographics, clinical and psychosocial factors, and behaviors at baseline. We dichotomized behaviors (recommended vs. not): smoking (no vs. current), body mass index (BMI <18.5 or ≥30 kg/m2), physical activity (>150 vs <150 minutes/week), diet (score of ≥2 vs 0-1), and hemoglobin A1c (<7 vs ≥7) if diabetes. Relationships between predictors and behaviors at 2 years were estimated by multinomial adjusted logistic regression models.

Results: Among 5,209 participants at baseline, mean age was 60 years, mean eGFR was 48 ml/min/m2, and 51% had diabetes. In multivariable analyses, baseline behaviors were most strongly associated with behaviors at 2 years. Higher SF-12 physical component scores, which relate to better physical function and pain control, associated with recommended behaviors at 2 years. In models that did not adjust for baseline behaviors, no smoking was associated with older age, female sex, and non-White race, but the other behavior associations were not notably changed.

Conclusions: Interventions to increase healthy behavior engagement should be implemented and tested to evaluate whether they improve physical function and pain control, and possibly mitigate CKD progression.

Funding: NIDDK Support

Associations with Recommended Behaviors at 2 years. ORs and 95% CI reported.

Table

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age (per 10 years)</td>
<td>1.00</td>
<td>(0.95, 1.05)</td>
<td>0.21</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>0.99</td>
<td>(0.96, 1.01)</td>
<td>0.43</td>
</tr>
<tr>
<td>Medical (no vs. yes)</td>
<td>0.98</td>
<td>(0.95, 1.01)</td>
<td>0.23</td>
</tr>
<tr>
<td>Medication (yes vs. no)</td>
<td>0.96</td>
<td>(0.94, 0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Higher physical activity (yes vs. no)</td>
<td>2.09</td>
<td>(1.68, 2.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lower all-cause mortality</td>
<td>0.90</td>
<td>(0.85, 0.96)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

PO2022

Impact of Participation in Food Assistance Programs Among NHANES Dialysis Patients from 2001-2016

Hannah Chen, Lea Borgi. Brigham and Women’s Hospital, Boston, MA.

Background: Food insecurity and malnutrition are recognized risk factors for poor outcomes and mortality among end-stage renal disease (ESRD) patients on dialysis. However, little is known about the effect(s) of participation in food assistance programs such as Supplemental Nutrition Assistance Program (SNAP) on outcomes among dialysis patients.

Methods: This is a cross-sectional analysis of dialysis patients in the National Health and Nutrition Examination Survey (NHANES) cohorts from 2001-2016. Food assistance program participation was self-reported as part of the NHANES interview. Differences in baseline characteristics were determined through null hypothesis testing. Logistic and linear regressions were used to examine the association between food assistance program participation and outcomes including hospitalizations and albumin as
a marker of nutrition status. The analyses were adjusted for demographics, BMI, diabetes, hypertension, and hyperlipidemia.

Results: A total of 156 dialysis patients were analyzed across all NHANES cohorts. Dialysis patients receiving food assistance were more likely to be younger, female, and obese (p<0.05). Food assistance participants had significantly larger household size, but lower income and lower levels of post-secondary education (p<0.05). These patients also reported significantly higher daily sugar intake. Dialysis patients receiving food assistance were significantly more likely to report very low food security and less likely to report full food security. Specifically, they reported more concerns regarding food running out, food not lasting, and not being able to afford balanced meals. Approximately 30% of dialysis patients report food insecurity but do not participate in food assistance programs. When adjusted to be representative of the non-institutionalized U.S. population, there was a non-significant trend towards increased hospitalization among dialysis patients on food assistance programs (OR 1.73 [95% CI: 0.42-7.12]). There was a non-significant negative correlation between food assistance program participation and serum.

Conclusions: Food assistance programs are not widely used among dialysis patients, even when patients report food insecurity. Food assistance program participation among dialysis patients did not significantly impact hospitalizations and serum albumin.

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Background: Food insecurity has been associated with CKD and its progression. Trends in food insecurity among adults with CKD have not been well characterized in the US population, particularly across racial/ethnic groups.

Methods: Data from NHANES from 2003-2016 were used to estimate the prevalence of food insecurity among individuals with CKD (defined by albuminuria or eGFR 15-59 ml/min/1.73 m2) overall and by racial/ethnic group. We included individuals aged 20 years and with a household income≤400% of the federal poverty level (n=3180). Food insecurity was defined as ≥3 yes responses on the 18-item questionnaire. Racial/ethnic groups were defined as non-Hispanic white (NHW) and non-NHW. Survey years were collapsed into time periods 2003-2006, 2007-2010, and 2011-2016. Prevalence rates were estimated after standardization to the 2010 age population distribution from the US Census.

Results: Overall prevalence of food insecurity in adults with CKD was 19.9%. During the period, the age-standardized prevalence rate of food insecurity increased from 5.7% to 32.8% among NHW and from 23.2% to 35.8% among non-NHW (p-trend=0.001). After adjusting for age, sex, education level, and annual household income, non-NHW had a significantly higher prevalence of food insecurity compared to NHW in 2007-2010 but not in 2003-2006 or 2011-2016 (Figure).

Conclusions: From 2003 to 2016, food insecurity among both NHW and non-NHW increased significantly among non-NHW compared to NHW during 2007-2010. One potential explanation may be the US economic recession during that period. Targeted interventions such as medically tailored meals for individuals with CKD and poverty may not in 2003-2006 or 2011-2016 (Figure).

PO2024 Approach to Nutritional Protein Intake in Hemodialysis Patients with Hyperphosphatemia: Associations with Mortality in the DOPPS
Suguru Yamamoto,2 Brian Biber,3 Hiroata Komada,3 Hiroki Kitabayashi,3 Takanozu Nomura,4 Alexi Cases,3 Christian Combe,3 Ronald L. Pisoni,1 Bruce M. Robinson,5 Masafumi Fukagawa.2 Arbor Research Collaborative for Health, Ann Arbor, MI; 3Nephrology, Graduate School of Medical and Dental Sciences, Niigata, Japan; 4Kyowa Kirin Co., Ltd., Tokyo, Japan; 5Tokai University School of Medicine, Isehara, Japan; 6Universitat de Barcelona, Barcelona, Spain; 7Université de Bordeaux, Bordeaux, France.

Background: Pt’s undergoing hemodialysis (HD) have poorer nutritional status than the general population, and worse nutritional status is associated with poor outcomes. Hyperphosphatemia is common in HD pts due to abnormal mineral and bone metabolism. Nephrologists manage hyperphosphatemia by prescribing phosphate binders and/or promoting dietary protein restriction; the latter may, however, adversely affect nutritional status. We address the hypothesis that, even in the presence of hyperphosphatemia, liberalizing dietary protein leads to better outcomes.

Methods: The analysis includes 11,628 HD pts in 12 countries in DOPPS phase 4 (2009-2011), from 254 facilities where the medical director reported facility practices. The primary exposure variable was response to the following question: “For pts with s. albumin 3.0 g/dl and phosphate 6.0 mg/dl, do you typically recommend to (A) increase or (B) not change/descrease dietary protein intake?” The primary outcome was all-cause mortality, analyzed by Cox regression. Linear regression was used to model associations between the exposure and intermediate nutrition markers. Models were adjusted for country, case-mix, and lab values.

Results: In the case scenario, 91% of medical directors in N. America recommended to increase protein intake compared to 58% in Europe (range=16-83% in 7 countries) and 56% in Japan. Advice to increase dietary protein intake was associated with 0.33 mg/dl higher s. creatinine levels (95% CI: 0.08-0.57) while clinically meaningful associations were not observed for s. albumin and phosphorus. Advice to increase dietary protein intake was weakly associated with lower mortality-HR (95% CI)=0.89 (0.77-1.03). The association with survival was stronger in pts with age ≥70 yrs and for those without diabetes (p=0.08 and 0.20 for interaction).

Conclusions: In this large international cohort study, the medical director’s preference to recommend increase in dietary protein intake for HD pts with low albumin and high phosphorus levels was most common in N. America and associated with higher s. creatinine levels and potentially lower all-cause mortality. Further research into the possible benefits of protein intake liberalization for HD pts, even in the presence of hyperphosphatemia, is warranted.

Funding: Commercial Support - This abstract was specifically supported by Kyowa Kirin Co., Ltd. The DOPPS Program support and additional support for specific projects and countries can be found here: https://www.dopps.org/AboutUs/Support.aspx
**PO2026**

Mediterranean Diet and the Risk of CKD: A Systematic Review and Meta-Analysis

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**Background:** Mediterranean diet has been shown to be associated with lower risk for cardiovascular disease. However, its association with chronic kidney disease (CKD) remains inconclusive as the results were not consistent among population-based studies. Thus, this study aims to assess the association between Mediterranean diet adherence and CKD prevention.

**Methods:** Ovid MEDLINE, EMBASE, and the Cochrane Library were searched from database inception to March 2020 without language restrictions. We included studies describing the risk for CKD in community-dwelling subjects ≥ 18 years of age. CKD was defined by eGFR < 60 mL/min/1.73m². Mediterranean diet adherence was assessed by standardized food frequency questionnaires. Meta-analysis and meta-regression analysis were used to evaluate the risk of CKD and the association between clinical factors and incidence of CKD, respectively.

**Results:** Of 168 citations, a total of ten (n = 19,151) and five studies (n = 9,099) were included in the systematic review and meta-analysis, respectively. Only studies adopting Mediterranean Diet Scale (MDS) were included in the meta-analysis. The mean score was 4.0 ± 0.1 points. The mean age was 53.1 ± 8.2 years. The mean eGFR was 77.3 ± 29.6 mL/min/1.73m². The average total daily energy intake was 1,989.4 ± 258.8 kilocalories per day. Up to 50.4% were male, 7.1% were black, and 14.9% had a history of diabetes mellitus. With the mean follow-up duration of 11.5 ± 9.5 years, the pooled adjusted odds ratio (OR) for CKD was 0.897 (95% CI, 0.865-0.930; I² = 9.5 years; p = 0.001). There was no significant association between age, black race, eGFR, and total daily energy intake vs. CKD incidence. The incidence of CKD was 0.028 events per person-year (95% CI, 0.012-0.044).

**Conclusions:** Mediterranean diet adherence was assessed by a 1-point increase of MDS was associated with 10% lower risk of CKD. However, this only applies to healthy individuals without a history of pre-existing CKD, whether Mediterranean diet adherence slows CKD progression is to be discovered.

**Funding:** NIDDK Support

**PO2027**

Attitudes Toward Plant-Based Eating (PBE), Self-Reported Habits, and Relationship to BMI and Blood Pressure in a Population of Inner-City CKD/ESKD Patients

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**Background:** The benefits of a PBE dietary pattern are well described, yet there is scarcity in the literature on the attitudes of CKD/ESKD patients regarding PBE as well as their self-reported habits.

**Methods:** A face-to-face survey was conducted in a random convenience sample patients from CKD clinic (15), Transplant clinic (12), and the Dialysis Unit (4). Pts were asked to answer questions assessing their attitudes and understanding of PBE using a 5-point Likert scale, and to rate their daily vegetable intake. There was no difference noted in answers among the clinics so all data were analyzed together. All comparisons are by t-test unless noted.

**Results:** Mean age was 54.7±1.7 yrs. There were 16 (53%) men and 14 (47%) women, with 25 Black (81%), 12 people (40%) had an income < $20K, with 10 (33%) between $20K and $40K. 30 (103%) were employed, 64.5% (20) were interested in learning more about PBE; 35% had never heard of it. 227% reported consuming animal protein 1-3x/d or more. 20 (57%) reported consuming plant-based foods less <1/d or never. Pts who did not eat plant-based foods had a higher BMI than those who consumed plants 30.9±3.5 vs 29.1±1.86, p<0.05 (30.9±3.5 vs 26.9±1.86, p<0.05 and 77.9±3.5 vs 66.3±4.1, p=0.019). 46.4% thought it would be difficult to find things to eat at restaurants, 51.7% thought it would be difficult to buy food or groceries on a budget; 46.4% thought they could not get all the protein they need from plant-based foods without eating animal meat or products; 40.7% thought it would be hard to get all the vitamins and nutrients but 63.1% thought it would be easy to find recipes that taste good if they followed PBE.

**Conclusions:** In our population: 1. The majority of pts were interested in learning about plant-based diet but ate few to no vegetables on a daily basis. 2. Possible obstacles to introducing PBE in this populations are misconceptions including the difficulty of affording food, getting enough protein and finding something to eat when eating out, believed by almost half of those surveyed. 3. Intensive educational programs targeted towards our population should be developed as pts who ate more vegetables had lower BMI and both systolic and diastolic BP and in general PBE has been shown beneficial for pts with CKD/ESKD.

**Funding:** NIDDK Support

**PO2028**

Higher Estimation of Dietary Phosphorus Content with More Plant-Based Protein in Hemodialysis Patients Across Race/Ethnicity Using 3-Day Food Records with Interviews

Amanda R. Tortorici,1 Connie Rhee,1 Amy S. You,1 Elani Streja,1 Keith C. Norris,2 Kamyar Kalantar-Zadeh,1 1University of California Irvine, Orange, CA; 2University of California Los Angeles David Geffen School of Medicine, Los Angeles, CA.

**Background:** Dietary phosphorus (P) restrictions are commonly recommended based on the estimated phosphorus (P) content of foods, not accounting for P type or its absorbability. Whereas plant-based diets have important benefits, they are traditionally not recommended to dialysis patients given perceived higher P content in plant vs. animal-based proteins, although P is less absorbable in plant foods. We examined dietary differences across race/ethnicity in a group of hemodialysis (HD) patients from several dialysis centers in Southern California.

**Methods:** The self-administered 3-day diet diary with face-to-face interview was conducted by a trained dietitian among 80 in-center HD patients, and the data were entered into a diet software (Nutrition Data System for Research), and dietary components of the individuals and subgroups were obtained.

**Results:** Patients were 57±15 years and included 25% Blacks, 36% Hispanics and 18% non-Hispanic Whites. Table shows dietary data across race/ethnicity. [Figure] Shows the association of the phosphorus-to-protein ratio with the percentage of plant protein, correlation coefficient r was 0.58 (p<0.001) for all including 0.28, 0.61 and 0.38 for Blacks, Hispanics and Whites, respectively.

**Conclusions:** Whereas estimated dietary potassium was not substantially different across race/ethnicity or different plant- vs. animal based protein proportions, dietary phosphorus content analyses may not account for varying phosphorus bioavailability across sources, which may lead to incorrect assumptions that higher plant-based protein for dialysis patients is associated with more phosphorus burden.

**Funding:** NIDDK Support

**Analyses of 3-day diet diary across race/ethnicity**

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>P vs protein ratio</th>
<th>Plan vs total protein, %</th>
<th>P, mg/1000cal</th>
<th>Protein, mg/1000cal</th>
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</thead>
<tbody>
<tr>
<td>Blacks</td>
<td>1.0±0.7</td>
<td>25%</td>
<td>558±110</td>
<td>1,084±214</td>
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<td>Hispanics</td>
<td>1.3±0.6</td>
<td>25%</td>
<td>614±187</td>
<td>1,309±275</td>
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<tr>
<td>Whites</td>
<td>1.2±0.2</td>
<td>36%</td>
<td>660±127</td>
<td>1,025±260</td>
</tr>
</tbody>
</table>

**PO2029**

Benefits of Home-Delivered, Low-Sodium Meals in Hemodialysis Patients

Luis M. Perez, Hsin-Yu Fang, Brett Burrows, Alexis King, Sadia anjum Ashrafi, Kenneth R. Wilund. Renal and Cardiovascular Research Laboratory University of Illinois at Urbana-Champaign, Urbana, IL.

**Background:** Patients undergoing maintenance hemodialysis (HD) therapy are routinely counseled to reduce dietary sodium intake to reduce sodium retention, volume overload (VO), and hypertension. Unfortunately, low-sodium trials in HD are sparse and mostly indicate that dietary education and behavioral counseling alone are ineffective in reducing sodium intake. The purpose of this study is to determine if 4-weeks of a low-sodium home delivered meals intervention will reduce interdialytic weight gain (IDWG) and subsequent VO and hypertension in patients undergoing HD when compared to 4-weeks of a usual diet.

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**
Methods: We recruited 20 subjects (55±12 years, BMI 40.7±16.6 kg/m², 45% male, 65% NA, 70% DM, 50% CVF) from a HD clinic in central IL. Participants followed a usual-control diet for the first 4 weeks. PurFoods, LLC prepared and shipped 3 low-sodium kidney meals (<700 mg sodium, potassium, and phosphorus each) per day to patients in the following 4 weeks. We collected monthly IDWG, bioelectrical impedance, standardized blood pressure, 3 days (HD, non-HD, and weekend day) of dietary recalls, and blood at baseline (0M), after a usual diet (1M), and post-intervention meals (2M).

Results: Home-meal delivery significantly reduced both dietary sodium intake, IDWG, BP, and VO in HD patients. It will be important to determine if these changes can be sustained long-term with additional counseling and in larger sample sizes. The long-term benefits and cost-effectiveness of this approach also needs to be evaluated.

Funding: Commercial Support - Renal Research Institute

Changes in Volume-Related Parameters

PO2030

Performance of GLIM for Nutritional Assessment of Hemodialysis Patients: Comparison with Subjective Global Assessment (SGA) and Malnutrition-Inflammation Score (MIS)

Carla M. Avesani,1 Alice Sabattino,4 Alessandro Guerra,2 Juan J. Carrero,3 Giovanni maria Rossi,1 Peter Stenvinkel,1 Enrico Fiaccadori,4 Bengt Lindholm,1 Karolinska institutet Department of Clinical Sciences Intervention and Technology, Huddinge, Sweden; 2Università degli Studi di Genova, Genova, Italy; 3Karolinska Institutet, Stockholm, Sweden; 4Parma University Hospital, Parma, Italy.

Background: There is a need for methods to identify and monitor malnutrition in maintenance hemodialysis (MHD) patients. We assessed GLIM (Global Leadership Initiative on Malnutrition) performance and evaluated agreement and survival prediction of GLIM vs. SGA and MIS in MHD pts.

Methods: We investigated two cohorts, MHD Italy (121 adult pts from Italy; 67% men, BMI 25±4 kg/m² and MHD Brazil (169 elderly [age 60±7] yrs) pts from Brazil; 71% men, 66% men, BMI 25±4 kg/m²), followed for 40 (27; 46) and 17 (12; 31) months (median and 25%; 65%), respectively. GLIM comprises: 1. Screening and 2. Confirming malnutrition by phenotypic and etiologic criteria. For 1., presence of >1 criteria from protein energy wasting definition was used. Pts at risk were re-tested with GLIM's phenotypic criteria: non-volitional weight loss or low BMI (<20 kg/m², <70y, or <22 kg/m² if ≥70y) and reduced muscle mass (MAMC<90%). As dialysis is a catabolic procedure, all pts were positive for the etiologic criteria. For SGA and MIS, a score ≥5 and ≥8 was considered for malnutrition, respectively.

Results: Malnutrition was present in 38.8% by GLIM, 25.6% by SGA and 29.7% by MIS in the MHDItaly cohort, and in 47.9% by GLIM, 59.8% by SGA and 49.7% by MIS in the MHDBrazil cohort. Cohen’s kappa coefficient (k) showed only “fair” agreement between GLIM and SGA and MIS respectively (Table). Cox regression analysis adjusted for gender and age showed that in the MHDItaly cohort, only pts malnourished by MIS had higher risk for mortality (HR=2.42; 95% CI:1.28 to 4.59; P=0.007) while in the MHDBrazil cohort, pts malnourished by GLIM (HR=2.09; 95% CI:1.1.3 to 3.86; P=0.02), SGA (HR=1.96; 95% CI 1.01 to 3.79; P=0.04) and MIS (HR=2.24; 95% CI 1.20 to 4.16; P=0.01) had higher risk for mortality.

Conclusions: In MHD pts, GLIM showed low agreement with SGA and MIS, raising question on its validity and usefulness in renal care. Only malnutrition by MIS predicted mortality risk in MHDItaly cohort, but in the MHDBrazil cohort, malnutrition by all three methods predicted higher mortality risk.

PO2031

Dietary Fiber Intake, Cardiovascular Risk Factors, and Kidney Function: A Mediation Analysis


Background: Higher fiber intake may be associated with higher eGFR but the mechanisms underlying this association are poorly understood. Considering that higher fiber intake is linked to improved cardiovascular (CV) risk factors, we hypothesize that the effect of fiber intake on eGFR could be mediated by these CV factors.

Methods: CARTaGENE is a population survey of healthy adults. We used multiple linear regression to study the association between fiber intake and eGFR while adjusting for confounding factors, including age, sex, diabetes, hypertension, dyslipidemia, body mass index (BMI), smoking, prior CV disease, physical activity and caloric intake. We assessed whether CV risk factors lie in the causal pathway between fiber intake and eGFR through mediation analyses.

Results: We included 9,854 of the CARTaGENE participants with a completed food questionnaire (mean age: 53 years, 56% males). The main comorbidities were hypertension (25%), diabetes (8%) and cardiovascular disease (7%). The median daily fiber intake was 17.2g (IQR 10.7-23.7) and the mean eGFR was 87.3±14.6 mL/min 1.73 m². After adjustment for the above factors, fiber intake was associated with higher eGFR and serum HDL levels, and lower BMI, glycated hemoglobin and triglyceride levels (Table). Other risk factors were found to be non-significant. The mediation analysis demonstrated that only 10% of the effect of fiber intake on eGFR was mediated through BMI and triglyceride levels.

Conclusions: Higher dietary fiber intake is associated with higher eGFR and better control of certain cardiovascular risk factors. While the association between fiber intake and kidney function may be marginally mediated by healthy weight and triglyceride levels, further studies are needed to understand the mechanisms underlying this association.

Association between dietary fiber intake and clinical variables.

PO2032

Interplay Between Dietary Phosphorus and Protein Intake with Mortality in a Prospective Hemodialysis Cohort

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Background: Current dietary recommendations for dialysis patients suggest that high phosphorus (P) diets may be associated with negative outcomes such as increased serum P and death. However, caution must be practiced to ensure dietary P intake is not compromised at the expense of dietary protein intake. We hypothesized that higher concentrations of dietary P intake is associated with higher mortality among a diverse cohort of hemodialysis (HD) patients.

Methods: Among 415 patients from the prospective multi-center Malnutrition, Diet, and Renal Disparities in Kidney Disease Study, we conducted standardized collection of dialysis and treatment characteristics every six months starting in 2011. We examined the association of quartiles of dietary P scaled to 1000 kcal (mg/ kcal), as measured by food frequency questionnaires, with all-cause mortality using Cox models adjusted for expanded case-mix+laboratory+nutrition covariates. To model the association between continuous daily dietary P intake scaled to protein (mg/g) and mortality, we conducted analyses in which dietary P/protein intake was examined as a restricted cubic spline.

Results: In baseline analyses, patients in the lowest quartile of dietary P scaled to 1000 kcal had increased mortality risk compared to those in the highest quartile: adjusted HR (95%CI) 1.80 (1.05, 3.09). In analyses examining the association between continuous dietary P/protein (mg/g) intake and mortality using a cubic spline, we observed that there was a monotonic decrease in death risk with higher dietary P/protein intake.

Conclusion: Contrary to current practice, we found that lower intakes of dietary P scaled to protein and caloric intake were each associated with higher mortality risk. National nutrient databases indicate that foods with lower vs. higher P/protein ratios tend to be from animal proteins vs. plant proteins and dairy. Further studies are needed to clarify the relationship between sources of dietary P intake and mortality in HD patients.

Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

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PO2033

Protein Supplements and Proteinuria: A Case-Control Study in Military Candidates

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Background: Man has long wanted to improve both image and physical performance using supplements some of which include proteins. Low protein diets are recommended by guidelines to attenuate the progression of chronic kidney disease. In healthy individuals, however, protein intake does not seem a risk factor. This study assessed whether protein supplements could cause proteinuria in a healthy population.

Methods: We performed a case-control study at the Military Hospital of Oporto including 1541 military academy candidates who had urinalysis in 2017. Among them, 102 (6.6%) had proteinuria (dipstick test +/++) and these were compared to a random sample of 106 non-proteinuric candidates. Telephone interviews collected data on comorbidities, exercise, smoke, alcohol habits, drugs, supplements, height and weight. Protein supplements were accessed as risk factors for proteinuria using the Pearson Chi-square test.

Results: Answers were obtained from 49 cases and 52 controls. Of these 101 candidates, 88 were males, had a median age of 19 and mean body mass index of 24.1±2.4kg/m2. Most (97%) exercised for a mean weekly time of 6±3.7h: 40% practiced only resistance training; the rest both resistance and strength. Half used supplements at some point in time and 32 were current users. All used protein powder, mainly whey protein. Additional supplements (mostly amino acids) were used by 13. The weekly powder intake ranged from 3 to 14 scopes (20.3±31.0 scope). No significant association was found between the use of protein supplements and proteinuria (p=0.51). Similarly, no difference was found in creatinine, urea or other laboratory parameters. Supplements were significantly used more by those who practiced strength, as compared with resistance-training subjects.

Conclusions: One third of Portuguese military candidates used protein supplements. Increased use was noted in strength training most likely due to peer pressure. Proteinuria was found in 6.6%, similar to screenings in other healthy populations. No relation was found between protein supplements and proteinuria which could mean that the kidneys of healthy individuals are capable of dealing with a higher metabolic strain after increasing protein loads. However we acknowledge that proteinuria as a marker of disease has limitations and that the cumulative evidence and exposure time of protein supplements was not considered and may be relevant.

PO2034

Continuous Intradialytic Amino Acid Infusion from the Start of Dialysis Is Better to Avoid Catabolism under the High-Volume Pre-Dilution Online Hemodiafiltration

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Background: Amino acid infusion during dialysis is useful for improving nutritional status (Clin Nephrol 3:234, 1975). Usually, amino acid is infused 60 to 90 minutes before the end of dialysis, but it is reported that continuous administration from the start of dialysis is better (Kidney Int 21: 500, 1982). Moreover, these effects are unclear in high-volume pre-dilution on-line HDF (HVPO-HDF). The optimal administration method of amino acid infusion during the HVPO-HDF was analyzed.

Methods: The subjects were 10 patients receiving HVPO-HDF (7 males, 4 diabetics, median age 77.2±5.5 years). We compared the pre- and post-dialysis plasma amino acid levels and the total amino acids amount in the waste fluid when the amino acids infusion was performed from the start of dialysis (Group A) and from 1 hour before the end of dialysis (Group B). The treatment time is 4 hours. The mean blood flow rate was 200 ml/min. The dialysate flow rate was 600 ml/min. The replacement fluid flow rate was 400 ml/min and total replacement fluid volume was 90 ml. Hemodialyzer FX-21M Nipro (Nipro Ltd) was used.

Results: In pre-dialysis plasma levels of total amino acid (TAA), Group A and Group B showed the same level (247±267 mmol/ml and 262±319 mmol/ml, respectively). In the essential amino acid (EAA) and non-essential amino acid (NEAA), similar results were obtained (827±145 mmol/ml and 847±99 mmol/ml of EAA, 1644±216 mmol/ml and 1120±193 mmol/ml of NEAA, respectively). Moreover, the losses of amino acids were also similar (99.1±13 mg and 880±1204 mg of TAA, 84±58 and 4544±453 mg of EAA, 402±644 mg and 432±862 mg of NEAA, respectively). In Group A, post-dialysis plasma levels of amino acids were significantly lower than in Group B (206±630 mmol/ml and 382±636 mmol/ml of TAA, 94±193 mmol/ml and 22±439 mmol/ml of EAA, 1120±193 mmol/ml and 1577±260 mmol/ml of NEAA, respectively, p < 0.01).

Conclusions: The result of high post-dialysis plasma levels despite the same loss of amino acids suggests more catabolism from muscle to blood in Group B. The continuous intradialytic amino acid infusion is better to avoid catabolism under HVPO-HDF.
yet attenuated relationship was observed among A2 patients. Odds of faster UACR slope was higher only in patients with LDL ≤ 160 mg/dL and with index UACR≥300 mg/g. For A3 patients, there was no association between LDL level and UACR slope.

Conclusions: Among patients with baseline UACR < 300 mg/g, both low and very high LDL were associated with higher odds of having fast UACR change. Yet, among those with higher albuminuria, the relationship with LDL and UACR change was null. More studies are needed to delve into the mechanism between LDL and CKD progression in order to further manage patients kidney health.

Funding: Veterans Affairs Support

PO2038

The Combination of Malnutrition Inflammation and Limitations in Functional Status Is Associated with a Very High Risk of Mortality in Hemodialysis Patients: Results from the DOPPS
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Background: The malnutrition-inflammation-complex (MIC) is a risk factor for mortality and lower quality of life in hemodialysis (HD) patients. The identification of MIC and its risk factors, which include the limited ability to perform functional status (FS), is key to improve the patient experience on HD. Our study investigates the association of MIC and FS combinations with mortality in HD patients.

Methods: We analyzed data from a cohort of 5465 HD patients from Australia, France, Germany, Italy, Japan, New Zealand, Spain, Sweden, and United Kingdom, enrolled in the Dialysis Outcomes and Practice Patterns Study phases 4 (2009-2011) and 5 (2012-2015). MIC syndrome was defined as low serum albumin (<3.8 g/dL) and high serum C-reactive protein (>3mg/L in Japan; >10 mg/L elsewhere). Poor functional status was defined as the sum of scores from the self-reported limitations in the Katz Index of Independence in Activities of Daily Living (0 to 5) and the Lawton-Brony Instrumental Activities of Daily Living Scale (score ranges from 0 to 8) less than 11. We investigated the association between combinations of MIC (+/+), FS and FS (low/high) with death, using Cox proportional hazards models adjusted for possible confounders including patient demographics, comorbidity history, catheter use, serum creatinine, phosphorus levels, WBC count, hemoglobin level, and time on dialysis therapy.

Results: The prevalence of different combinations were: MIC-/HD FS 57%, MIC-/ Low FS 24%, MIC+/HD FS 9%, and MIC+/Low FS 10%. Patients with MIC+/HD FS were younger, better nourished, and had lower prevalence of comorbidities. Compared to the reference group, the hazard ratios [HR (95% CI)] for all-cause mortality were 1.56 (1.24-1.98) for MIC-/ low FS, 1.75 (1.32-2.32) for MIC+/ HD FS, and 2.97 (2.31-3.82) for MIC+/ low FS groups. The adjusted HRs for infection-related mortality were 1.57 (0.91, 2.71) for MIC-/low FS, 1.67 (0.84, 3.31) for MIC+/HD FS, and 5.45 (3.15, 9.45) for MIC+/low FS groups.

Conclusions: The combination of MIC and low FS is a strong predictor of mortality, and infectious mortality in particular, in HD patients. Identification of patients with MIC and FS.

PO2039

High-Amylose Resistant Starch (RS) Cookies Supplementation Does Not Decrease Trimethylamine N-Oxide (TMAO) Plasma Level in Hemodialysis (HD) Patients
Denise Mafra,1 Julie ann Kemp,1 Henrique F. Santos,1 Hugo E. de Jesus,1 Marta Espigalho,1 Bruna Paiva,1 Bengt Lindholm,2 Peter Bergman,2 Peter Stenvinkel.1 1Federal University Fluminense, Rio de Janeiro, Brazil; 2Karolinska Institutet, Stockholm, Sweden.

Background: TMAO is generated from dietary nutrients by the gut bacteriome and it is associated with cardiovascular mortality in HD patients. Thus, to reduce its generation, nutritional strategies have been proposed. The aim of this study was to analyze the TMAO levels and potential changes in TMAO-associated bacterial taxa in HD patients after RS supplementation.

Methods: This is a randomized, double-blind, placebo-controlled trial with HD patients that were allocated to RS or placebo group to receive alternately 9 cookies/d (dialysis days) and 1 sachet/d (non-dialysis days) containing 16g/d of RS (Hi-Maize 260, Ingredion®) or manioc flour as the placebo, during 4 weeks. Plasma TMAO, choline, and betaine levels were measured with LC-MS/MS. Fecal bacteriome composition was evaluated by high-throughput sequencing of 16S ribosomal RNA gene V1–V3 region, followed by a search for TMAO-associated taxa.

Results: Thirty-one participants finished the study, 15 in RS group (53.3 %); 56.0 ± 7.5 yrs; 50.0 ± 36.6 months on HD and BMI 26.1 ± 5.0 kg/m² and 16 in the placebo group (31.2 %); 53.5 ± 11.4 yrs; 44.3 ± 26.4 months on HD and BMI 26.6 ± 5.2 kg/m². After four weeks of supplementation no significant changes in TMAO, choline and betaine plasma levels were observed (Table 1). Notably, after the RS supplementation, TMA-producing bacterial taxa such as Ruminococcus torques group [0.026 (0.023 - 0.04) vs. 0.017 (0.017 - 0.02), p = 0.06] and Streptococcus had decreased the relative abundance, while Prevotellaceae family and Enterococcus increased their relative abundance in placebo group. However, the differences did not reach statistical significance. Additionally, the relative abundance of TMA-producing bacterial taxa was low in both groups.

Conclusions: RS supplementation did not influence TMAO plasma levels nor fecal taxa potentially linked to TMAO in HD patients, suggesting that RS did not modify the composition of gut bacteriome that convert its precursors into TMAO.

Funding: Government Support - Non-U.S.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

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Effects of RS supplementation or placebo on plasma TMAO, choline and betaine levels

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**PO2040**

**Public Health Effects of Sterilized, Used Hemodialyzers for Water Purification in Rural Ghana**

Jommander, Bagah; Boehm; Grisch; G. Raimann,3 Philip K. Nahr,1 Seth Johnson,1,2 Linda L. Donald,1 Harrison K. Matti,1 Maria E. Ferris,1 Mathieu Lamolle,1 Hongbin Zhang,3 Friedrich K. Port,1 Nathan W. Levin,1 Easywater for everyone, Accra, Ghana; 2Department of Field Epidemiology and Applied Biostatistics, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; 3Health Service, Ada, Ghana; 4Arbor Research Collaborative for Health, Ann Arbor, MI; 5Graduate School of Public Health and Health Policy, New York City, NY; 6Renal Research Institute, New York, NY; 7University of North Carolina System, Chapel Hill, NC; 8Water for Everyone, Geneva, Switzerland.

**Background:** Consumption of contaminated water is a risk factor for infectious diarrhea and according to estimates of the World Health Organization the remains the most often reported cause of death in children and the elderly. Our organization “Easy Water for Everyone (EW/E)” uses a membrane filtration device with repurposed hemodialyzers and we have previously reported remarkable public health effects (Raimann for EWE, SciRep 2020). Here we report the impact our project had on the incidence of diarrhea in two villages in rural Ghana.

**Methods:** This prospective study was conducted with approval from Ghana Health Service and involved the quantification of self-reported diarrhea 4 months before and after implementation of a membrane filtration device in a school and a primary healthcare center. Using a mixed-effects generalized linear model, the odds of developing diarrhea in presence of the membrane device were estimated. We additionally tested the association of age on the estimate, and conducted a subset analyses in those younger than 15 years old. Analyses were conducted in R version 4.0 and odds ratios (OR) reported as OR (95% CI).

**Results:** We studied 927 villagers (55% female, 43% <15 yrs and 33% >50yrs) and the incidence rate of diarrhea was 0.30 per subject month per village-month before and 0.26 after implementation of the device. We found a statistically significant association between the device and incidence of diarrhea [OR 0.79 (0.67 to 0.95)] with significantly higher odds of diarrhea in the younger [OR 1.32 (1.07 to 1.63)] and the elderly [OR 1.45 (1.06 to 1.99)].

**Conclusions:** Our study supports provision of clean drinking water as means to prevent diarrhea and its possible adverse sequelae such as acute kidney injury (AKI). Additionally, we conclude the youngest and the eldest in the population are at highest risk of diarrhea.

**PO2041**

**Development and Validation of a Multifrequency Bioimpedance Spectroscopy Equation to Predict Appendicular Skeletal Muscle Mass in Hemodialysis Patients**

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**Background:** Sarcopenia is prevalent and associated with poor outcomes in patients with chronic kidney disease (CKD). Although bioimpedance analysis is accepted by major consensus statements as an alternative for muscle mass assessment, it can be affected by hydration status in CKD patients. The Body Composition Monitor (BCM), a multifrequency bioimpedance spectroscopy device, has been widely used to assess body composition and dry weight in hemodialysis patients because it can distinguish normally hydrated lean tissues from overly hydrated tissues. Therefore, our study aimed to develop and validate an equation for obtaining appendicular skeletal muscle mass (ASM) from BCM using dual-energy X-ray absorptiometry (DXA) as the reference among hemodialysis patients.

**Methods:** A total of 322 consecutive body composition measurements with BCM and DXA in 263 hemodialysis patients were randomly divided at a ratio of 2:1 into development and validation groups. Stepwise multiple regression modeling was applied to develop the ASM prediction equation. Tests for agreement included mean differences and Bland-Altman plots. We evaluated the model as a diagnostic tool for sarcopenia using cutoffs of ASM defined by the Asian Working Group for Sarcopenia (AWGS). We further explored the association between ASM predicted by the BCM equation and all-cause mortality in two independent cohorts: one with 326 stage 3–5 CKD patients and one with 629 hemodialysis patients.

**Results:** BCM yielded the following equation: ASM (kg) = −1.838 + 0.395 × total body water (L) + 0.105 × body weight (kg) + 1.213 × male sex – 0.026 × age (years) (R² = 0.914, standard error of estimate = 1.35 kg). In the validation group, Bland-Altman analysis showed no significant bias of 0.098 kg and limits of agreement ±2.440 kg. Using the AWGS criteria, the model was found to have a sensitivity of 94.1%, a specificity of 98.8%, a positive predictive value of 84.2%, and a negative predictive value of 99.6% for the diagnosis of sarcopenia. Low ASM predicted by the BCM equation was associated with significantly worse overall survival among CKD patients but not hemodialysis patients.

**Conclusions:** The new BCM equation provides a feasible and valid option for assessing ASM in hemodialysis patients. Its utility in clinical practice requires further research.

**Funding:** Private Foundation Support

**PO2042**

**Indoxyz Sulfate Reduces the Inducibility of NLRP3 Inflammation in Hemodialysis Patients**

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**Background:** The NLRP3 inflammasome is a cellular component of innate immunity responsible for the maturation of interleukin-1β (IL-1β). Studies have shown that the basal activity of the NLRP3 inflammasome is increased in the immune cells of hemodialysis (HD) patients, but the inducibility of the NLRP3 inflammasome upon canonical stimulation has not been studied.

**Methods:** Peripheral blood mononuclear cells (PBMCs) isolated from 13 HD patients and 18 volunteers without a history of chronic kidney disease (CKD) were treated with a combination of lipopolysaccharide (LPS) and nigericin to induce NLRP3 inflammasome activation. Likewise, THP-1 monocytic cell-derived macrophages, with or without indoxyz sulfate (IS) pretreatment, underwent the canonical NLRP3 inflammasome stimulus as well. The activity of the inflammasome was determined by immunoblot analysis.

**Results:** Despite the high plasma levels of IL-1β in HD patients, caspase-1 and IL-1β in the PBMCs of HD patients remained predominantly immature and were not stimulated in response to the canonical stimulus. Further investigations showed that while IS treatment alone facilitated the secretion of IL-1β from THP-1-derived macrophages, IS pretreatment reduced the inducibility of NLRP3 inflammasome in response to LPS and nigericin, characterized by the low mature rate of caspase-1. The PBMCs derived from the HD patients and the macrophages exposed to IS both had low expression levels of NLRP3 inflammasome components, suggesting insufficient supplies of inflammasome machinery.

**Conclusions:** The low stimulation response of the NLRP3 inflammasome attributed to indoxyz sulfate probably contributes to a breach of the immune defense system, which may explain the high infection risk in HD patients.

**Funding:** Clinical Revenue Support

**PO2043**

**Prevalence and Risk Factors of High-Altitude Hyperuricemia in the Bai Ethnic Group**

Chenni Gao, Xiaonong Chen. Shanghai Jiao Tong University Medical School Affiliated Ruijin Hospital Department of Nephrology, Shanghai, China.

**Background:** The Bai ethnic group is one of the 55 minorities in the People's Republic of China. Hyperuricemia is not rare among this ethnic partly due to the chronic exposure to high altitude. However, the prevalence of hyperuricemia in the Bai ethnic group remains unclear.

**Methods:** We collected retrospectively the demographic characteristics and laboratory measurements of 1393 Bai ethnic adults undergoing annual medical examination during Jan 2019 to Dec 2019 in the People's Hospital of Jianchuan County (average altitude 2300m), Yunnan Province. We investigated the prevalence of hyperuricemia as well as its clinical features and risk factors.

**Results:** Of the 1393 participants enrolled in the study, the prevalence of hyperuricemia was 24.8%, and the prevalence was significantly higher in male (53.2% vs men vs. 11.0% in women, P<0.001). The prevalence of hyperuricemia increased from 9.2% among participants aged 30-40 years to 30.1% among participants aged 50 years and older. Also, the prevalence elevated from 17.2% among participants with normal body mass index (BMI) to 35.5% among those who were overweight/obese. Interestingly, we found a positive correlation between hemoglobin level (Hb) and serum uric acid (β=2.19, P<0.01). Logistic regression analysis revealed main risk factors for hyperuricemia in the Bai ethnic group included age, sex, BMI, systolic blood pressure (SBP) and Hb.

**Conclusions:** Hyperuricemia is common in the Bai ethnic group. Besides traditional risk factors such as age, sex and BMI, polythecemia secondary to chronic exposure to high altitude may also contribute to the hyperuricemia.
PO2044
Changes in the Gut Microbiota After a Controlled Feeding Study in Individuals with CKD and Healthy Controls

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Background: Diet has been shown to alter the gut microbiota composition and function. However, controlled diet studies assessing the gut microbiota in CKD patients are limited. We assessed the differences in the gut microbiota composition before and after a week of controlled meals in patients with moderate-to-advanced CKD and healthy adults.

Methods: In a secondary analysis, we studied patients with CKD (n=7, eGFR 29.5±55mL/min/1.73m2) vs. controls (n=7) matched for sex, age, and race. Participants ate a diet controlled for macronutrients (protein 0.8g/kg/d), fiber (25g/d), P (1500mg/d), Ca (1400mg/d), K (3500mg/d), and Na (2400mg/d) for 1 week. Fecal samples were obtained before and after the dietary intervention. Fecal DNA was extracted and used to amplify the V4 region of the 16S rRNA gene. Sequencing was performed via Illumina MiSeq platform and analyzed using QIIME2 and LEfSe.

Results: The Gut microbial diversity did not differ between patients with CKD or controls and was not affected due to the dietary intervention. At baseline, control individuals had a higher relative abundance of Blautia and an unclassified genus within Coriobacteriaceae, while CKD patients had a higher relative abundance of Lachnobacterium. After receiving a week of controlled meals, CKD patients had a higher relative abundance of Anaerostilbos and Clostridium, while controls had a higher relative abundance of Parabacteroides and Sutterella. Comparing data before and after dietary treatment within groups, CKD individuals had a lower relative abundance of Lachnobacterium and higher Bacteroides and Holdemansia. Meanwhile, healthy controls had a lower relative abundance of unclassified Mogibacteriaceae, and a higher relative abundance of Anaerostilbos, Parabacteroides and Sutterella.

Conclusions: While there were no major changes in microbial diversity, healthy controls and CKD patients responded differently to a week of controlled meals.

Funding: NIDDK Support, Other NIH Support - T32 AR065971-04

PO2045
Mitochondrial Dysfunction and Uremic Toxins from Gut Microbiota in CKD Patients: Is There a Link?

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Background: Dysbiosis in patients with chronic kidney disease (CKD) is associated with increased production of uremic toxins, such as indoxyl sulfate (IS), p-cresyl sulfate (p-CS) and indole-3-acetic acid (IAA), which are linked to oxidative stress and may be related to mitochondrial dysfunction with alterations in peroxisome proliferator activated gamma receptor coactivator 1 alpha (PGC-1α), respiratory nuclear factor 1 (NRF-1) and mitochondrial transcription factor (TFAM). The aim of this study was to verify possible associations between metabolites produced by gut microbiota and genes related to mitochondrial function (PGC-1α, NRF-1, TFAM) in CKD patients.

Methods: This was a cross-sectional, observational study, involving 46 patients with CKD: 20 patients on hemodialysis (HD) (12 men, 44.2 ± 8.9 years) and 26 non-dialysis patients (8 men, 57.6 ± 6.2 years, GFR 25.0 ± 13.0 mL/min), selected by non-probabilistic sampling of convenience. Plasma levels of IS, p-CS and IAA were assessed by high-performance liquid chromatography (HPLC). The analysis of the gene expression of PGC1-α, NRF-1 and TFAM were performed by real time Polymerase Chain Reaction (RT-PCR) in peripheral blood mononuclear cells (PBMCs). For statistical analysis, software R, version 3.5.0 (R Core Team, Vienna, Austria) was used and the results were expressed as mean ± standard deviation, with a significance level of p <0.05.

Results: As expected, the levels of uremic toxins were higher in HD patients than in non-dialysis patients [IS: 31.1 ± 14.3 mg/L vs 2.9 ± 1.7 mg/L (p <0.001); p-CS: 53.4 ± 34.6 mg/L vs 14.6 ± 10.8 mg/L (p <0.001)]; IAA: 2560.1 ± 1379.6 ug/L vs 1050.4 ± 984.8 ug/L). There was no significant difference in the mitochondrial parameters between PGC1α and NRF1 between the groups of patients. In the HD group was observed a positive linear correlation between TFAM and p-CS (r = 0.978, p <0.001); as well as between PGC1α and NRF1 (r = 0.8, p = 0.006). However, in both groups there was no correlation between mitochondrial genes and uremic toxins.

Conclusions: The uremic toxins levels were significantly higher in HD patients; however, we did not find any correlations with the parameters of mitochondrial function analyzed.

Funding: Government Support - Non-U.S.

PO2046
Dysbiosis of Gut Microbiota in Adult Idiopathic Membranous Nephropathy with Nephrotic Syndrome

Jian Zhang. Division of Nephrology, Department of medicine, Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

Background: Gut bacterial microbiota is altered in patients with chronic kidney disease (CKD) and those on dialysis. However, it is not yet clear what bacterial composition changes occur in patients with idiopathic nephrotic syndrome. We present in this report the changes in gut bacterial microbiota in idiopathic nephrotic syndrome patients with membranous nephropathy.

Methods: A total of 156 individuals were recruited for this study. Of these, 80 were CKD3–5 stage patients without nephrotic syndrome, 48 patients had idiopathic nephrotic syndrome and pathological diagnosis of membranous nephropathy, and 30 were age- and sex-matched healthy controls. The gut microbiome composition was analyzed using a 16S ribosomal RNA gene-based sequencing protocol.

Results: The results indicated that the nephrotic syndrome (NS) patients had a significantly different alpha and beta diversity compared with the CKD3–5 group and healthy controls (p < 0.01). At the phylum level, the NS patients showed increased Fusobacteria and Proteobacteria but reduced Firmicutes when compared with the healthy controls. At the genus level, Megamonas, Megaplasma, Akkermansia, and the butyrate-producing bacteria Lachnospira, Roseburia, and Fusobacteria were more abundant in the controls (LDA score > 3) than the CKD3–5 and NS patients. Compared with the healthy controls, we found that Parabacteroides was increased in CKD3–5 and NS patients. In addition, Oscilispora and Ruminococcus were more abundant in CKD patients than in the other two groups (LDA score > 3). At the genus level, ten bacterial taxa were more prevalent in the healthy controls. Providencia and Myrobiotes were more prevalent in NS patients.

Conclusions: Our findings highlight that, NS patients had a significantly different alpha and beta diversity and decreased gut microbiota-derived short-chain fatty acids, such as butyrate. However, large-scale prospective studies should be performed to identify the cause and effect factors of these changes in the microbiota in NS patients.

Funding: Government Support - Non-U.S.

PO2047
The Alter of Gut Microbiota in Dialysis Patients and Its Influence on the Prognosis for ESRD Patients

Jian Zhang, Dan Luo, Huaixia Xiong, Hui-qun Li. Department of Nephrology, the Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

Background: Previous studies have found that alteration in gut microbiota occurred in end-stage renal disease (ESRD) patients with or without dialysis, and are associated with complications such as inflammation and cardiovascular events. However, it has not been clarified whether gut microbiota are influenced by dialysis intervention in ESRD patients.

Methods: The fcal samples of 73 ESRD patients were collected, including 33 pre-dialysis ESRD patients, 19 peritoneal dialysis (PD) patients, and 21 hemodialysis (HD) patients; 19 healthy fecal samples were also collected as control in this study. The 16S rRNA sequencing and the bioinformatics was used to analyze the the composition and function of gut microbiota. The clinical outcomes of the patients were tracked from April 2017 to the end of May 2020.

Results: Compared with the pre-dialysis patients, Bacteroides decreased significantly in HD patients. At the genus level, a total of 14 genera showed differences between patients before and after dialysis. Pre-dialysis patients have a increased abundance of Parabacteroides, Prevotella and Oscillibacter, and the decreased abundance of Lachnospira, Klebsiella, Akkermansia and Roseburia. HD could repair the abnormal changes of these flora in pre-dialysis patients. We could not found any bacteria difference function between PD and pre-dialysis patients in phylum and genus level. The PICRUSt analysis showed that PD and HD could change the signal transduction and metabolic pathways of ESRD patients. It was found that Bacteroidetes and SMB53 were associated with the occurrence of cardiovascular events. Blautia, Faecalibacterium, and Veillonella were associated with peritonitis in PD patients.

Conclusions: Our results suggested that compared with healthy control, the composition and function of gut microbiota of pre-dialysis patients were changed, HD could restored the relative abundance of beneficial bacteria and reduced some potential pathogenic bacteria. Some gut microbiota were associated with prognosis in all of ESRD patients and peritonitis in PD patients.

Funding: Government Support - Non-U.S.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Effect of Intradialytic Oral Nutritional Supplementation with and Without Exercise on the Skeletal Muscle Quantity and Quality of Adult Hemodialysis Patients
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Background: The muscle mass (MM) is one of the major tissues affected by the chronic kidney disease. Patients undergoing chronic hemodialysis (HD) have loss of MM due to many factors. Intradialytic oral nutritional supplementation (ONS) and exercise (EX) have been shown to improve the amount and quality of MM and physical function (PF).

Methods: Patients were randomized in two different groups: 1) ONS and 2) EX + ONS. Patient’s realized 30 minutes of aerobic EX using static bicycles and 30 minutes of resistance EX using Thera-band Bands. Quantity and quality of MM were measured with anthropometrics and computed tomography (CT). PF was measured by short physical performance battery (SPPB), six-minute walk test (6 MWT) and handgrip strength (HGS).

Results: Twenty-three patients conclude the study. Both groups improved their weight (ONS: baseline, 53 ± 4.4kg; final: 54.3 ± 4.9kg; p = 0.020 and ONS + EX: baseline, 57.2 ± 9.2kg; final: 59 ± 9.2kg; p = 0.001) and the AMC (ONS: baseline, 227 ± 20mm; final: 241 ± 19mm; p = 0.040 and ONS + EX: baseline: 235 ± 27mm, final: 250 ± 31; p = 0.047). In the ONS group we observed decreases in the 6MWT: baseline: 417 ± 53.9m, final: 405 ± 52m; p = 0.016 and improvements in the SPPB; baseline: 10.8 ± 1.3, final: 11.2 ± 1.4, p = 0.005) with no change in the intramuscular lipid infiltration (baseline: 53.5 ± 5.8% vs. 53.5 ± 5.8%; p = 0.83) and the AMC (baseline: 235 ± 27mm, final: 250 ± 31; p = 0.047).

Conclusions: Exercise training for 6 months improves the MM composition of HD patients measured by CT and this was reflected with the improvements in the PF tests and no changes were observed in MM composition in the ONS group.

Funding: Private Foundation Support

Muscle Mitochondrial Function and Physical Performance Are Associated with Branched-Chain Amino Acid Levels in Patients with CKD
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Background: Muscle mitochondrial function and physical performance are impaired in patients with chronic kidney disease (CKD). Previous studies suggest that decreased branched-chain amino acids (BCAA) levels are associated with muscle catabolism in patients with CKD. We hypothesized that BCAA is lower in patients with CKD and branched-chain amino acids (BCAA) levels are associated with muscle catabolism in patients with CKD.

Methods: In a cross-sectional study, we evaluated 63 participants [20 with CKD stage 3-4, 13 with ESRD, and 30 controls] and 23 patients with CKD stages 1-3a, 3b-5, HD, and PD enrolled from 2018 to 2020. All patients were hospitalized and received our CKD educational program, and did not have sleep complaints. The diagnosis and assessment of the severity of SBD were evaluated using PULSION-Mc306 and SAS2100 systems. The 3% oxygen desaturation index and SpO2 were measured during sleep. SBD was defined as 3% oxygen desaturation index (ODI)>15.0 and SpO2<92% in this study.

Results: The proportion of the patients with CKD1-3a, CKD3b-5, HD, and PD were 28%, 53%, 11%, and 8%, respectively. 31% of the patients were diagnosed with SBD in all CKD patients. In a generalized linear model, 3% ODI>15.0 and SpO2<92% were significantly correlated with apnea hypopnea index (p<0.05, r=0.87 and p<0.05, r=-0.45, respectively). Further, it became clear that the proportion of 3% ODI>15 and SpO2<92% was significantly higher in PD patients (50%) than in other CKD patients. Furthermore, 3% ODI was significantly correlated with BMI and HDL cholesterol levels in PD patients (p<0.05, r=0.67 and p<0.05, r=0.54, respectively).

Conclusions: We reported for the first time that the prevalence of SBD was very high and that the severity of SBD was significantly associated with BMI in patients with PD. These findings suggest that the extracellular fluid overload and excess glucose exposure due to PD fluid might accelerate SBD in patients with PD. Further clinical studies are needed to determine whether PD-associated SBD might influence the development of cardiovascular disease in CKD patients.

Funding: Government Support - Non-U.S.

Effects of Resistant Starch (RS) Type 2 Cookies on Gut Microbiota Profile in Hemodialysis (HD) Patients
Denise Mafra, Julie Ann Kemp, Marta Esgalhado, Bruna Paiva, Hugo E. de Jesus, Henrique F. Santos. Federal University Fluminense, Niterói, Brazil.

Background: Dysbiosis is recognized as a new cardiovascular risk factor in HD patients. In this context, nutritional strategies as the use of high amylose RS have been proposed to modulate the gut microbiota in HD patients. The aim of the present study was to evaluate the effects of RS supplementation on gut microbiota modulation in HD patients.

Methods: This double-blind, placebo-controlled clinical trial evaluated HD patients randomized in two groups, RS or placebo. They received 9 cookies/day (16g of RS - Hi-MAize 260, Ingredion®), in the HD days and 1 sachet/day in non-HD days for 4 weeks.

Results: Twenty-three patients concluded the study: 10 in the RS group (3 ♂, 52.3 ± 12.3 yrs, BMI 24.6 ± 3.9 Kg/m2) and 10 in the placebo group (8 ♂, 55.1 ± 11.1 yrs, BMI 25.6 ± 4.9 Kg/m2). Microbial diversity (Shannon index) and richness (ACE) were similar in both groups at baseline. RS supplementation increased mainly the relative abundance of the genus Ruminococcus 2 and maintained genus Blautia, while the placebo group decreased both of these genera, as showed in the Fig 1. After RS supplementation the beta diversity (PCA) changed, increasing the short-chain fatty acid producers, which are related to benefits effects.

Conclusions: The RS supplementation was able to change the gut microbiota in HD patients. Linking these results with our previous studies, which RS was able to reduce the inflammatory and oxidative stress markers and uric acids plasma levels in HD patients, we suggest that RS can be a good nutritional strategy to modulate the gut microbiota in HD patients.

Funding: Government Support - Non-U.S.
Gut Dysbiosis and Mortality in Hemodialysis Patients

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Background: Persistent inflammation plays a pathogenic role in CKD-associated protein-energy wasting, cardiovascular disease, and mortality. Gut dysbiosis, characterized by decreased microbial diversity, promotes inflammation. The gut microbiota is markedly altered in patients with ESKD. Therefore, we aimed to determine the relationship between gut dysbiosis and mortality in an ESKD cohort.

Methods: In an observational study, we examined the associations between microbial diversity and mortality in ESKD patients undergoing maintenance hemodialysis (n=109) using Cox proportional hazards models. The gut microbiota was assessed by 16S rRNA sequencing. Microbial diversity was calculated using the Simpson index. Participants were stratified into higher- (above the median) and lower-diversity (below the median) groups and were followed up for a median of 2.1 years. Next, in a matched case-control study, we compared the microbial composition between nonsurvivors and survivors.

Results: Kaplan-Meier analyses revealed a significant association between higher diversity and a lower risk of death (P<0.015). After adjustment for patient characteristics and comorbidities, the risk of death among patients with higher diversity was 74% lower than that among patients with lower diversity (hazard ratio, 0.26; 95% CI, 0.07 to 0.95). Nonsurvivors and survivors were matched 1:4 for age and sex. We observed significantly lower values of microbial diversity and higher levels of proinflammatory cytokines (IL-6 and TNF-α) among nonsurvivors (n=14) than survivors (n=56). Notably, the relative abundance of Succinivibrio and Anaerostipes, two short-chain fatty acid-producing bacteria, was reduced in nonsurvivors compared with survivors.

Conclusions: A unique gut microbial composition is associated with an increased risk of mortality in patients with ESKD and may be used to identify subjects with a poor prognosis. Our findings need to be validated in a larger independent cohort.

Funding: Private Foundation Support

Insulin Resistance and Pancreatic Beta-Cell Function in Calcium Kidney Stone Formers

Olive W. Tang,1 Kevin Mitchell,2 Jie Tang.2 Johns Hopkins Medicine, Baltimore, MD; 2 Alpert Medical School of Brown University, Providence, RI.

Background: Diabetes mellitus is common among individuals with kidney stones; however, the risk factors associated with glucose dysregulation in this population is unclear.

Methods: We characterized the independent associations between vitamin D, urinary measures of dietary intake (sodium, magnesium), and urinary ammonia and citrate with homeostasis model assessment of β-cell (HOMA-B) and insulin resistance (HOMA-IR) in prevalent calcium kidney stone formers without diabetes mellitus recruited from Lifespan Kidney Stone Clinic (N = 96). We used linear regression with adjustment for demographics, body mass index, hypertension, hyperlipidemia, parathyroid hormone, and serum uric acid.

Results: The study population had a mean age of 53 years, 48% were male, and 83% were Caucasian. The mean 25-hydroxy-vitamin D (25D) was 30 ng/mL, 1,25-dihydroxy-vitamin D (1,25D) was 55 pg/mL, 24-hour urine sodium was 145 mmol, urine ammonia was 50 mg/dL, urine citrate was 590 mg/dL, and urine magnesium was 102 mg/dL. Mean HOMA-B was 172.1, and mean HOMA-IR was 5.4. Urine sodium was negatively associated with HOMA-B, but not HOMA-IR. Urine ammonia was positively associated with HOMA-IR, but not HOMA-B. Urine citrate was positively associated with both HOMA-B and HOMA-IR (Table 1).

Conclusions: In our cohort of calcium kidney stone formers, high salt intake and low urine citrate were associated with worse beta-cell function. High urine ammonia and citrate were associated with increased insulin resistance.

Funding: Clinical Revenue Support

Table 1. Association of risk factors with HOMA-B and HOMA-IR in prevalent calcium kidney stone formers from the Lifespan Kidney Stone Clinic, N = 96

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>HOMA-B</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-hydroxy-vitamin D, ng/mL</td>
<td>-0.1 (2.1, 0.1)</td>
<td>-0.1 (2.1, 0.0)</td>
</tr>
<tr>
<td>1,25-dihydroxy-vitamin D, ng/mL</td>
<td>-0.2 (-3.1, 0.1)</td>
<td>-0.2 (-3.1, 0.1)</td>
</tr>
<tr>
<td>Urine sodium, mEq/L</td>
<td>0.7 (0.1, 0.1)</td>
<td>0.7 (0.1, 0.1)</td>
</tr>
<tr>
<td>Urine ammonia, mg/dL</td>
<td>0.1 (2.3, 2.1)</td>
<td>0.1 (2.3, 2.1)</td>
</tr>
<tr>
<td>Urine citrate, mg/dL</td>
<td>-0.2 (-0.2, 0.1)</td>
<td>-0.2 (-0.2, 0.1)</td>
</tr>
<tr>
<td>Urine magnesium, mg/dL</td>
<td>0.0 (-0.0, 0.0)</td>
<td>0.0 (-0.0, 0.0)</td>
</tr>
</tbody>
</table>

*p < 0.05

**p < 0.01
Methods: Among 3,958,837 US veterans that had a sK between 2004-2006, there were 589,019 that had an index HK event (sK >5.0 mEq/L) during this period where we could ascertain INPT/OPT status. We then identified patients who had a recurrent HK event 7-365 days after the index HK and had at least one normal sK ≤5.0 mEq/L in between events. We examined time to recurrence in 30-day intervals according to whether the index sK was INPT or OPT. Patients who’s INPT/OPT status at HK recurrence could not be ascertained were excluded.

Results: HK recurrence over one year occurred in 103,155/589,019 (17.5%) patients, or 17,215/51,262 (34%) and 85,940/537,757 (16%) of patients with index INPT and OPT event, respectively. The 103,155 patients with HK recurrence had a mean patient age of 68±11 years, consisted of 98% males, 14% African Americans, 56% diabetics, and 60% with estimated glomerular filtration rate <60 mL/min/1.73m². In patients with HK recurrence, 50% (n=5,167) developed this event 6 months after the initial HK (table). Among patients who had an OPT index HK, 56% developed recurrence 6 months after index HK event. However, 51% of the patients who had an INPT index HK event developed recurrence within 60 days of the index HK.

Conclusions: A significant proportion of VA patients with HK developed another HK event within one year. Hospitalized patients with HK developed recurrence faster than patients in the OPT setting despite requiring 7 days between HK events and normalization of sK between events. This could be due to the fact that hospitalized patients are usually sicker or they were monitored more closely by the healthcare providers, therefore it is easier to catch HK recurrence in INPTs than OPTs.

Funding: Other U.S. Government Support

PO2056
Workplace Outreach Program Facilitates Referral into Physician Care and Diagnosis of CKD
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Background: Chronic kidney disease (CKD) is often unrecognized and undertreated. Timely diagnosis can improve disease management and slow CKD progression. We asked whether a workplace outreach program facilitates CKD diagnosis and improves management of CKD.

Methods: An annual workplace health assessment that included eGFR testing was offered to employees. Those with confirmed CKD by repeat eGFR >60 mL/min/1.73 m² or by albumin to creatinine ratio test were eligible to participate in a CKD outreach program. A study coordinator made up to 3 phone calls in an effort to contact each eligible employee, to provide an explanation of CKD risk and to offer a physician consultation to discuss test results and referral into care. Those who accepted the phone call (participation group) were compared to those who were not reached by phone (control group). Using logistic regression models that adjusted for prevalent CKD, we analyzed claims data to estimate the effect of outreach participation on nephrologist visits, physician visits, and new CKD diagnoses 5 months after the outreach. Changes in eGFR levels were evaluated at the following annual health assessment.

Results: Of the 398 eligible employees, 156 participated in the outreach program; the remaining 242 served as the control group. CKD risk factor profiles at baseline were similar between participants and controls. Participants had 3-fold greater odds of visiting nephrologists, 60% greater odds of visiting physicians and 80% greater odds of being diagnosed with CKD, compared with the controls. Participants had 40% lower odds of an annual eGFR decline >5 mL/min/1.73 m² compared with controls (Table). One participant initiated kidney dialysis, compared with none in the control group.

Conclusions: A workplace CKD outreach program facilitates diagnosis of CKD and improves disease management including referral to a nephrologist.

Funding: Commercial Support - Quest Diagnostics supports annual health assessments and the CKD outreach program for employees and their spouses. It also provided funds for the analysis presented in the abstract

Effect of the CKD Outreach Program on Disease Management

PO2057
A Pilot Randomized Clinical Trial to Embed Technology-Enabled Group-Based Exercise Programming in the Clinic: The Exercise Is Medicine in Chronic Kidney Disease Trial
Susan Ziolkowsi,1 Shuchi Anand,1 Ahad A. Bootwalwa,2 Jianheng Li,2 Nhat M. Pham,3 Jason Cobb,1 Felipe Lobelo,2 Stanford University School of Medicine, PALO ALTO, CA; Emory University School of Medicine, Atlanta, GA.

Background: Physical activity (PA) is associated with improvement of cardiovascular health, transplant outcomes, and survival in CKD. We evaluated the feasibility and effectiveness of integrating referral from nephrology clinics to a technology-enabled and/or group-based exercise program.

Methods: We conducted a pilot trial to test the ACSM Exercise is Medicine (EIM) framework in persons with eGFR <45 not on dialysis in San Jose, CA and Atlanta, GA. Participants were randomized to 1. mobile health (mHealth) group: wearable PA trackers + counseling, or 2. EIM group: mHealth + twice weekly small group exercise sessions. Physical and mental health assessments were done at baseline, 8, and 16 wks. Multilevel mixed models evaluated group differences.

Results: Of 56 participants, 86% belonged to a racial/ethnic minority. In intention-to-treat analyses, the EIM group increased moderate-vigorous PA compared to the mHealth group (time x intervention p=0.02) at 8 wks, no differences were observed between group daily step count. In as-treated analyses, daily step count, distance covered, light and moderate-vigorous PA improved in the EIM group and declined in the mHealth group at 8 wks (p=0.05) but group differences faded at 16 wks. No differences in physical function or mental health were found.

Conclusions: We successfully integrated recruitment, assessment, and group-based fitness interventions into clinical settings servicing minority patients with advanced CKD. Despite poor baseline measures, improvements in PA were observed in the EIM group, particularly in persons who participated in exercise sessions.

Funding: Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2058
Effect of Exercise on Quality of Life and Functional Capacity in Patients with CKD

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Background: Chronic kidney disease patients have lower activity levels when compared to normal population, compounded by sedentary lifestyle and is associated with increased mortality, which might reduce with exercise

Methods: Patients with chronic kidney disease were evaluated for 12 weeks of supervised exercise program. The subjects were divided into 2 groups: Group I (CKD stage 3-5) and Group II (CKD on maintenance hemodialysis). Serum hemoglobin (Hb), calcium (Ca), phosphorous (Pi), and albumin (Alb) were done at baseline and at 12 weeks. Symptom burden was assessed using Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACT-F) and Leicester Uremic Symptom (LUS) Scale. Quality of life using SF-36 questionnaire, functional capacity using Duke Activity Status Index, Physical activity using Godin-Shephard Leisure time Exercise Questionnaire and Nutritional status using modified Subjective Global Assessment at baseline and at 12 weeks. Subjects in Group I were advised aerobic and resistance exercises at home, with once in 3 weeks activity using Godin-Shephard Leisure time Exercise Questionnaire and Nutritional status using modified Subjective Global Assessment at baseline and at 12 weeks. Subjects in Group II underwent aerobic and resistance exercise in the pre-dialytic and intra-dialytic period during each dialysis visit

Results: Group I included 28 patients, while group II had 30 patients. At baseline, Hb and Albamin were significantly different between groups, while other parameters and scores were similar. At baseline, SF-36 and FACT-F significantly correlated positively with Hb, Alb, Ca & Pi, while SGA correlated significantly with Alb, Ca & Pi. At end of study, in group I there was a non-significant increase in SF-36 (p=0.41), and DUKES (p=0.17), with a non-significant decrease in LUS (p=0.36), FACT-F (p=0.83) and SGA (p=0.113), while in group II there was a significant increase in SF-36 (p=0.001), with non-significant increase in Dukes (p=0.75), and a significant decrease in LUS (p=0.001), SGA (p=0.05) and FACT-F (p=0.001)

Conclusions: Exercise increased the quality of life and decreased symptom burden but there was an increase in fatigue perception in patients on dialysis. However, LUSS reduced with reduced FACT-F which could mean decrease in symptom burden but persistence of fatigue. In patients not on dialysis there was no significant increase in quality of life or decrease in symptom burden.

PO2060
Changes in Body Composition, Muscle Strength, and Fat Distribution Following Renal Transplantation

Susan Zolkowski,1 Simin Goral,2 Jin Long,3 Joshua F. Baker,3 Justine Shults,4 Babette Zemel,5 Peter P. Reese,3 Francis P. Wilson,5 Mary B. Leonard.1
1Stanford University School of Medicine, Stanford, CA; 2University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; 3The Children’s Hospital of Philadelphia, Philadelphia, PA; 4Lucile Packard Children’s Hospital at Stanford General Pediatrics, Palo Alto, CA; 5Yale University School of Medicine, New Haven, CT; 6University of Pennsylvania, Philadelphia, PA.

Background: The impact of renal transplantation on body composition and muscle quality has not been established. Low muscle mass relative to fat mass (relative sarcopenia) has been associated with mortality and disability but has not been examined following transplantation.

Methods: DXA measures of fat mass index (FMI) and appendicular lean mass index (ALMI; representing muscle mass), CT measures of muscle density (low density Z-scores represented increased intramuscular adipose tissue), and leg muscle strength were assessed in 60 transplant recipients (ages 20-60 years) at transplantation, and 6, 12, and 24 months after transplantation. ALMI relative to FMI (ALMI/FMI) is an established index of relative sarcopenia. Measures were expressed as age, sex, and race-specific Z-scores and compared with 327 healthy controls.

Results: At transplantation, ALMI, ALMI/FMI muscle strength and muscle density Z-scores were lower vs. controls (all p≤0.001). Transplant recipients received glucocorticoids throughout. The prevalence of obesity increased from 18% to 45%. Although ALMI increased following transplantation (p=0.001) and was comparable to controls from 6 months onward, gains were outpaced by increases in FMI, resulting in persistent ALMI/FMI deficits (mean Z-score -0.31 at 24 months, p=0.02 vs controls). Fat gains were disproportionately high in distribution (p=0.05). Muscle strength improved but remained low compared with controls independent of ALMI (p<0.05). Exercise increased in the early months following transplantation (p=0.05) but remained lower than controls (p=0.02).CONCLUSIONS: The two-year interval following renal transplantation was characterized by gains in muscle mass and strength that were outpaced by gains in fat mass resulting in persistent relative sarcopenia.

Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: We included 36 participants with CKD (mean eGFR=38) and 19 controls. Mean age was 61±13 years, 51% male, and 25% had diabetes. Diabetes and CKD were independently associated with lower ATMax (-0.12 mM/s, p<0.01 and -0.19 mM/s, p<0.01, respectively). Accelerometry counts per minute (r=58, p=0.01) was more strongly correlated with ATMax than HAP scores (r=46, p<0.01) with no interaction by CKD status (p=9). Accelerometry counts explained 43% of the difference in ATMax between CKD and controls and HAP scores 15% after adjustment.

Conclusions: Objective PA was more strongly associated with ATMax and explained more of the differences in ATMax between CKD and controls than self-reported PA. Further studies should demonstrate if exercise interventions can improve muscle ATMax in CKD.

Funding: NIDDK Support, Private Foundation Support

Figure 1. Association of ATMax with log-transformed accelerometry counts

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**PO2063**

**Serum and Skeletal Muscle Acylcarnitines And Physical Function in CKD Stage 5-SD**

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Background: Sarcopenia is highly prevalent among those with advanced CKD. The metabolite signature of skeletal muscle in patients with CKD is poorly studied. We hypothesized that skeletal muscle metabolites would be different between serum and muscle in those with CKD 5-SD as compared to healthy adults.

Methods: Subjects: 34 subjects participated; 17 with CKD (10 CKD-5, 7 CKD 5D) undergoing renal transplant and 17 healthy donors. All had blood drawn and transversus abdominis muscle biopsy during surgery. Physical Function tests done the week before were: Sit to stand (STS), 6 minute walk test (6MW), 4m gait speed (fast and usual). Metabolomics: Targeted mass spectrometry (MS) was performed on serum and muscle using the Biocrates Absolute IDQ. Differences were tested between those with and without CKD.

Results: There were no differences in age, height, weight or BMI between CKD and healthy subjects. Physical Function: The CKD group had poorer performance for the STS (13 vs 19), 6MW (434 vs 589m), fastest gait speed (1.62 vs 2.00 m/s) and usual gait speed (1.18 vs 1.34m/s), all p<0.05. Metabolomics: The heatmap depicted two distinct signatures in both serum and skeletal muscle between CKD and donors. Serum demonstrated 59 significantly different metabolites, especially in fatty acid metabolism with increases in short and medium chain acylcarnitines C4-C12, and nine hydroxylated and dicarboxylated acylcarnitines in CKD (p<0.05). Lower 6MW distance was independently associated with levels of C10:14 even after adjusting for CKD status and age in multivariate regression analyses. Skeletal muscle demonstrated significant differences in 42 metabolites, with consistently higher acylcarnitine levels in recipients, including short chain (i.e. C4.1, C5.1, C6.1), long chain and dicarboxyls.

Conclusions: Our data demonstrates patients undergoing renal transplant have increased acylcarnitine levels in serum and muscle that are independently associated with poor physical performance. These results suggest impaired b-oxidation of fatty acid metabolism that affects physical function. Understanding these pathways will allow targeted therapeutics to improve the disabling sarcopenia observed in patients with CKD.

Funding: NIDDK Support
PO2064

Metabolic Acidosis and Muscle Metabolic Health Are Important Determinants of Fatigue in Persons with CKD

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Background: Chronic kidney disease (CKD) is associated with a high prevalence of physical frailty, reduced physical function and fatigue, contributing to increased morbidity, mortality risk, and poor quality of life. Impaired muscle mitochondrial oxidative capacity (ATPmax) underlies poor physical endurance in persons with CKD. Metabolic acidosis may mediate effects of CKD on ATPmax. Little is known about the relevance of metabolic acidosis and ATPmax on patient-reported fatigue in CKD.

Methods: We performed a cross-sectional analysis of 58 participants (39 CKD and 19 non-CKD) from the CKD Muscle Mitochondrial Energetics and Dysfunction (MEND) study. Muscle metabolic health of the tibialis anterior leg muscle was measured from the time course of phosphocreatine after exercise using 31P Magnetic Resonance Spectroscopy. Fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F) scale. Metabolic acidosis (MA) was determined from serum bicarbonate (< 22 mEq/L). Linear regression was used to test associations adjusting for age, sex, body mass index (BMI), and diabetes.

Results: The cohort included 48% female and 29% diabetes with a mean age of 61±12 years and a mean BMI of 28±19ml/min per 1.73m² in CKD age, sex, body mass index (BMI), and diabetes.

Methods: We performed a cross-sectional analysis of 58 participants (39 CKD and 19 non-CKD) from the CKD Muscle Mitochondrial Energetics and Dysfunction (MEND). Muscle metabolic health of the tibialis anterior leg muscle was measured from the time course of phosphocreatine after exercise using 31P Magnetic Resonance Spectroscopy. Fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F) scale. Metabolic acidosis (MA) was determined from serum bicarbonate (< 22 mEq/L). Linear regression was used to test associations adjusting for age, sex, body mass index (BMI), and diabetes.

Results: The cohort included 48% female and 29% diabetes with a mean age of 61±12 years and a mean BMI of 28±19ml/min per 1.73m² in CKD age, sex, body mass index (BMI), and diabetes. ATPmax is directly associated with fatigue. MA might play an important role in the association of muscle metabolic health with fatigue in CKD. Further research is needed to examine the impact of treating MA on improvement in muscle metabolic health, fatigue, and quality of life in CKD.

Funding: NIDDK Support, Other NIH Support - Dialysis Clinics Incorporated

PO2065

Blood Pressure in Young Adults with CKD and Associations with Cardiovascular Events and CKD Progression

Alexander J. Kula,1,2 Nisha Bansal,2 David K. Prince,3 Joseph T. Flynn.1,2 Seattle Children’s Hospital, Seattle, WA; 3University of Washington, Seattle, WA.

Background: Young adults (age 18-40yrs) with CKD are a poorly studied subset of CKD patients. Blood-pressure management for young adults with CKD relies on extrapolating findings from studies conducted in older adults or children. Our objective was to perform an observational study exclusively in young adults with CKD to test the association between BP and adverse outcomes.

Methods: Participants aged 21-40yrs of age enrolled in the Chronic Renal Insufficiency Cohort Study were included (n=317). Exposures included baseline systolic BP (SBP) category, <120, 120-129, 130, and >130 higher baseline SBP. Outcomes included cardiovascular (CV) events, including heart failure, myocardial infarction, stroke, or all-cause death, and CKD progression, defined as 50% eGFR decline or ESRD. We used cox-proportional hazard models to test association between baseline SBP with outcomes. Adjusted models included age, race, eGFR, diabetes, and prevalent CV disease for CV event models and urine albumin to creatinine ratio for CKD progression.

Results: As seen in Figure 1, incidence rates for HF, death, CV events, and CKD progression were greater in higher SBP categories. In adjusted models, a baseline SBP ≥130 was significantly associated with CV events (HR: 3.32, 95% CI: 1.53-7.20) and CKD progression (HR: 1.63, 95%CI: 1.02-2.59) compared with SBP<120. Every +10 in SBP was significantly associated with CKD progression (HR: 1.13, 95%CI: 1.02-1.26) in adjusted models.

Conclusions: There is a graded association of higher SBP with greater risk of CV events and CKD progression in young adults with CKD. Among those with SBP>130, 5.8% per year had a CV event and risk was 3-fold higher compared with SBP<120; and 20.7% per year had CKD progression and risk was nearly 2-fold higher. These data suggest that higher SBP is an important risk factor for adverse outcomes in young adults with CKD.

Funding: NIDDK Support

PO2066

Angiotensin Converting Enzyme Inhibitor and Angiotensin Receptor Blocker Use Among Hypertensive US Adults by Albuminuria Status, 2013-2018

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Background: Since 2003, U.S. hypertension (HTN) guidelines have recommended angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) therapy for urine albumin/creatinine ratio (UACR) ≥300 mg/g. Our objective was to assess the prevalence of ACEi/ARB use for UACR ≥300 mg/g among adults with HTN and to examine the association between UACR and ACEi/ARB use.

Methods: We studied adults with HTN in the National Health and Nutrition Examination Surveys 2013-2018. Respondents were classified as having HTN if they had systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, were currently using anti-hypertensive medications, or reported being told by a clinician they had HTN. ACEi/ARB use was assessed by review of medication containers by study staff. Modified Poisson regression was used to estimate crude and adjusted prevalence ratios (PR) for the association between ACEi/ARB use and UACR ≥300 mg/g, for sex, race/ethnicity, diabetes, systolic blood pressure (continuous), chronic kidney disease stage, and having a reported routine site for healthcare.

Results: Among 7,377 adults with HTN, 83.4% had UACR 0-29 mg/g, 13.5% had UACR ≥300 mg/g, and 3.2% had UACR ≥300 mg/g. ACEi/ARB use was 43%, 54%, and 48% in UACR categories 0-29, 30-299, and ≥300 mg/g, respectively. This represents approximately 1.5 million adults with UACR ≥300 mg/g who are not receiving ACEi/ARB therapy. Adjusted ACEi/ARB use was minimally associated with UACR ≥300 mg/g (PR = 1.09, 95% CI 1.03-1.17 for UACR 30-299 mg/g; PR = 0.96; 95% CI 0.83-1.10 for UACR ≥300 mg/g; reference = UACR <30 mg/g).

Conclusions: Nationally representative data indicate a large gap in guideline-concordant ACEi/ARB use among adults with HTN and UACR ≥300 mg/g. Improving uptake of ACEi/ARB therapy presents a substantial opportunity for prevention of cardiovascular disease and kidney disease progression for adults with HTN.

Funding: NIDDK Support

PO2067

Increased Residual Cardiovascular Risk in US Veterans with Moderately Elevated Baseline Triglycerides, Well-Controlled LDL Cholesterol Levels on Statins, and Decreased Renal Function

Sarah Leatherman,1 Ryan E. Ferguson,1 Cynthia Hau,1 Craig B. Granowitz,2 Kelly M. Harrington,1 Sephy Philips,2 Peter P. Toth,2 Deepak L. Bhatt,2 William E. Boden,1 VA Boston Healthcare System, Boston, MA; 2Amarin Corp, Bridgewater, NJ; 3Brigham and Women’s Hospital, Boston, MA; 4CGH Medical Center, Sterling, IL.

Background: Recent studies have suggested a causal role for elevated triglycerides (TG) in incident cardiovascular (CV) events. Using a large cohort of U.S. veterans with statin-controlled LDL-C levels (40-100mg/dL), we explored whether increased residual CV risk existed in patients with elevated baseline TG levels versus those with normal TG levels in the subset who had reduced eGFR (<60 ml/min).

Methods: We identified veterans receiving a statin but not a TG-lowering agent from the VA Corporate Data Warehouse, a database of the VA electronic health record,
from 2010-2015. We compared CV event rates (nonfatal MI, stroke, unstable angina, or coronary revascularization) between the elevated TG (150-499 mg/dL) and normal TG (<150 mg/dL) groups. We calculated crude event rate ratios, rate ratios, and 95% CI for both groups, and adjusted event rate ratios for age, sex, baseline blood pressure, glomerular filtration rate, and weight.

Results: We included 152,266 veterans (predominantly male and white) in the analysis cohort of whom 43,670 (29%) had elevated TG levels. These subjects were younger and had higher BMIs. Table 1 details the crude and adjusted CV event rates. The overall crude and adjusted CV event rate ratios were 1.28 (95% CI 1.23,1.33) and 1.12 (95% CI 1.07,1.16), respectively.

Conclusions: In this large cohort of veterans, those with elevated TG levels and moderately decreased renal function showed a significant increase in CV events despite well-controlled LDL-C on statins compared to veterans whose baseline TG was in a normal range.

Funding: Commercial Support - Amarin Corp

Crude prevalence, crude and adjusted rate ratios of cardiovascular outcomes

<table>
<thead>
<tr>
<th>Category</th>
<th>Crude Rate Ratio (95% CI)</th>
<th>Adjusted Rate Ratio (95% CI)</th>
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<tbody>
<tr>
<td>All CV outcomes</td>
<td>1.28 (1.23, 1.33)</td>
<td>1.12 (1.07, 1.16)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>1.36 (1.29, 1.43)</td>
<td>1.18 (1.12, 1.24)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.36 (1.29, 1.43)</td>
<td>1.18 (1.12, 1.24)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>1.45 (1.39, 1.51)</td>
<td>1.29 (1.23, 1.36)</td>
</tr>
</tbody>
</table>

Rate ratio for each outcome based on generalized linear model with Poisson errors. Composite CV outcome was the 1st occurrence of all individual CV endpoints. Analysis based on 150,151 subjects with complete data.

PO2068

Deep Learning Analysis of Derived Cardiac Function Metrics for the Detection of CKD and Subsequent Outcome Prediction in Community-Dwelling Individuals

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Background: Whether subtle abnormalities in cardiac function exist in community-dwelling individuals and can be used toagnostically discern those with reduced kidney function and incident adverse outcomes over follow up is unknown.

Methods: The Irish Longitudinal Study on Ageing (TILDA) is a prospective nationally representative cohort study based on random sampling of the community-dwelling general population aged ≥50 years in Ireland. Wave 1 was performed between June 2009–June 2011. Participants underwent a detailed health assessment including blood tests, and an active stand test using the Finometer, which measures continuous blood pressure and heart rate for 10 mins while supine at rest, then throughout the standing test and for 2 mins thereafter. Cardiac function metrics are derived: left ventricular ejection time (LVET), cardiac output, and total peripheral resistance. CKD-EPI equation was used to estimate eGFR. All participants had ≥2 measurements of LVET and cardiac output over 3 years, eGFR <60 ml/min/1.73 m2 within 2 years and during the period between 2008 and 2019 were included. The first date where the eGFR value became <60 was defined as the index date. Patients without serum creatinine (SCr) record within 38 months from the index date were excluded. Anemia status (yes/no) was defined by the age-sex specific hemoglobin value estimated.

Conclusions: Deep Learning analysis of repeated measures of derived cardiac function metrics discerned community dwelling individuals with CKD and subsequent outcomes. This method has potential for population level risk discrimination.
PO2071

Estimation of Sodium Consumption by Novel Formulas Derived from 12-Hour Urine Collection

Pitchaporn Sonuch, Surasak Kantachuvessiri. Mahidol University Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand.

Background: 24-hour urine sodium excretion is the gold standard for estimating sodium intake. Several equations have been used to estimate 24-hour urine sodium excretion from spot urine samples. However, a validated formula for predicting 24-hour urine sodium excretion from 12-hour urine collection has not been established. This study aims to establish novel equations for predicting 24-hour urine sodium excretion from 12-hour urine collection and to also validate spot urine equations for predicting 24-hour urine sodium excretion.

Methods: 299 adults were recruited from hospital personnel. Participants were asked to perform a 12-hour daytime, nighttime, and a random spot urine collection in 1 day. Pearson correlation was used to compare measured 24-hour sodium excretion to the estimated values from three different methods. A multivariate linear regression analysis was performed to create novel equations. Bland-Altman method was used to estimate bias and agreement between the equations.

Results: The mean 24-hour urine sodium excretion was 4,055 ± 1,712 mg/day (male 4,307 ± 1,694 and female 3,882 ± 1,710 mg/day, P = 0.0078). The 24-hour urine sodium excretion in non-healthcare workers was higher than in healthcare workers (4,442 ± 1,865 and 3,617 ± 1,406 mg/day respectively, P < 0.001). Estimated urine sodium excretion from 3 different equations using spot urine samples showed moderate correlation with actual 24-hour urine sodium excretion (r = 0.54, P = 0.001 for Kawasaki; r = 0.57, P = 0.001 for Tanaka; r = 0.66, P = 0.001 for INTERSALT). Novel equations for predicting 24-hour urine sodium excretion was then developed using variables derived from 12-hour daytime urine collection, 12-hour nighttime urine collection, and random spot urine samples which showed strong correlation with actual measured values (r = 0.88, P = 0.001, r = 0.83, P = 0.001, r = 0.67, P = 0.001 respectively. Bland-Altman plots indicated good agreement between predicted values and actual 24-hour urine sodium excretion using the new equations, with biases for 12-hour daytime urine collection of +0.28 mmol/day (95%CI: -5.09 to 4.53), for 12-hour nighttime urine collection of 0.85 mmol/day (95%CI: -4.86 to 6.56), and for random spot urine sample of 0.90 mmol/day (95%CI: -6.66 to 8.45).

Conclusions: The associations between predicted values and actual measured sodium excretion were stronger using 12-hour daytime urine collection and 12-hour nighttime urine collection can accurately predict 24-hour urine sodium excretion.

Funding: Government Support - Non-U.S.

PO2072

Serum Magnesium, Blood Pressure, and Risk of Hypertension: Insights from the Chronic Renal Insufficiency Cohort (CRIC) Study

Simon Correa,1,2 Xavier E. Guerra Torres,3 Sushrut S. Waikar,4 Finninn R. McCausland,1,2 Brigham and Women’s Hospital, Boston, MA; 3Harvard Medical School, Boston, MA; 4Hospital Universitario Principe de Asturias, Alcala de Henares, Spain; 5Boston Medical Center, Boston, MA.

Background: Magnesium (Mg) has been implicated in regulation of blood pressure (BP). Mg deficiencies in serum Mg (sMg) are common in CKD and ESRD due to decreased intestinal absorption, impaired renal handling and diuretics use. Studies assessing the association of sMg and BP are scarce, and the association of sMg with the risk of developing hypertension (HTN) is unknown.

Methods: We analyzed data from 3,866 participants from CRIC. Adjusted linear regression models assessed the association of sMg with SBP and DBP at baseline and adjusted smoothing splines were fit. Adjusted logistic regression models explored the association of baseline sMg with baseline HTN (CRIC-defined HTN: SBP ≥140 or DBP ≥90 or anti-HTN drug use; AHA-defined HTN: SBP ≥130 or DBP ≥80 or anti-HTN drug use) and sub optimally controlled blood pressure (SBP ≥120 or DBP ≥80). Adjusted cox-proportional hazard models stratified by clinical site explored the association of baseline sMg with incident HTN. All models were adjusted for demographics, CV comorbidities, eGFR, proteinuria, serum albumin, GFG-23, calcium, phosphate, total PTH, Na, K, urine Na, and urine K.

Results: Median sMg was 2.0 mg/dL (25th-75th percentile 1.9 to 2.1 mg/dL). Higher sMg at baseline was associated with lower SBP (β = -2.63 mmHg, 95% CI -5.01 to -0.25, per 1 mg/dL) and lower DBP (β = -2.75 mmHg, 95% CI -4.16 to -1.34, per 1 mg/dL) (Fig 1A, 1B). Higher sMg was associated with a lower risk of AHA-defined HTN at baseline (HR ≤OR 0.25, 95% CI 0.12-0.55, per 1 mg/dL), a lower risk of sub optimally controlled BP (aOR 0.22, 95% CI 0.10-0.53, per 1 mg/dL) but not with a higher risk of CRIC-defined HTN (aOR 0.77, 95% CI 0.30-1.20, per 1 mg/dL). In time-to-event analyses, higher baseline sMg was associated with a numerically lower risk of incident CRIC-defined HTN (aHR 0.68, 95% CI 0.40-1.13, per 1 mg/dL).

Conclusions: Higher sMg is associated with lower SBP, lower DBP and a nominally lower risk of incident HTN. Monitoring and optimal control of sMg should be considered in patients with CKD for improved BP control.

PO2073

Cardiac Structure and Function and Long-Term Risk of ESKD in African Americans: The Atherosclerosis Risk in Communities (ARIC) Study

Manabu Hishida,1,2 Junichi Ishigami,1 Lena Mathews,3 Morgan Grams,4 Josef Coren,5 Scott D. Solomon,6 Kunihiro Matsushita,7 Welch Center Johns Hopkins University, Baltimore, MD; 2Nagoya Daigaku Daigakuin Igakubu Kenkyuka Igakubu, Nagoya, Japan; 3Brigham and Women’s Hospital, Boston, MA.

Background: Cardiovascular disease and end-stage kidney disease (ESKD) disproportionately affect African Americans. Whether cardiac structure and function is associated with the risk of ESKD in this population is not well-characterized.

Methods: In 1,929 African American ARIC participants who underwent echocardiography between 1993-1995 (mean age 58.5 [SD 5.6] years, 36% male), we explored the association of left ventricular mass index (LVMi), fraction shortening (FS), left atrial diameter (LAD), and LV end-diastolic diameter (LVEDD) with the subsequent risk of ESKD using Kaplan-Meier method and multivariable Cox models.

Results: During a median follow-up of 22.3 years, 82 participants developed ESKD (incidence rate 3.0 per 1,000 person-years). The cumulative incidence of ESKD was highest in the top quartile (bottom quartile for FS of all echo parameters (Figure), although the risk separation was most evident for LVMi. The association of LVMi with ESKD remained significant even after accounting for potential confounders like blood pressure and clinical history of cardiovascular disease (HR 2.46 [1.13-5.38] in the top vs. bottom quartile). FS, LAD, or LVEDD were not independently associated with ESKD.

Conclusions: Among African Americans, higher LVMi was robustly and independently associated with the risk of ESKD. Our findings support the importance of LVMi or its pathophysiology in CKD progression in African Americans.

PO2074

Myeloperoxidase and the Risk of Atrial Fibrillation in the Chronic Renal Insufficiency Cohort (CRIC) Study

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Background: Myeloperoxidase (MPO) catalyzes the formation of reactive oxygen intermediates and is associated with adverse CV outcomes and progression of chronic kidney disease (CKD). We wished to determine the association of MPO with hospitalization for atrial fibrillation (AFib) in patients with baseline CKD.

Methods: We evaluated 3,872 participants with MPO measured at baseline in the CRIC Study, a large prospective multicenter cohort of non-dialysis dependent CKD. The association of MPO with hospitalization due to AFib was evaluated through adjusted Cox proportional hazard models in all study participants, and separately in subjects with and without AFib at baseline. Models were adjusted for age, sex, race, DM, SBB, coronary artery disease, CHF, eGFR (CKD-EPI), proteinuria, ACEi- ARB, beta-blocker and diuretic use.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

636
PO2075
The Association Between Pre-Donation Hypertension and Early Post-Donation Systolic Blood Pressure in Older Living Kidney Donors
Fawaz Al Ammary, Abimerki Muzzaal, Daniel C. Brennan, Dorry L. Segev, Allan Massie. Johns Hopkins University School of Medicine, Baltimore, MD.

Background: One mechanism underlying predonation hypertension in older (age≥50) living kidney donors is a reduced number of nephrons. The 50% nephron mass reduction associated with donor nephrectomy may exacerbate predonation, controlled hypertension. In light of evolving hypertension guidelines, we aim to study systolic blood pressure (BP) trajectory in older donors with- vs. without hypertension.

Methods: We conducted a national registry study of 11,969 older living kidney donors from 2010-2018. We modeled the association between predonation hypertension and postdonation systolic BP using a mixed linear model with donor-level random intercept adjusting for age, sex, race, predonation systolic BP (SBP), BMI, and year of donation. We modeled odds of having 6-month postdonation systolic BP ≥130 mmHg and ≥140 mmHg using multivariable logistic regression.

Results: 1,161 of 11,969 older donors (9.7%) had hypertension. Median (IQR) predonation systolic BP was 130 mmHg (122-140) among donors with hypertension vs. 124 mmHg (115-132) among those without (p<0.001). After adjustment for baseline characteristics including predonation systolic BP, hypertension was associated with a 2.4, and 3.9 mmHg increase in postdonation systolic BP (p<0.001). Hypertension was associated with 39% higher odds of having 6-month postdonation systolic BP ≥130 mmHg (aOR≥130 mmHg = 1.50, p<0.001) and 50% higher odds of having 6-month postdonation systolic BP ≥140 mmHg (aOR≥140 mmHg = 1.50, p<0.001).

Conclusions: Predonation hypertension was associated with higher risk of uncontrolled 6-month postdonation systolic BP among older donors, even after adjusting for postdonation systolic BP. Our findings call for programs to monitor postdonation systolic BP in donors with hypertension to ensure adequate BP control following nephrectomy.

Funding: NIDDK Support

PO2076
Temporal Trends of the Burden of CKD Among Hospitalized Aortic Stenosis Patients in the Province of Quebec, Canada
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Background: Aortic stenosis (AS) is associated with valvular calcifications which are highly prevalent in chronic kidney disease (CKD). The aim of this study was to describe the temporal trends of comorbid CKD status in patients hospitalized for AS and evaluate the impact of these two conditions on 1-year mortality in the province of Quebec, between 2000 and 2017.

Methods: Using the Quebec Integrated Chronic Disease Surveillance System, we identified patients a 20 years with incident AS using ICD-9 and ICD-10 codes, in the hospital discharge database. We then combined hospital discharges and physician billing claims databases to identify patients with comorbid CKD status in the two years prior to the AS diagnosis. Three subgroups of CKD status were considered: 1) non-CKD, 2) pre-dialysis and 3) dialysis. To allow comparison over time, direct adjustment using age distribution of the 2016-2017 AS population was used for proportion, 1-year all-cause and cardiovascular mortality.

Results: We included 108,780 patients with incident AS (Women: 51.8%; mean age (aSD): 76.4 ±11.7; non-CKD: 74.2% (n=80,768); pre-dialysis: 24.6% (n=26,809); dialysis: 1.1% (n=1,203). During the study period, the age-adjusted proportion of AS patients with non-CKD comorbid status decreased by 14% (80.7% [95% CI 77.6-84.0] to 66.9% [95% CI 67.2-71.9]). Inversely, the age-adjusted proportion of AS patients with pre-dialysis and dialysis comorbid status increased by 58% (18.5% [95% CI 16.9-20.2] to 29.3% [95% CI 27.8-30.9]) and 46% (0.7% [95% CI 0.5-1.1] to 1.1% [95% CI 0.8-1.4]), respectively. Age-adjusted 1-year all-cause and cardiovascular mortality decreased over time but remained higher in patients with comorbid CKD. In 2015-2016, age-adjusted relative risk (RR) of 1-year all-cause mortality was significantly higher in pre-dialysis (RR=1.56 [95% CI 1.44, 1.69]) and dialysis (RR=2.04 [95% CI 1.62-2.61]) compared to non-CKD patients. Age-adjusted RR of 1-year cardiovascular mortality was also significantly higher in pre-dialysis (RR=1.83 [95% CI 1.66-2.03]) and dialysis (RR=2.28 [95% CI 1.68-3.09]) compared to non-CKD patients.

Conclusions: Proportion of patients with incident AS and comorbid CKD increased from 2000 to 2017. One-year all-cause and cardiovascular mortality improved over time but remained higher in AS patients with comorbid CKD.

PO2077
Troponin Level in Relation to Angiographic Coronary Artery Disease in CKD Patients
Sachin Bhatia,1 Bhavin Chokshi,1 Balaram Krishna J. Hamamantulu,2 Belinda Jim,2 Jacob Medical Center, Bronx, NY; 2Mount Sinai Beth Israel Hospital, New York, NY; 1Wayne State University School of Medicine, Detroit, MI; *James J Peters VA Medical Center, Bronx, NY.

Background: An association between cardiac troponin I (cTI) in the diagnosis of angiographic coronary artery disease (CAD) is unclear in the CKD population. We evaluated the association between cTI findings of angiographic significant CAD in CKD patients with traditional risk factors.

Methods: Data was collected from left cardiac catheterizations (LCHs) performed between 2006-2017 at Jacobi Medical Center. CAD outcomes were defined as: none, mild (<50% stenosis), moderate (50-69% stenosis), severe (≥70% stenosis of any major epicardial artery). ROC characteristics of cTI as biomarker for severe CAD was performed in patients with CKD stages 3-5. C-Statistic/AUC were used to compare pretest probabilities for severe CAD based on CAD risk factors (age, race, HTN, HLD, DM, smoking), abnormalities on ECHO and ECG, cTI level, and CKD stage.

Results: 798 LCHs were included. Fig1a shows that cTI level is only significantly higher in severe CAD as compared to no CAD among CKD 1-2 patients. ROC showed cTI >0.3ng/mL displayed peak sensitivity (59%), specificity (62%). Multivariate analysis for predictors of severe CAD among 223 CKD patients was stratified at cTI >0.3 and cTI <0.3. Among cTI <0.3 subgroup, age >65(OR 4.6, 95% CI 1.49-27.9, p=0.012) and eGFR<30(OR 2.92; 95% CI 0.94-9.00; p=0.06) were associated with severe CAD. Among cTI >0.3 subgroup, none of the clinical factors were significantly associated with severe CAD. Fig1b shows that the addition of dichotomized cTI > or < 0.3 to CAD risk factors did not significantly change the AUC value.

Conclusions: cTI levels are not associated with different levels of CAD in patients with eGFR<60. The addition of cTI>0.3 does not alter the predictive value of severe CAD when other cardiac risk factors are considered. It will be important to study if the change in cTI during a cardiac event would be more predictive in the CKD population.
PO2078

Pediatric vs. Adult Ambulatory Blood Pressure Monitoring (ABPM)
Criteria for the Diagnosis of Hypertension (HTN) and Detection of Left Ventricular Hypertrophy (LVH) in Adolescents

Kumail Merchant,1 Parus P. Shah,2 Paula Singer,1 Laura J. Castellanos,1 Christine B. Sedina,1,2 Cohen Children’s Medical Center, Queens, NY; Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

Background: Normative values for clinic blood pressure (BP) measurements in adolescents were recently updated to align with adult HTN guidelines (CPG 2017). However, the most widely accepted pediatric normative values used to diagnose HTN by ABPM criteria have not been updated. The objective of this study was to compare pediatric ABPM criteria (pHTN) with adult ABPM criteria (aHTN) for the diagnosis of HTN and detection of LVH in adolescents.

Methods: ABPM and ECHO reports from adolescents age 12-18 years performed from 2015-2019 at a single center were analyzed. The concordance of HTN diagnosis based on pHTN (AHA 2014) was compared to aHTN from ACC/AHA 2017 (overall BP ≥125/75 mmHg, wake BP ≥130/80 mmHg, sleep BP ≥110/65 mmHg) using Cohen’s kappa statistic. Logistic regression adjusted for body mass index (BMI) z-score and receiver operating curves (ROC) were used to compare the ability of pHTN vs. aHTN to detect LVH (left ventricular mass index [LVMI] >95th percentile reference values and LVMI >51g/m²).

Results: Of 306 adolescents (15.9±1.6 years, 73.5% male), 140 (45.8%) had HTN based on pHTN compared to 228 (74.5%) based on aHTN. There was poor agreement in the diagnosis of HTN between pHTN and aHTN (59.3%, N=137, kappa 0.41). 1.0% (N=3) had HTN by pHTN only while 29.7% (N=91) had HTN by aHTN only. Although a higher prevalence of LVH was captured by aHTN only, 9 (5.6%) adolescents who had LVH >95th percentile did not have HTN by either criteria. In logistic regression, adjusted for BMI z-score, there were no significant differences between pHTN and aHTN in the detection of LVH >95th percentile (OR 1.24, CI 0.66-2.31, p=0.51) or >51g/m² (OR 1.06, CI: 0.47-2.40, p=0.89). ROCs for pHTN were not significant for detecting LVH >95th percentile (0.50, p=0.91) or >51g/m² (0.55, p=0.45). However, the ROC for aHTN was significant for detecting LVH >95th percentile (0.59, p=0.045) but not >51g/m² (0.63, p=0.07).

Conclusion: Pediatric HTN criteria appear to have better sensitivity than adult HTN criteria for the diagnosis of HTN in adolescents. aHTN appears to better predict LVH than pHTN, although neither criteria diagnosed all patients who had LVH. A consideration to align the ABPM criteria for the diagnosis of HTN in adolescents with adult guidelines is warranted.

PO2079

Effect of Psychiatric Diagnosis and Selective Serotonin Reuptake Inhibitors (SSRIs)/Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) Use on BP Using 24-Hour Ambulatory Blood Pressure Monitoring (ABPM)

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Background: Hypertension (HTN) and psychiatric disorders frequently co-exist. Psychiatric conditions and their treatment by SSRIs/SNRIs affect serotonin & norepinephrine and may cause variation in blood pressure (BP). There is limited data to assess this variation by using ABPM.

Methods: Subjects who underwent psychiatric evaluation & ABPM within six months of each other between 1/2012 to 12/2017 were identified. Demographics, comorbidities, medications, ABPM, lab data were retrospectively collected. Subjects were divided into group-subjects with no psychiatric diagnosis & no psychiatric medicine (Group 1), subjects with psychiatric diagnosis & on SSRIs/SNRIs (Group 2) and subjects with psychiatric diagnosis & no medication (Group 3). BP systolic & diastolic levels (daytime, nighttime) were compared between groups controlling for age, sex, race, HTN, DM and smoking. Single and multivariable linear regression models were used to analyze group differences.

Results: Total of 475 subjects met inclusion criteria–Group 1=135, Group 2=232, and Group 3=108. First, Group 1 was compared with Group 2 for daytime systolic & diastolic, nighttime systolic & diastolic BP. In multivariable analysis adjusted for age, sex, race, HTN, DM, and smoking, subjects in Group 2 had higher nighttime systolic BP (22.7±11.05 mmHg; 8.36; 95% CI: 4.21-12.51; P<0.0001) and nighttime diastolic BP (8.2±6.4 mmHg; 4.6±11.9; 2.7 P<0.0001) to determine whether higher nighttime systolic & diastolic BP in Group 2 were due to psychiatric diagnosis or effect of SSRIs/SNRIs, we compared ABPM between Group 1 & Group 3. In adjusted model, there was no statistically significant difference between Group 1 & 3 for daytime or nighttime systolic & diastolic BP suggesting higher nighttime BP in Group 2 was associated with psychiatric diagnosis during sleep with serotonin & norepinephrine with SSRIs/SNRIs use. Further prospective studies using ABPM are needed to determine the risk of nocturnal hypertension with SSRIs/SNRIs use that could adversely impact cardiovascular outcomes.

PO2080

Obesity-Related Renal Damage in Adolescent Women: Body Surface Area Matters

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Background: Obesity is a potentially modifiable risk factor for the development and progression of kidney disease. In children and adults, the attention has been paid to the prevalence of early signs of kidney dysfunction among overweight and obese adolescents by examining routine labs including creatinine for hyperfiltration and albuminuria.

Methods: De-identified electronic health record (EHR) data were extracted for female adolescents aged 12-21 years, who received health care services from 1/1/2011 to 12/31/2015 in NYC from 12 academic health centers and community health centers that are part of PCORnet NYC Clinical Data Research Network (NYC-CDRN). Data were analyzed using SAS (v 3.25) on 60,549 unique subjects. Patient characteristics observed and by subgroups were examined using standard statistical tests. BMI groups were coded according to NHANES as underweight, normal weight, overweight or obese. Multiple linear regression analyses will control for covariates.

Results: Mean creatinine values were similar between normal weight, overweight and obese BMI groups, yet after calculating eGFR and adjusting for BSA, significant and alarming differences appeared. Obese adolescent women had significantly higher eGFR, estimated by CKD-EPI and the Schwartz formula according to age, compared to normal weight subjects. Only subjects in the obese group (BMI>30) exhibited hyperfiltration (eGFR>135 ml/min).

Conclusions: Obese adolescent women present with significant alteration in kidney function that without intervention will lead to ESRD, and adverse outcomes associated with the deleterious effects of adiposity. Awareness should be raised to consider body size when estimating GFR in adolescents.

Funding: Other NIH Support - This project was supported in part by the National Center for Advancing Translational Sciences, National Institutes of Health, through The Rockefeller University, Grant Number UL1 TR000445. The Rockefeller Center for Biomedicine at The Rockefeller University, The Sackler Institute for Nutritional Science at the New York Academy of Sciences, and the Patient-Centered Outcomes Research Institute (PCORI) PCORnet Contract # CDRN-1306-03961., Private Foundation Support

PO2081

Urinary Magnesium Predicts Risk of Cardiovascular Disease in Pre-Dialysis CKD Patients

Qiongling Yuan,1 Hui Xu,1 Jinwei Wang.2 on behalf of the C-STRIDE study group.1 Yonghua Hospital Central South University, Changsha, China; 2Peking University First Hospital, Beijing, China.

Background: 24h Urinary magnesium concentration (24h U Mg), an indicator of intestinal magnesium absorption, may provide a better insight in the connection of CKD progression.

Methods: We examined 3179 participants aged 18 to 74 years pre-dialysis patients in the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE) study. We performed a time-to-event analysis of the data using Kaplan-Meier Survival model, Cox proportional hazard and competing risks Fine and Gray sub-distribution hazard models.

Results: During the median follow-up of 4.19 (IQR 3.432-5.09) years, lower incidence rate of ESRD events was observed with increases in 24h UMg (Figure 1). Higher incidence rate of CVD events was seen with increases in 24h UMg (Figure 2). After adjustment for demographic and traditional ESRD risk factors, 24h UMg was strongly associated with risk of CVD (HR of 1.509 [95% CI 1.031:2.208] Table 1).

Conclusions: 24h U Mg risk variants display a modest association with CVD in pre-dialysis CKD patients.

Funding: Government Support - Non-U.S.
Table 1 Association of 24h UMg with CVD events among pre-dialysis CKD patients

<table>
<thead>
<tr>
<th>UMg category</th>
<th>Model 1</th>
<th>Model 2</th>
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<tr>
<td>Total CVD patients (n=359)</td>
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<tr>
<td>&lt;95%</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>&lt;95%</td>
<td>1.88 (0.62, 5.66)</td>
<td>1.90 (0.62, 5.66)</td>
</tr>
<tr>
<td>&gt;95%</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
</tbody>
</table>

** Statistically significant at 0.05.

Model 1: Age, gender
Model 2: Age, gender, CVD, HBP, DM, drinking, smoking, UA, HCO3-, TC, LDL, eGFR, BMI, ACR, iPTH, HGB, sP, sMg, sCa, sK, sNa, UNa, UK

Conclusions: Although non-dipping was not associated with LVMI or LVH in adolescents with WCH, the fair prevalence (34.7%) of non-dipping among this population is of note. Given adult studies demonstrating the progression of non-dipping to poor CVD outcomes, these potentially high-risk patients should be monitored closely.

PO2083

Left Atrial Strain Measurements Are Associated with Cardiovascular Outcomes in Patients with ESRD

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Background: Left atrial (LA) strain is a marker of diastolic dysfunction, heart failure and atrial fibrillation that has been validated in populations without chronic kidney disease. There are few studies of LA strain in patients with end-stage renal disease (ESRD), among whom cardiovascular (CV) mortality is high and there are no accepted methods of CV risk stratification. We sought to examine associations of LA reservoir strain with CV hospitalization and mortality in a cohort of patients with ESRD on dialysis, and to investigate prognostic utility of strain measurements for CV outcomes.

Methods: 190 ambulatory participants with ESRD on dialysis in the Cardiac, Endothelial Function and Arterial Stiffness in ESRD (CERES) study underwent 2D echocardiography at one study visit. The composite outcome, CV hospitalization or death, was adjudicated over a median of 2 years. Hospitalizations attributed to missing dialysis were not counted as events. LA and left ventricular (LV) structure and function were captured by a single technician, and de-identified images were read by a single reader using GE EchoPac software. Associations of LA reservoir strain with the composite outcome were analyzed with cox survival analyses, adjusting for age, gender, comorbidities, and systolic blood pressure.

Results: Mean age was 56 years, 1/3 were women, and the median time since dialysis initiation was 3.5 years. 45% were diabetic and 14% had a history of heart failure. Participants were relatively euvoletic, based on well-controlled blood pressure and weight. Mean (SD) LA volume index was 40ml/m2(±12), mean LA reservoir strain was 24%(±6.9). There were 61 events: 40 hospitalizations and 21 deaths. In the adjusted model, HR (95%CI) per SD LA volume index was 1.4(1.04, 1.9); LA reservoir strain HR(95%CI) per SD was 0.67(0.47, 0.94). A risk model including age, LA reservoir strain and LV global longitudinal strain had an a-statistic(95%CI) of 0.72(0.63, 0.81) for the composite outcome.

Conclusions: Our results suggest that LA strain is independently associated with CV hospitalizations and death among patients with ESRD on dialysis. Strain measurements have the potential to contribute to CV risk stratification in this population. Larger studies are necessary to validate our findings.

Funding: NIDDK Support

PO2084

Under Diagnosis of Pediatric Hypertension

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Background: Pediatric hypertension is associated with target organ damage in children and cardiovascular morbidity in adults. Therefore, prompt diagnosis and treatment are critical. Application of clinical practice guidelines is inconsistent.

Methods: Using electronic health record data (from 8 community centers), we evaluated the proportion of children (3-18 years) with elevated blood pressures (>90th percentile) who were appropriately diagnosed as either hypertension or elevated blood pressure over 1 year (2016-17), and provided guideline directed follow-up, by age, sex, race/ethnicity and weight.

Results: The sample included 6233 children with elevated blood pressure, 15% were appropriately diagnosed. These children were more likely to be older, white, and obese. 55 children met criteria for hypertension with 23 being appropriately diagnosed, there was no difference by patient characteristics. Of children with blood pressure ≥95th percentile, 13% had follow-up within 1 month; they were more likely to be older, female, of Hispanic ethnicity or ‘other’ race. Of children with blood pressure ≥90th percentile, 41% had follow-up within 6 months, and were more likely to be older, of either white, Hispanic, Asian race or Hispanic ethnicity.

Conclusions: We found persistent underdiagnosis of pediatric hypertension and elevated blood pressure as well as disparities in the diagnosis of elevated blood pressure and guideline-directed follow-up among diverse children in a community setting. New strategies are needed to improve compliance with guidelines.

Funding: Other NIH Support - National Heart, Lung, and Blood Institute of the National Institutes of Health; National Institute on Drug Abuse

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Underline represents presenting author.

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Background: Visit-to-visit blood pressure variability (BPV) is associated with cardiovascular (CV) events in individuals with chronic kidney disease (CKD) stages 3-5. We examined the associations of BPV with CV events, death, and end-stage kidney disease (ESKD) among veterans with CKD stages 1-5 and hypertension, and if treatment with a thiazide or loop diuretic modified these associations.

Methods: In a matched cohort study, patients seen between 2010-2016 with non-dialysis CKD and hypertension on single-agent therapy with a non-diuretic were propensity with a thiazide or loop diuretic modified these associations. 3-5. We examined the associations of BPV with CV events, death, and end-stage kidney disease (ESKD) in patients with CKD and hypertension. Diuretic use attenuated the association of BPV was also associated with MI, heart failure, stroke, and death, but not with ESKD

Results: We included 31,394 new users of diuretics and 31,394 patients initiating their second agent. BPV, defined as the coefficient of variation of outpatient systolic blood pressure over 6 months after prescription of the second antihypertensive, was divided into their second agent. BPV, defined as the coefficient of variation of outpatient systolic blood pressure over 6 months after prescription of the second antihypertensive, was divided into quintiles. Cox proportional hazards regression measured associations of BPV with time to CV events (first among myocardial infarction [MI], hospitalization for heart failure, or ischemic stroke), each component of the primary outcome, all-cause death, and ESKD.

Results: We included 31,394 new users of diuretics and 31,394 patients initiating other agents. Over a median (IQR) follow up time of 939 (404-1,606) days, there were 7,326 CV events, 16,357 deaths, and 2,029 ESKD events. Higher BPV was associated with composite CV events (Figure). Diuretic exposure attenuated these associations at the fourth and fifth quintiles of BPV (interaction P<0.03 at the 4th and .04 at the 5th quintile). BPV was also associated with MI, heart failure, stroke, and death, but not with ESKD (Figure). Diuretic treatment did not modify these associations. Conclusion: BPV was associated with CV events and all-cause death but not ESKD in patients with CKD and hypertension. Diuretic use attenuated the association of BPV with CV events at the highest quintiles of BPV. Future studies should test whether diuretics improve CV outcomes in those with high BPV.

Funding: Private Foundation Support

Poster

PO2085

Associations of Blood Pressure Variability with Cardiovascular Events, Death, and ESKD in Patients with CKD

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Background: Hypertension and CVD: Epidemiology, Risk Factors, and Prevention

Hypertension (HTN) is often underdiagnosed and undertreated. Masked HTN can reach 49% in chronic kidney disease (CKD) in children. The prevalence of HTN in systemic lupus erythematosus (SLE) varies from 30 to 77%. A small study demonstrated that children with SLE are prone to have blunted dipping. Nocturnal HTN and blunted dipping are independent predictors for all-cause cardio-vascular morbidity/mortality, independent of 24-hr systolic blood pressure (BP) levels.

Methods: Patients (<21 years) with lupus nephritis (LN) were enrolled. Clinical, laboratory, ambulatory blood pressure monitor (ABPM) and echo were reviewed. Max dose of steroids was 20 mg (1 patient). Variables included age, gender, ethnicity, CKD stage, BMI, MMR level, complement levels, dsDNA, proteinuria.

Results: Of the 10 patients (8 F, 2 M), 8 were Hispanic, 2 African American. 9 had CKD stage 1, 1 had CKD stage 2, and mean age was 16.2 ± (11-20y). Class III LN was in 4 patients, class IV and V in 5 patients each. BP during the previous 3 visits were normal in 8 patients and 6 patients were on BP medications. Based on ABPM data, 3 of 6 treated patients had uncontrolled HTN. Of the 4 patients without BP treatment 2 had pre-HTN. Blunted dipping was seen in 6 patients. Echo was done for 5 patients with ABPM.
abnormalities. Left ventricular mass index (LVMI), relative wall thickness (RWT) and ejection fraction were normal. Left ventricle was dilated in 1 patient. Observed intraocular pressure (IOP) was high, and on examination, the patient's vision was somewhat impaired. The patient was treated with diuretics, and the intracranial pressure (ICP) was reduced. There was no change in the patient's vision.

**Conclusion:** Masked HTN and blunted nocturnal dip is common in adolescents with SLF and can be missed if ABPM is not applied in clinical practice. Additional studies are required to find risk factors and management strategies.

**Discussion:**

See table below.

**Case Description:**

**Discussion:**

We describe 2 adolescent cases of hypertension diagnosed by clinic BP and target organ damage but not confirmed by ABPM. Both patients had EST done as part of their evaluation because they were first seen by cardiologists at the study center who frequently employ EST as part of evaluation for hypertension. The cut-off value of 180mmHg for EESP was employed in this report as a previous study had identified 181 mmHg as the most discriminatory systolic BP threshold for predicting hypertension at follow-up. The discrepant results between the ABPM and EST BP in our patients with target organ damage may indicate that multiple diagnostic tools may be required to confirm the diagnosis of hypertension. Both tests could be viewed as complimentary as ABPM is not recommended during exercise which is a part of everyday life. Furthermore, a normal ABPM may not exclude a diagnosis of hypertension in patients with elevated clinic BP and target organ damage. Further studies are needed to confirm these findings in a larger population, and to better understand how these 2 tests may perhaps be used adjunctively to diagnose hypertension.

**Table 1**

<table>
<thead>
<tr>
<th>Variable at Baseline</th>
<th>Group A (N = 90)</th>
<th>Group B (N = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (SD)</td>
<td>61.3 (15.9)</td>
<td>67.7 (10.7)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>44 (48.9%)</td>
<td>31 (69.1%)</td>
</tr>
<tr>
<td>CKD 1-5, N</td>
<td>55 (72.2%)</td>
<td>46 (67.6%)</td>
</tr>
<tr>
<td>SBP, mean (SD mmHg)</td>
<td>163.0 (16.4)</td>
<td>162.6 (16.4)</td>
</tr>
<tr>
<td>DBP, mean (SD mmHg)</td>
<td>89.9 (12.4)</td>
<td>88.4 (12.9)</td>
</tr>
<tr>
<td>MAP, mean (SD mmHg)</td>
<td>110.4 (10.5)</td>
<td>112.7 (10.4)</td>
</tr>
<tr>
<td>Central SBP, mean (SD mmHg)</td>
<td>142.7 (20.7)</td>
<td>142.7 (20.7)</td>
</tr>
<tr>
<td>Central DBP, mean (SD mmHg)</td>
<td>90.5 (14.5)</td>
<td>89.5 (14.5)</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Change from Baseline</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mean (SD mmHg)</td>
<td>-20.0 (16.3)</td>
<td>-15.2 (12.1)</td>
</tr>
<tr>
<td>DBP, mean (SD mmHg)</td>
<td>-11.0 (14.0)</td>
<td>-6.9 (9.7)</td>
</tr>
<tr>
<td>MAP, mean (SD mmHg)</td>
<td>-14.7 (10.9)</td>
<td>-9.5 (12.4)</td>
</tr>
<tr>
<td>Central SBP, mean (SD mmHg)</td>
<td>-21.5 (33.8)</td>
<td>12.5 (16.8)</td>
</tr>
<tr>
<td>Central DBP, mean (SD mmHg)</td>
<td>-13.4 (21.9)</td>
<td>-7.0 (9.27)</td>
</tr>
</tbody>
</table>

**PO2089**

**Hypertension with Target Organ Damage and Discrepancy Between Ambulatory Blood Pressure Monitoring and Exercise Blood Pressure**

**Results:**

There were 90 and 21 patients in groups A and B, respectively. At baseline, demographics were similar in both groups (Table 1). At endpoint, Group A had more patients at targeted blood pressure (BP) (55.6% vs 33.3% at 140/90 mmHg; 21.1% vs 19% at 130/80 mmHg), and larger reduction in both brachial and central BP parameters (Table 2). The mean (SD) of number of office visits were 3.1(1.0) and 2.9(1.1), in Groups A and B, respectively. In Group A, mean aorta compliance was increased 23.3% and 1.7% in the subgroups that met and did not meet target BP, respectively. Mean number of medications at baseline/endpoint were 1.7/2.6 and 1.9/2.0 in groups A and B, respectively. At endpoint, Group B had negligible change in distribution of drug classes, while Group A had significant increased use of calcium channel blockers (dihydropyridine) and beta-blockers.

**Conclusions:** Impedance cardiography is a simple, noninvasive method for evaluating underlying hemodynamic drivers of HTN. Hypertension management is more effective when guided by hemodynamic state.
Intensive Blood Pressure Lowering on Incident Strokes in the SPS3 Trial

The Influence of Baseline Diastolic Blood Pressure on the Effects of Intensive Blood Pressure Lowering on Incident Strokes in the SPS3 Trial

PO2092

The Influence of Baseline Diastolic Blood Pressure on the Effects of Intensive Blood Pressure Lowering on Incident Strokes in the SPS3 Trial

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Background: While observational analysis suggested higher risk of recurrent stroke with low baseline DBP, intensive SBP lowering did not increase recurrent stroke risk in those with low baseline DBP and previous stroke.

Methods: SPS3 was a 2x2 factorial RCT that examined the effects of intensive vs. standard (<130 vs. 130-149 mmHg) SBP control and combination versus aspirin alone antipatelet therapy on stroke outcome in 3020 participants. We examined whether the effects of intensive SBP lowering on stroke were modified by baseline DBP using spline regression models.

Results: Mean baseline age was 55 ± 11 yrs and DBP 95 ± 14 mmHg. There were 264 death/ESKD events over 4714 years of follow-up. Compared to usual BP control, low BP goal resulted in lower levels of follow-up SBP, MAP and DBP across baseline DBP tertiles (Fig 1). Despite the lower follow-up MAP and DBP values, there was no evidence that low BP goal increased the risk of death/ESKD in those with low baseline DBP (Fig 2). Interaction of baseline DBP and BP intervention for death/ESKD was not significant (p = 0.22).

Conclusions: The effect of BP lowering on the risk of death/ESKD was not modified by low baseline DBP. Hence, low baseline DBP by itself should not be an impediment for intensive BP lowering in CKD.

Funding: NIDDK Support, Other NIH Support - NHLBI, Veterans Affairs Support

Figure 1. Mean follow-up SBP, DBP and MAP by BP arm in baseline DBP tertiles

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

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Early GFR Decline with Intensive BP Lowering and the Risk of Death and ESKD: Mediation Analysis of AASK Study
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Background: Intensive BP lowering decreased the risk of death in CKD in SPRINT but there are concerns that its acute, hemodynamic kidney effects might increase ESKD risk.

Methods: AASK Study (N=1094) was a RCT of low vs. usual mean arterial pressure (92 vs.102 to 107 mmHg) on kidney outcomes. Using the change in measured iothalamate GFR from baseline to the average of months 3 and 6 (early GFR change), we examined the acute effect of the intervention on subsequent death/ESKD in a mediation analysis. We partitioned the total effect of BP intervention on death/ESKD that was mediated through early GFR change (indirect effect) and independent of early GFR change (direct effect). We also used SIMEX method to access the impact of measurement error in early GFR change on the findings.

Results: We included 976 AASK participants with GFR measurements at baseline, 3 and 6 months. Mean baseline GFR was 55±11 ml/min/1.73m². There were 223 deaths, 293 ESKD events and 445 death/ESKD events during an average of 7.2±3.3 years of follow-up. BP separation was maintained through the trial (Fig 1, panel A) with an early decline in GFR in the lower BP group but GFRs in the two arms that were similar at the end of the trial (Fig 1, panel B). After adjustment for covariates listed in the footnote to Fig 2, we observed a borderline significant beneficial total effect of the BP intervention on death/ESKD and a slightly stronger direct effect (Fig 2). The HR for the indirect effect was slightly > 1, consistent with the possibility of a small adverse effect of early GFR change.

Conclusions: Intensive BP lowering appears to have a largely beneficial direct effect and a small deleterious indirect effect on death/ESKD in CKD.

Funding: NIDDK Support, Other NIH Support - NHLBI, Veterans Affairs Support

A Novel Marker of Resistant Hypertension in CKD
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Background: Inflammation, oxidative stress (OS), atherosclerosis and resistant hypertension (RH) are common features of chronic kidney disease (CKD) leading to higher risk of death from cardiovascular disease. These effects seem to be modulated by impaired anti-oxidant, anti-inflammatory and reverse cholesterol transport actions of high-density lipoprotein cholesterol (HDL). Recently, monocyte count to HDL-cholesterol ratio (MHR) has emerged as a potential marker of inflammation and OS, demonstrating to be relevant in CKD. Our research was aimed to assess, for the first time, its reliability in RH.
Methods: We performed a retrospective study on 214 patients with CKD and arterial hypertension admitted between January and June 2019 to the Unit of Nephrology and Dialysis of Policlinico G. Martino in Messina, Italy. 72 patients were diagnosed with RH, defined as blood pressure >140/90 mmHg despite use of three different classes of antihypertensive medications (one of which must be a diuretic) at the maximum tolerated doses.

Results: MHR appeared inversely related to eGFR (p = 0.0163; P = 0.0172). MHR was significantly higher among RH patients compared to non-RH ones (12.39 [IQR 10.67 - 16.05] versus 7.30 [5.49 - 9.06] (Figure 1); P < 0.0001). Moreover, MHR was significantly different according to the number of anti-hypertensive drugs per patient in the whole study cohort (F = 46.723; P = 0.001) as well as in the non-RH group (F = 14.19; P = 0.001). Lastly, MHR values differed according to gender, being higher among males (9.41 [6.75 - 12.07] versus 8.02 [5.94 - 10.57]; P = 0.0463).

Conclusions: MHR may be a reliable biomarker due to the connection between HDL and monocytes. HDL prevents and reverses monocyte recruitment and activation into the arterial wall and impairs endothelial adhesion molecule expression. Our study suggests that MHR can reflect renal status and OS in CKD patients with RH, in order to implement appropriate treatment strategies.

PO2098
Primary Aldosteronism in CKD
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Background: Primary aldosteronism (PA) is a common cause of secondary hypertension, with unilateral causes of PA are potentially cured with adrenalectomy. Treatment of PA in CKD is often avoided for concerns of safety and efficacy.

Methods: We conducted a retrospective cohort study of patients with PA and CKD (eGFR <60 ml/min/1.73m²) at 3 institutions (2009-2019). eGFR was calculated using CKD-EPI. Statistical comparison utilized the student’s t-test, Chi-square test, and Wilcoxon rank-sum test.

Results: Of 250 patients included, mean age was 56.6yrs (±10.5), and 64% were female. Median plasma aldosterone concentration was 29.0 ng/dl (IQR:20.3-47.4), median plasma renin activity was 0.2 ng/ml/hr (IQR:0.1-0.6) and aldosterone-renin ratio was 119 (ng/dl)/(ng/ml/hr) (IQR:63.5-240.0). Median eGFR on initial evaluation was 49.0 ml/min/1.73m² (IQR:40.3-58.2). Adrenal vein sampling (AVS) was performed in all patients; unilateral PA was diagnosed in 67.6% (n=169). Adrenalectomy was performed in 163 subjects. Surgical pathology demonstrated adrenocortical adenomas in 66.9%, nodular hyperplasia in 4.9%, and nodular hyperplasia with a dominant nodule in 10.4%. The median tumor size was 1.2 cm (IQR:1.0-1.8). No differences were detected in baseline MAP, number of anti-hypertensive medications (AHM), serum creatinine, or potassium levels between adrenalectomy patients and those medically managed. Adrenalectomy patients had significantly lower AHM requirements at 1 month (2.0 vs. 4.5; AHM requirements at 1 month (2.0 vs. 4.5; P = 0.001)), 6 months (2.0 vs. 3.0, p=0.002) and 12 months after surgery (2.0 vs. 4.0, p<0.001) compared with medically managed patients. Adrenalectomy patients demonstrated stable eGFR from baseline to 12 months postoperatively, while medically managed patients had a statistically significant decrease in eGFR from baseline to 12 months (p=0.040). There was no difference between groups in cardiovascular outcomes.

Conclusions: Patients with CKD and unilateral PA experience significant and durable decrease in AHM requirement and demonstrate stabilization of eGFR after adrenalectomy when compared to medically managed patients. AVS was successful despite reduced eGFR. This study demonstrates that patients with CKD and suspected PA should undergo evaluation to determine whether they have surgically curable disease, as there is a clear benefit in medication reduction and stabilization of eGFR at 12 months.

PO2099
Bilateral Nephrectomy in a Patient with Refractory Hypertension Prior to Development of ESKD
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Introduction: Renal denervation (RDN) reduces increased sympathetic activation in refractory HTN (rHTN) while preserving kidney function, and trials in both the US and Europe demonstrate a 7-12 mmHg placebo subtracted reduction in systolic BP. Bilateral nephrectomy (BLN), originally performed in ESKD patients in the 1970s for HTN is an effective treatment, but is reserved for ESKD pts. We present a case of life threatening rHTN in a pt with Stage 3b CKD that was unresponsive to open surgical renal denervation (OS RDN) but responded extremely well to BLN.

Case Description: A 43 y/o white woman with stage 3b CKD (eGFR 38 ml/min/1.73m²) presented with a resting SBP between 180-240 mmHg on maximal doses of 8 different antihypertensive medications including spironolactone and minoxidil. She required frequent hospitalizations for symptomatic HTN with IV CCBS and beta blockers. Workup included an evaluation of all secondary causes including drug screening, urine metanephrines, renal MRI, and renin/aldo ratio. In an effort to avoid BLN, she initially underwent bilateral OS RDN by severing all neural tissue entering the kidney. Renal vein renin levels were 9.1, 7.8 ng/ml/hr pre OS RDN and 0.7, 1.4 ng/ml/hr post. Despite an initial drop in BP to 140/70 mmHg on only 2 medications, within 4 wks of OS RDN, her BP rose to 240/120 on 4 medications and she was symptomatic. At this point, BLN was performed as the only remaining option. Understanding of the need for RRT following BLN, the patient consented to proceed. Follow up BPs have been in the 130/80 mmHg range on reduced dose 12.5mg bid alone.

Discussion: Neither OS RDN nor pre-ESKD BLN for rHTN have been previously reported. Advancements in endovascular RDN are becoming more effective, but still only lower systolic BP by 7-12 mmHg placebo subtracted. Our case failed to respond to OS RDN, where we were guaranteed completed resection of the nerves and surrounding connective tissue, and suggests the effects of any form of RDN may be limited. BLN for rHTN in pts on RRT was started in the 1970s. Almost 50 yrs later, despite enormous improvements in medications, there is still a role for this procedure, and it emphasizes how little we still know about the etiology of HTN. Requiring this in a patient pre-ESKD was extreme but we felt a life-saving requirement. She will be referred for transplantation.
PO2100
Rostral Ventrolateral Medullary Compression: A Rare but a Cardinal Cause of Refractory Hypertension (RfHTN)
Mirinali Sarkar, Susanne B. Nicholas. University of California Los Angeles, Los Angeles, CA.

Introduction: RfHTN is defined as uncontrolled HTN with BP >140/90 mmHg despite at least 5 different classes of maximally tolerated antihypertensive agents, including a diuretic and a mineralocorticoid receptor antagonist. RfHTN may be underdiagnosed.

Case Description: A 43-year-old female with a history of mitral valve prolapse, iron deficiency anemia, mild asthma and migraine presented for management of uncontrolled severe HTN. Her HTN became increasingly resistant following use of pheniramine and fenfluramine for two years and a recent hysterectomy, with persistently elevated blood pressure (BP) up to 250/100 mmHg. Her medications included: hydralazine, lopressor, procardia, demadex, diovan, catapres and aldactone. On physical exam, her BP was 230/136 mmHg with regular pulse of 96 beats/min and no papilledema or bruits. Renal function and aldosterone levels were normal. Renal ultrasound/doppler, captopril scan, and angiograms showed no renal artery stenosis or coarctation of the aorta, and 24-hour urine metanephrines were normal. Her echocardiogram showed concentric left ventricular hypertrophy with ejection fraction of 60%. Minoxidil was initiated and procardia and lopressor were maintained, with no effect on BP. A high-resolution brain MRI with spectroscopy showed a venous angioma in the right superior temporal lobe and CT angiogram showed irregularity of the basilar artery with outpouching at the left posterior communicating artery and right anterior choroidal artery. She was diagnosed with neurogenic arterial HTN from neurovascular compression (NVC) of the rostral ventrolateral (RVL) medulla. Left retro-sigmoid craniotomy was performed for NVC decompression, but aborted eight hours later for fear of precipitating a massive stroke.

The patient continues to have RfHTN despite maximal medical therapy and has now developed complications including a cerebral ICA dissection, CKD stage 3, heart failure, and severe refractory HTN.

Discussion: NVC is related to neurogenic HTN when occurring in the RVL medulla.

This case highlights that brain MRI be performed in patients with intractable resistant HTN when all other secondary causes are ruled out.

PO2101
Adjunctive Mesenchymal Stem Infusion Boosts Recovery of GFR After Renal Revascularization for Atherosclerotic Renovascular Disease
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Background: Atherosclerotic renovascular disease (ARVD) reduces renal blood flow (RBF), GFR and accelerates poststenotic kidney (STK) tissue injury. Renal revascularization alone often fails to restore GFR in ARVD. Whether adjunctive infusion of autologous mesenchymal stem cells (MSC) can modify reparative processes during restoration of RBF is unknown.

Methods: We measured RBF (MDCT), GFR (iolyticum clearance), systolic blood pressure (SBP), in 16 human subjects with ARVD, before and 3 mo after MSC delivery and stent PTRA. MSC were administered at 3 dose levels (1, 2.5 and 5.0x10^5 MSC/kg, n=7,5,4 patients each) into STK, after stent PTRA. A cohort with ARVD n=17 matched for age, SBP and GFR studied under identical protocol treated with stent PTRA alone served as controls.

Results: SBP decreased in MSC + PTRA and PTRA alone groups 145±20 to 135±19, P=0.022, and 147±20 to 137±16 mmHg, p= 0.02. RBF increased in both MSC + PTRA and PTRA alone treated groups following the three-month hiatus 23±1 to 29±1 mls/min, p=0.015 and 31±2 to 37±3 mls/min, p=0.017. By contrast, GFR increased in the MSC + PTRA group 64±20 to 73±34 ml/min/p=0.017 whereas GFR did not change in the PTRA group 63±7 to 65±8 ml/min, p=0.35. The increases in RBF and GFR were higher in the group treated with the highest MSC dose Fig1.

Conclusions: These data reinforce the dissociation between restoring RBF and recovery of GFR in ARVD. Adjunctive therapy with autologous MSC was associated with a dose-related increase in GFR after restoring blood flow, consistent with the ability of MSC to repair microvascular injury. Further clinical trials to characterize the durability and extent of these reparative pathways are warranted.

Funding: NIDDK Support

PO2102
Percutaneous Angioplasty of Renal Artery Stenosis Most Beneficial in Patients with AKI Requiring Acute Hemodialysis
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Background: Treatment of atherosclerotic renal artery stenosis (RAS) is still controversial and several studies have shown that percutaneous transluminal renal angioplasty with stenting (PTRAS) is not superior to medical treatment, and the procedure is commonly reserved for malignant hypertension, flash pulmonary edema or deterioration of kidney function. The benefit of endovascular intervention among acute kidney injury (AKI) patients requiring hemodialysis secondary to severe RAS has not been studied. We studied the effects of PTRAS in patients with atherosclerotic RAS, specifically those who presented with AKI indicated for hemodialysis.

Methods: 109 PTRAS were performed in 92 patients with RAS from 2003 to 2019 in a tertiary hospital. Eleven patients presented with AKI secondary to high grade RAS and underwent PTRAS after starting acute hemodialysis. Data collected included demographic parameters, medical background, indication for intervention, technical procedure parameters and complications and long term data including dialysis treatment and mortality. Patients were categorized as responders or non-responders based on improvement in kidney function and discontinuation of dialysis.

Results: A total of 109 procedures were performed in 92 patients with severe renal artery stenosis. Eleven patients (12%) underwent PTRAS for severe high grade stenosis causing renal hyperperfusion and hemodialysis-dependent AKI. After PTRAS, 8 of 11 patients (73%) improved kidney function and discontinued dialysis. The average time on dialysis was 17 days (range 3-35 days) to PTRAS and 22 days (range 3-42 days) to recovery of kidney function, which occurred 6.5 days (range 1-24 days) after PTRAS. Two of the 8 patients later required long term hemodialysis. Only two cases were reported with mild complications.

Conclusions: In patients with hemodialysis dependent AKI, PTRAS should be considered as a rescue treatment as kidney function may recover even after prolonged time on dialysis.

PO2103
Outcomes of Cardiac Surgery in CKD Stage 3 vs. Stage 4 and 5
Aimen Liaquat,1 Elias Basili,1 Jonathan J. Taliercio,1 Ali Meahi,1 Remy Daou,1 Susana Arrigain,2 Victoria Konig,1 Jesse D. Schold,1 Serge C. Harb,1 Per Wierup,1 Sevag Demirjian,1 Georges Nalhoul,1 Cleveland Clinic, Cleveland, OH; 2Universite Saint-Joseph, Beirut, Lebanon.

Background: Pre-operative kidney dysfunction is associated with worse outcomes following cardiac surgery. However, few studies have assessed the outcomes of advanced Stage 4 and 5 Chronic Kidney Disease (CKD) patients.

Methods: Using our Electronic CKD registry, we compared the outcomes of 988 patients with CKD stages 3 vs. 4 and 5 undergoing Coronary Artery Bypass Graft (CABG) and/or valvular cardiac surgery. We compared length of stay (LOS), ICU days, days on pressors, and days intubated as continuous values and as proportion above the 50th percentile using Kruskal-Wallis and Chi-square tests. We estimated Fine and Gray’s competing risks cumulative incidence function of days to post-operative AKI requiring
dialysis (AKI-D) with mortality as a competing risk during hospitalization. We also compared the proportion developing AKI-D with Chi-square test.

Results: Among 988 total patients with cardiac surgery, 115 (12%) had CKD stage 4/5 and 873 (88%) had CKD stage 3. Average age was 71.2 ± 9.5 and 590 (59.7%) were male. Patients with CKD 4/5 had a higher proportion of diabetes (60% vs. 37%). Compared to CKD 3 patients, CKD 4/5 patients required longer intubation (33% more than 2 days compared to 20%, P=0.003), more pressures (47% more than 3 days vs. 32%, P=0.003), longer ICU LOS (median of 5 days vs. 4 days, P=0.001), longer post-operative LOS (median 12 days vs. 9, P<0.001). 24 patients (20.9%) with CKD 4/5 developed post-operative AKI-D vs. 42 (4.8%) in the CKD 3 group (p < 0.001). The cumulative incidence of End-Stage-Kidney Disease (ESKD) with death as a competing risk at 15 days was 5% (95% CI 4, 8) in CKD 3 group vs. 24% (15, 33) in CKD 4/5 group (p < 0.001).

Conclusions: Advanced CKD stages 4/5 is associated with worse outcomes following cardiac surgery including prolonged ICU stay, intubation duration, days on pressors, development of AKI-D and ESKD.

### Post-operative Outcomes in CKD Stage 3 Vs. Stage 4 and 5

<table>
<thead>
<tr>
<th>Factor</th>
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<th>Stage 3 (N=115)</th>
<th>Stage 4 + 5 (N=15)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>SICU-d</td>
<td>0</td>
<td>4.0 (1.9-7.0)</td>
<td>7.0 (3.1-13.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary ESR (PSD)</td>
<td>30</td>
<td>2.64 (1.7-4.2)</td>
<td>2.64 (1.7-4.2)</td>
<td>0.65</td>
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<tr>
<td>Initiation (day-1, PSD)</td>
<td>59</td>
<td>33.9 (29.3)</td>
<td>36.5 (27.6)</td>
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<tr>
<td>Post AKI-D duration</td>
<td>0</td>
<td>24.6 (8.0)</td>
<td>42.6 (29.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In Hospital Death</td>
<td>0</td>
<td>12.5 (7.1)</td>
<td>12.5 (7.1)</td>
<td>0.73</td>
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<tr>
<td>Post LOS</td>
<td>0</td>
<td>11.8 (8.3)</td>
<td>12.8 (8.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Presented as Median [P25, P75] or N (column %).

p-values: b=Kruskal-Wallis test, c=Pearson’s chi-square test

### PO2104

**Cardiovascular Events and Mortality in Adults with Kidney Failure after Major Noncardiac Surgery**

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**Background:** People with kidney failure have a high incidence of major surgery. Despite this surgical exposure, there is a paucity of literature investigating postoperative CV events and death. We aimed to determine the risk of these outcomes based on surgery type.

**Methods:** This retrospective cohort study used administrative health data from Alberta, Canada from April 2005 to February 2017. Adults (≥18 years) with kidney failure (receipt of chronic dialysis or two outpatient eGFR measures <15 mL/min/1.73m²) admitted to hospital for a surgical procedure were included. Surgery type, categorized using ICD-10 codes from hospitalization data, was examined for association with acute myocardial infarction (AMI) and death within 30 days of surgery using multivariable logistic regression. We adjusted for demographics, comorbidities, preoperative laboratory measures, procedure urgency, and kidney disease specific variables.

**Results:** 3398 people with kidney failure had a major surgery (1905 hemodialysis; 903 peritoneal dialysis; 903 non-dialysis). Most of the cohort was male (61.0%), the median age was 61.5 years (IQR 50.0, 72.7), and over half of the procedures were urgent (56.9%). 198 people (5.8%) had an AMI or died within 30 days of major surgery. Kidney transplantation had the lowest frequency of the outcome and were the reference group. After adjustment, vascular, skin and soft tissue, intraabdominal, musculoskeletal, retroperitoneal, anorectal, and neurosurgical procedures had statistically higher odds of AMI or death compared to kidney transplantation (Figure 1).

**Conclusions:** Major non-transplant surgery in people with kidney failure is associated with a high risk of AMI and death, which has implications for the direction of future perioperative research in this population.

**Funding:** Government Support - Non-U.S.

### PO2105

**Race Differences in Cardiovascular Events After Percutaneous Coronary Intervention-Induced AKI**

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**Background:** AKI portends a higher risk of subsequent cardiovascular disease (CVD). Although racial differences in AKI incidence have been found, it is unclear if the risk of CVD events following AKI also varies by race.

**Methods:** We quantified racial differences in the association of AKI with CVD events 1-year following percutaneous coronary intervention (PCI), using the Duke Databank for Cardiovascular Disease (DDCD). The DDCD captured all patients who underwent PCI at Duke between January 1, 2003 and December 31, 2013 with a combination of structured (forms) and electronic health record (EHR) data. Patients were followed prospectively for CVD events. AKI was defined as a ≥1.5-fold increase in serum creatinine from outpatient reference value before PCI to the peak value within 7 days post-PCI or a 0.3 mg/dl increase from the reference value within 48 hours. The primary outcome was a CVD composite including all-cause death, myocardial infarction, stroke, and revascularization. Cox models from date of AKI to outcome were adjusted for demographics, baseline cardiac comorbidities, medication use (RAAS inhibitors and NSAIDS), indication and urgency of PCI, and BP at PCI and number of stents placed.

**Results:** Among 9432 patients (median age 63y; 33% women; 75% white; 20% black), 865 (9%) developed AKI. Among 8699 patients with follow-up, the cumulative incidence of CVD at 1-year was 21%. After adjustment, AKI vs no AKI was associated with 1.84 greater hazards for the composite CVD outcome [95% confidence interval (CI) 1.62 to 2.10]. Compared to whites, other race (HR 0.79, 95% CI 0.63 to 0.99) but not black race (HR 1.07, 95% CI 0.95 to 1.20) was associated with lower risk of subsequent CVD. There was no interaction between race and AKI (p-interaction 0.216). Results were similar with individual components of the outcome.

**Conclusions:** AKI vs. no AKI following PCI is associated with greater risk for CVD events, regardless of race. Efforts to offset long-term consequences of AKI should target all patients undergoing PCI.

**Funding:** Private Foundation Support
PO2106
Frailty Is Associated with Higher Risk of Cardiovascular Events and Mortality in Adults with CKD: Findings from the Chronic Renal Insufficiency Cohort (CRIC) Study
Mary Hanna,1 Ana C. Ricardo,1 Julia Brown,1 Eunice Carmona,1 Zahraa Hajiri,1 Natalie Meza,1 Jinsong Chen,1 Mildra R. Saunders,1 James P. Lash,1 1University of Illinois at Chicago College of Medicine, Chicago, IL; 2UChicago Medicine, Chicago, IL.

Background: Frailty is common in individuals with chronic kidney disease (CKD). In the general population, frailty is associated with increased risk of cardiovascular events and mortality, but this association has not been fully examined in the CKD population. The objective of this study is to evaluate frailty status as a predictor of cardiovascular events and death in individuals with CKD.

Methods: Among 2,537 CRIC Study participants, frailty status was assessed using five criteria (slow gait speed, muscle weakness, low physical activity, exhaustion, and unintentional weight loss). Frailty was defined as meeting ≥3 criteria, pre-frailty as meeting 2–3 criteria, and non-frailty as meeting zero criteria. Cox proportional hazards models were used to evaluate associations with atherosclerotic events, incident heart failure, and death.

Results: Baseline age was 57.5 years, 45.5% were female, mean eGFR was 46.9 mL/min/1.73m², and median urine protein was 0.13 mg/day. Frailty was present in 21% of the participants and 66% were pre-frail. During a median follow-up of 12.5 years, there were 349 atherosclerotic events, 398 incident heart failure events, and 398 deaths. In multivariable analyses, frail individuals had a higher risk of each outcome compared to non-frail individuals. Pre-frail individuals had a higher risk of atherosclerotic events compared to non-frail individuals (Table). Conclusion: In adults with CKD, frailty is associated with increased risk for cardiovascular events and death. Future studies are needed to evaluate the impact of interventions to reduce frailty in individuals with CKD.

Funding: NIDDK Support, Other NIH Support - NHLBI, Private Foundation Support

Association Between Frailty Status and Outcomes

PO2107
CKD Predicts Stroke Severity, Disability, and Early Recurrence in a Population-Based Cohort Study

Background: Chronic kidney disease (CKD) is associated with cerebrovascular disease and related mortality, and with under-utilisation of acute and preventative treatments, but any impact on initial event severity and recurrence risk is unclear. We aimed to determine whether CKD is associated with worse initial stroke severity and disability, and whether CKD is independently predictive of recurrent stroke and other vascular events.

Methods: In a population-based study of all TIA/stroke (Oxford Vascular Study), we studied initial stroke severity and disability using the National Institutes of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS), respectively, in relation to CKD in all patients presenting with TIA and stroke from April 1, 2002 to March 31, 2017. Associations between CKD and event severity, and between CKD and risk of recurrent vascular events (stroke, myocardial infarction, and sudden cardiac death) were examined using ordinal and Cox regression models, respectively, adjusted for age, sex, and known vascular risk factors, and stratified by TOAST subtype.

Results: Among 3178 patients with TIA (n=167), ischemic stroke (n=1802), and intracerebral haemorrhage (n=209), 1267 (40%) had CKD. CKD was independently associated with greater risk of ischemic stroke compared to TIA (adjusted OR=1.31, 95%CI=1.11-1.56, p=0.002) and with greater initial NIHSS (adjusted OR=1.28, 1.04-1.46; p=0.018), driven mostly by those with an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m² (adjusted OR=2.59, 1.44-4.66; p=0.001) for ischemic stroke; adjusted OR=4.06, 2.04-8.06; p=0.001 for initial NIHSS). Among patients with ischemic stroke, CKD was also associated with higher one-month mRS scores (adjusted OR=1.40, 1.13-1.74; p=0.002), driven by those with an eGFR < 30 mL/min/1.73m² (Adjusted OR=6.51, 3.04-13.97; p=0.001). Risk of early (< 90 days) recurrent stroke was increased with CKD (adjusted HR=1.60, 1.15-2.21; p=0.005) as was the risk of longer-term (0-15 years) composite vascular outcomes (adjusted HR=1.14, 1.05-1.40; p=0.01).

Conclusions: The consistent independent impact of CKD on initial event severity, early disability and recurrence risk suggests that there may be processes intrinsic to CKD leading to uniformly worse outcomes. Further research should determine whether there are CKD-specific treatments that may improve stroke outcomes.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO2108
Control of Blood Pressure in Elderly Patients with Heart Failure and Risk of Mortality
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Background: Blood pressure (BP) targets in elderly patients with heart failure (HF) are unclear and guidelines are based on expert consensus and extrapolation from populations without HF. Thus, our population-based prospective cohort study assessed if BP control <140/90 mmHg is associated with a decreased risk of mortality in elderly HF patients.

Methods: We included participants of the Berlin Initiative Study, all ≥70 yrs, with HF and treated with antihypertensive drugs at baseline (2009-2011). Demographics, lifestyle factors, medication, and comorbidities were obtained in face-to-face interviews and linked with administrative healthcare data. BP status was defined as normalized BP (systolic BP <140 and diastolic BP <90 mmHg) or non-normalized BP (systolic BP ≥140 or diastolic BP ≥90 mmHg) and updated every 2 yrs, so that each patient could contribute person-time to both exposure categories during follow-up. Time-dependent Cox proportional hazards models estimated adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of cardiovascular death and all-cause mortality associated with normalized BP compared with non-normalized BP in HF patients. Analyses were repeated in non-HF patients.

Results: There were 544 HF patients treated with antihypertensive drugs (mean age 82.8 yrs; 45.4% female). During a median follow-up of 7.5 yrs and compared with non-normalized BP, a decreased risk of cardiovascular death (HR, 1.79; 95% CI, 1.23-2.61) and all-cause mortality (HR, 1.48; 95% CI, 1.15-1.80) was observed. No increased risks of cardiovascular death (HR, 1.23; 95% CI, 0.87-1.74) or all-cause mortality (HR, 1.19; CI 0.95-1.49) associated with normalized BP were observed among 1079 non-HF patients.

Conclusions: BP <140/90 mmHg was not associated with a decreased risk of mortality in elderly HF patients. The increased risk requires further confirmation.

Funding: Private Foundation Support

Risk of cardiovascular death and all-cause mortality associated with normalized BP in older adults with HF

PO2109
Renal Outcomes of Sacubitril-Valsartan vs. ACE Inhibitors and Angiotensin Receptor Blockers in Heart Failure: A Systematic Review and Meta-Analysis

Background: Chronic kidney disease is an important comorbidity in heart failure patients through elevation in blood pressure and activation of the RAAS. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers have been linked to beneficial effects on clinical outcomes of HF patients with CKD; however, they have been found to increase the risks for renal impairment. Clinical trials on the angiotensin receptor neprilysin inhibitor, sacubitril-valsartan, have found that it causes kidney dysfunction less frequently. This study determined the effect of sacubitril-valsartan on renal outcomes among HF patients compared to ACEi and ARBs alone.

Methods: A comprehensive literature search was done through electronic databases and readings until November 2019. This analysis incorporated randomized controlled trials in which indicators of renal function of patients on sacubitril-valsartan were compared to those of patients on reference drugs–estimated glomerular filtration rate, serum creatinine, and increase in serum potassium levels.

Results: Four RCTs were included with a total of 14,377 subjects for analysis. Two of the studies used an ACEi (enalapril), while the remaining 2 used an ARB (valsartan). Compared with ACEi and ARBs, there was a nonsignificant difference between decline in glomerular filtration (RR 0.75, 95% CI 0.55 to 1.02; participants = 14737; studies = 4; I2= 53%), but a significant difference between rise in serum potassium level (RR 0.90, 95% CI 0.84 to 0.96; participants = 14334; studies = 4; I2= 66%), and elevation of serum creatinine level (RR 0.86, 95% CI 0.78 to 0.95; participants = 1470; studies = 3; I2= 72%).

Conclusions: In HF patients, sacubitril-valsartan shows possible protective effects of risk for renal impairment, and definite reduction of risks for both increasing serum creatinine and hyperkalemia, as compared to ACEi and ARBs.
PO2110
The Accuracy of Current Ankle-Brachial Index and Toe-Brachial Index Diagnostic Criteria for Peripheral Artery Disease Among Patients with CKD

Jing Chen,1,2 Hua He,2 Charlton C. Starcke,2 Yajun Guo,3 Siyi Geng,2 Chunjian Chen,2 Erin Mahone,2 Jodie R. Laurent,2 Christina L. Wiggins,2 Praktiti Mehta,4 Paige R. Pielert,4 Vecchi Batuman,4 L. Lee Hamm,4 Jiang He,4 1 Tulane University School of Medicine, New Orleans, LA; 2 Tulane School of Public Health and Tropical Medicine, New Orleans, LA.

Background: Ankle-brachial index (ABI) less than or equal to 0.9 and toe-brachial index (TBI) less than or equal to 0.7 are used as diagnostic criteria for peripheral artery disease (PAD). The sensitivity and specificity of the ABI and TBI diagnostic criteria have not been evaluated in patients with chronic kidney disease (CKD).

Methods: We performed ABI, TBI, and doppler ultrasound among 100 patients with CKD using standard methods. Color doppler ultrasound, which has a high level of diagnostic performance with a sensitivity of 93% and a specificity of 95% for diagnosing PAD, was used as the reference standard. Doppler ultrasound diagnostic criteria were determined by multiple ultrasound features including reduction in luminal diameter, monophasic waveform, peak systolic velocity ratio (PSV ratio) >2.0, and presence of special broadcasting. Stenosis greater than or equal to 50% based on doppler ultrasound imaging was used to diagnose PAD. Sensitivity, specificity, positive predictive value, and negative predictive value were estimated. The areas under the curve (AUCs) for ABI and TBI were calculated.

Results: Participants with PAD were older, and more likely to be male and have a history of cardiovascular disease. The average estimated glomerular filtration rate and proteinuria were similar among participants with and without PAD. The sensitivity, specificity, positive predictive value, and negative predictive value were 15.6%, 88.3%, 20.8%, and 92.5% for ABI, and 16.3%, 89.4%, 24.7%, and 95.9% for TBI, respectively.

Conclusions: These data indicate that current ABI and TBI diagnostic criteria have suboptimal accuracy in diagnosing PAD in CKD. New ABI and TBI diagnostic criteria with better sensitivity and specificity need to be developed.

Funding: NIDDK Support, Other NIH Support - P20 GM109036

PO2111
Efficacy and Safety of Roxadustat in Patients with Non-Dialysis-Dependent CKD, Anemia, and Heart Failure

Daniel W. Coyne,1 Steven Fishbain,2 Pablo E. Pergola,3 Lynda Szczecizh,4 Tyson T. Lee,5 Dustin J. Little,5 Kin-Hung P. Yu,4 1 Washington University School of Medicine in Saint Louis, Washington University in Saint Louis School of Medicine, Saint Louis, MO; 2 Northwell Health, Great Neck, NY; 3 Renal Associates PA, San Antonio, TX; 4 FibroGen Inc, San Francisco, CA; 5 AstraZeneca, Gaithersburg, MD.

Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Patients with heart failure (HF) represent an important clinical subgroup of patients with CKD.

Methods: Pooled data from three pivotal, phase 3, randomized, open-label, epoetin alfa-controlled studies of roxadustat for the treatment of anemia in patients with dialysis-dependent (DD) CKD were assessed in the subgroup of patients with a history of NYHA Class I or II HF at baseline. Endpoints were: mean change from baseline (CFB) in hemoglobin (Hb) averaged over weeks 28–52 regardless of rescue therapy, time to first blood/RBC transfusion during the treatment period, and mean monthly IV iron use during weeks 28–52. Safety and tolerability were assessed by reported treatment-emergent adverse events (TEAEs).

Results: In the DD-CKD study population, 25% (991/3980) of patients had HF (roxadustat=499; epoetin alfa=492). Baseline characteristics were generally similar. Mean (SD) Hb levels (g/dL) at baseline were 9.59 (1.30) in the roxadustat group and 9.65 (1.29) in the epoetin alfa group. Patients achieved significantly larger mean Hb increases (SEM) CFB in Hb levels (g/dL) with roxadustat vs. epoetin alfa (1.24 [0.04] vs. 0.94 [0.04]), corresponding to a LSM difference of 0.29 (95% CI: 0.18, 0.40) (p<0.0001). The hazard ratio for first blood/RBC transfusion during the treatment period in the roxadustat and epoetin alfa groups was 0.76 (95% CI: 0.54, 1.08) (p=0.1274). Mean (SD) monthly IV iron (mg) use was lower in roxadustat- vs. epoetin alfa-treated patients: 55.8 (288.8) vs. 68.6 (142.7) (p<0.0001), TEAE rates were comparable between treatment groups and similar to those in the overall DD-CKD study population.

Conclusions: Roxadustat was efficacious vs. epoetin alfa for increasing Hb levels and reducing mean monthly IV iron use in DD-CKD patients with HF. The safety and tolerability profile was similar to the overall population and consistent with that observed in this patient subgroup.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

PO2112
Safety and Efficacy of Roxadustat in Patients with Dialysis-Dependent CKD, Anemia, and Heart Failure

Poster

Thursday

H. Hamm,1 Jiang He,1,2 Vecihi Saikali,4 Dustin Little,5 Kin-Hung P. Yu,4 1 Renal Research, Gosford, NSW, Australia; 2 Northwell Health, Great Neck, NY; 3 Renal Associates PA, San Antonio, TX; 4 FibroGen Inc, San Francisco, CA; 5 AstraZeneca, Gaithersburg, MD.

Methods: Pooled data from three pivotal, phase 3, randomized, open-label, epoetin alfa-controlled studies of roxadustat for the treatment of anemia in patients with dialysis-dependent (DD) CKD were assessed in the subgroup of patients with a history of NYHA Class I or II HF at baseline. Endpoints were: mean change from baseline (CFB) in hemoglobin (Hb) averaged over weeks 28–52 regardless of rescue therapy, time to first blood/RBC transfusion during the treatment period, and mean monthly IV iron use during weeks 28–52. Safety and tolerability were assessed by reported treatment-emergent adverse events (TEAEs).

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Conclusions: Roxadustat was efficacious vs. epoetin alfa for increasing Hb levels and reducing mean monthly IV iron use in DD-CKD patients with HF. The safety and tolerability profile was similar to the overall population and consistent with that observed in this patient subgroup.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

PO2113
Roxadustat Reduces Low-Density Lipoprotein Cholesterol in Patients with Anemia of CKD

Poster

Thursday

Jimenez,1 Mohamed A. El-Shawalwy,1 Carol A. Pollock,2 Hamm,31 Steven Fishbain,2 Pablo E. Pergola,3 Willis Maksym,1 Kin-Hung P. Yu,1 1 Renal Research, Gosford, NSW, Australia; 2 The University of Sydney, Sydney, NSW, Australia; 3 FibroGen Inc, San Francisco, CA; 4 AstraZeneca, Warsaw, Poland; 5 University of Southern California Keck School of Medicine, Los Angeles, CA.

Background: Roxadustat is an oral hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor with positive safety and efficacy results in phase 3 studies in patients with anemia in CKD. The HIF pathway affects cholesterol metabolism; at high altitude, total and low-density lipoprotein cholesterol (LDL-C) decrease in healthy individuals. Roxadustat reduced LDL-C in phase 2 studies. We evaluated the effect of roxadustat on LDL-C in patients with anemia in non-dialysis-dependent (NDD) and dialysis-dependent (DD) CKD.

Methods: Data were pooled from three pivotal phase 3 studies in patients with NDD-CKD and three pivotal phase 3 studies in patients with DD-CKD, including the incident dialysis (ID; on dialysis <4 mo at randomization) population. Mean changes from baseline (CFB) in LDL-C (regardless of statin use) averaged over weeks 12–28 were analyzed using a mixed model of repeated measures and reported least-squares mean (LSM) treatment differences.

Results: In patients with NDD-CKD, there was a 17.2% reduction in LDL-C averaged over Weeks 12–28 in the roxadustat group (n=1650) compared with the placebo group (n=1430). The LSM treatment difference was statistically significant (p<0.0001). In the DD-CKD population, there was a 15.8% reduction in the roxadustat group (n=1650) and a 1.7% reduction in the epoetin alfa group (n=1741). The LSM treatment difference was statistically significant (p<0.0001). In patients with DD-CKD, there was a 21.5% reduction in the roxadustat group (n=680) and a 4.6% reduction in the epoetin alfa group (n=691). The LSM treatment difference was statistically significant (p<0.0001).

Keywords: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

468
Conclusions: Treatment with roxadustat vs. placebo or epoetin alfa lowered LDL-C in patients with NDD-CKD and DD-CKD, respectively.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

Table: LDL-C Results in NDD-, DD- and ID-DD-CKD Patients (FAS)

<table>
<thead>
<tr>
<th>Group</th>
<th>LDL-C (mg/dL)</th>
<th>NDD-NDD</th>
<th>DD-CKD</th>
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<tr>
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<td></td>
<td>112.1±22</td>
<td>113.9±20</td>
<td>112.3±21</td>
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<td>Change from baseline</td>
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PO2114
Roxadustat vs. Placebo or Epoetin Alfa Has No Clinically Meaningful Effect on Blood Pressure in Patients with Anemia of CKD
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Background: Hypertension (HTN) is a leading cause of chronic kidney disease (CKD) and often worsens as CKD progresses. Erythropoiesis-stimulating agents have been associated with an increase in blood pressure (BP) and other cardiovascular risks. Roxadustat is an oral hypoxia–inducible factor prolyl hydroxylase inhibitor that stimulates the production of erythropoietin and is approved for use in CKD patients with anemia. We evaluated the effect of roxadustat on BP in dialysis-dependent (DD) and non-dialysis-dependent (NDD) patients with anemia of CKD.

Methods: Pooled data from three, phase 3, randomized, placebo-controlled trials in NDD patients (n=4270), and three pivotal phase 3 randomized, active-controlled trials in DD patients (n=1526) and NDD patients (data censored after dialysis discontinuation; n=2354) were assessed. All DD patients and NDD patients (data censored after dialysis discontinuation) were included. Mean change from baseline (CBF) in mean arterial pressure (MAP) was assessed across Weeks 20–28 (NDD-NDD, SDD) and over weeks 8–12 (ID-DD); time to first exacerbation of hypertension (SBP ≥20 mmHg or DBP ≥10 mmHg and an increase from baseline ≥20 mmHg [SBP] or ≥15 mmHg [DBP]); and adjudicated hypertensive emergency were analyzed.

Results: In NDD-NDD, the least squares mean (LSM) difference between roxadustat and placebo in MAP (mmHg) was 0.67 (0.30) [95% CI: −0.09, 1.25]. Values for ID-DD and SDD patients were −0.35 (0.66) [95% CI: −1.65, 0.95] and −0.06 (0.42) [95% CI: −0.88, 0.76]. Hazard ratios (95% CI) for HTN exacerbation in NDD-NDD, ID-DD, and DD patients were 1.12 (0.95, 1.32), 1.02 (0.84, 1.25), and 1.06 (0.93, 1.21). Follow-up adjusted incidence rates [events/100 patient-exposure year] of adjudicated hypertensive emergency were 1.1 and 1.1 in roxadustat- and placebo-treated NDD-NDD, 2.2 and 2.5 in the overall roxadustat- and epoetin-alfa treated DD, and 1.7 and 1.7 in the subgroup of ID-DD.

Conclusions: Pooled analyses of phase 3 data across a continuum of patients with CKD and anemia showed that roxadustat did not have any clinically meaningful effect on BP, HTN exacerbation, or hypertensive emergency vs. placebo in NDD-NDD patients and epoetin alfa in DD-CKD patients.

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.

PO2115
Rivaroxaban Reduces Major Cardiovascular and Limb Events in Patients with CKD and Peripheral Artery Disease with Recent Lower Extremity Revascularization: Insights from VOYAGER PAD
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Background: In the VOYAGER PAD trial, rivaroxaban reduced cardiovascular (CV) and limb ischemic events (HR 0.85 vs placebo, 95% CI 0.76-0.96; p=0.009) in peripheral arterial disease (PAD) patients following lower extremity revascularization (LER). This analysis examines the prespecified subgroup of VOYAGER PAD patients with CKD.

Methods: VOYAGER PAD (NCT02504216) randomized 6564 PAD patients following LER to rivaroxaban 2.5 mg twice daily or placebo on a background of aspirin 100 mg daily. The primary endpoint was a composite of acute limb ischemia, major amputation for vascular cause, myocardial infarction, ischemic stroke or CV death. Intention-to-treat analyses utilized Kaplan Meier estimates and Cox proportional-hazards models.

Results: Mean baseline eGFR was 75±23 ml/min/1.73m² with 79, 20, 1 and <1% of patients with CKD stage ≥2, 3, 4 and 5 respectively. During 28-month median follow-up, rates of major CV and limb events were higher among patients with more severe CKD (placebo group event rate: 7.4/100 patient-years for eGFR ≥60, 10.0 for eGFR 30-60 and 9.8 for eGFR <30). Rivaroxaban reduced primary endpoint events with no heterogeneity by eGFR above or below 60 (mostly CKD stage 3) (Figure). Acute limb ischemia and major amputation were significantly reduced among patients with eGFR<60 (HR 0.77, 95% CI 0.63, 0.94) and <60 (HR 0.55, 95% CI 0.36, 0.86). Major bleeding was infrequent with no heterogeneity by CKD category.

Conclusions: Rivaroxaban reduced CV and limb events in patients with CKD, PAD following LER, a particularly high-risk population.

Funding: Commercial Support - Bayer

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Methods: We analyzed parameters related to volume status in these Phase 3 trials. Results: In these studies, 97% and 31% of pts, had HTN and CHF, respectively and 193 pts were treated with veverimer or placebo for up to 52 weeks. Treatment with veverimer (v placebo) had no effect on weight, BP, urine Na/creatinine ratio, volume-related adverse events, or increased use of diuretics or antihypertensives (Table). Conclusions: Veverimer, a novel non-absorbed HCl binder, effectively treats metabolic acidosis in CKD without adversely affecting BP or volume status.

Funding: Commercial Support - Tricida, Inc.

Data presented are mean (SD) or n (%)

PO2117

Optimal Medical Therapy Attainment by Dialysis Status in the ISCHEMIA-CKD Trial
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Background: The efficacy of an aggressive multiple risk factor intervention approach – optimal medical therapy (OMT) – to reduce major adverse cardiovascular events in patients with CKD has not been tested. Objective: to examine OMT goal attainment in patients with CKD on dialysis (CKD-D) and non-dialysis CKD (CKD-ND) in the ISCHEMIA-CKD trial.

Methods: OMT was recommended to all participants in ISCHEMIA-CKD. Longitudinal trajectories of individual OMT components (smoking cessation, systolic blood pressure (SBP) <140 mmHg, low density lipoprotein (LDL) cholesterol <70 mg/dL, high-intensity statin use, and aspirin use) were modeled over study follow-up. Covariate-adjusted percentage point difference in each OMT goal achieved at 24 months between CKD-D and CKD-ND patients (95% credible interval (CrI)) was estimated.

Results: There were 415 CKD-D and 362 CKD-ND patients at baseline. CKD-D were younger (61 v 67 yrs, p<0.001) and less often diabetic (53% v 62%, p=0.023). CKD-D patients were 7.9 % (0.7%, 14.8%) more likely than CKD-ND to attain the SBP goal during follow up. There was a steady and similar increase in proportional attainment of OMT during follow up.

Conclusions: OMT improved over time in advanced CKD-ND and CKD-D. CKD-D achieved the SBP goal more than CKD-ND, yet CKD-D were less likely to be treated with high-intensity statin. Future studies should explore systemic and patient-related barriers to attainment of OMT in this high-risk cohort.

Background: Patients with end-stage kidney disease (ESKD) are often sedentary and decreased functional capacity associates with mortality. The relationship between physical function and cardiovascular disease (CVD) has not been fully explored. Understanding the relationships between prognostically relevant measures of CVD and physical function and capacity may offer insight into whether exercise interventions could target specific elements of CVD.

Methods: 130 patients on haemodialysis underwent cardiovascular phenotyping with cardiac MRI (left ventricular (LV) structure and function, pulse wave velocity and native T1 mapping) and cardiac biomarker assessment. Participants completed the incremental shuttle walk test (ISWT) and sit-to-stand 60 (STS60) as field-tests of physical function and capacity. Separate linear regression analyses identified CV determinants of physical function measures. Multivariate models were adjusted for age, gender, BMI and diabetes.

Results: Mean age was 57±15 years, 73% were male and median dialysis vintage was 1.3 years (0.5, 3.4). In multivariate models, NT pro-BNP and global native T1 were independent determinants of ISWT and STS60 performance. LV ejection fraction was also an independent determinant of ISWT distance. However, age, gender and diabetes had the strongest relationship with physical function. Cardiovascular markers that were significant in multivariate models are shown in Table 1.

Conclusions: Markers of CV health could be targeted in exercise interventions to improve outcomes in patients with ESKD. NT pro-BNP, global native T1 and LV ejection fraction were independent CV determinants of physical function. The influence of age and diabetes on performance had the strongest relationship. Improving strategies for prevention and management of diabetes may ameliorate deconditioning in these patients.

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PO2119
The Relationship of Cardiovascular Morbidity with Death and End-Stage Kidney Failure in Patients with Diabetes and CKD Receiving Specialist Renal Care
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Background: Patients with diabetes (DM) and CKD have worse cardiovascular, renal and mortality outcomes than those with neither and either condition alone. However, relationships between these 3 outcomes remain unclear, especially in patients receiving specialist renal care. Aims: To determine the relationships of major adverse cardiovascular event (MACE), end stage kidney failure (ESKF) and death using competing risk analysis.

Methods: CKD,QLD is a large Australian registry of patients with CKD not on RRT receiving specialist renal care. Patients with DM enrolled between 1/1/2011 and 31/12/2016 inclusive were studied. Follow-up was censored by death, ESKF, MACE post enrolment, movement of patient interstate/overseas, loss to follow-up or censor date of 31/12/2017, whichever occurred first. Competing risk analysis was performed with MACE, ESKF and death in turn as the primary outcome whilst the other 2 were competing risks. Covariates examined were age, gender, ethnicity, incident status, access to services, biopsy, smoking, diabetes treatment, HBa1c, MACE prior to enrolment, eGFR, proteinuria, Hb, RAAS blocker and lipid lowering therapy.

Results: 2255 patients underwent 6615 patient-years follow-up (pyfu), mean 2.8y. The first event was MACE in 571 patients (24.2%), ESKF in 299 patients (12.6%) and death in 268 patients (11.3%), giving respective event rates of 86, 45 and 41 per 1000 pyfu. 1137 patients (48.3%) experienced no event. Table 1 summarises the results of the best fit multivariable model with each primary outcomes. p < 0.05 was deemed significant.

Table 1: summary of competing risk analysis with the different primary outcomes.

Comparison of the Combined Prognostic Significance of Red Blood Cell Distribution Width and Vascular Calcification in Patients with ESKD
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Background: Red blood cell distribution width (RDW) is a simple parameter that reflects the degree of red blood cell volume variability. Recent evidence has shown that increased RDW is associated with adverse clinical outcomes in end-stage kidney disease (ESKD) patients. Vascular calcification (VC) is another major independent risk factor for mortality among ESKD patients. This study investigated the combined prognostic effect of RDW and VC in ESKD patients starting dialysis.

Methods: We conducted a retrospective observational cohort study of 582 ESKD patients treated at a single center from January 2006 to July 2017. VC was assessed by the aortic calcification index (ACI) using abdominal computed tomography. Patients were divided into four groups based on the median ACI (17.12) and serum RDW value (14.3) as low ACI-low RDW, low ACI-high RDW, high ACI-low RDW, or high ACI-high RDW. The association between RDW and VC on the composite of cardiovascular events (CVEs) and death was investigated.

Results: During a median follow-up of 3.1 years (range, 1.5–5.5 years), 165 (28.3%) CVEs and 126 deaths (21.4%) occurred. The Cox regression analyses showed that the patients with low ACI-high RDW (adjusted hazard ratio, 1.93; 95% confidence interval, 1.185-3.157; P = 0.008) and high ACI-low RDW (adjusted hazard ratio, 1.92; 95% confidence interval, 1.171-3.152; P = 0.001) had a greater risk of the composite endpoint than patients with low ACI-low RDW. Patients with high ACI-high RDW had the greatest risk (adjusted hazard ratio, 2.367; 95% confidence interval, 1.465-3.824; P < 0.001). The interaction between ACI and RDW on CVEs and mortality was statistically significant (P = 0.023).

Conclusions: In ESKD patients starting dialysis, the combined effect of VC and high RDW was associated with a higher risk of CVEs and death. Also, high serum RDW amplified the risk associated with VC.

PO2121
Attention to the “Liddle” Details
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Introduction: Laboratory data provide clues to the etiology of resistant hypertension. We present one such case where in a presumptive diagnosis of Liddle’s syndrome was made, and appropriate therapy initiated. Yet the hypertension failed to be controlled despite multiple antihypertensive medications.

Case Description: A 26-year-old African American male was evaluated 8 years ago for a history of resistant hypertension. He was compliant with five blood pressure medications yet his systolic blood pressures were greater than 180mmHg. He denied smoking or consuming licorice products. No family history of early deaths, hypertension, or strokes. He reported having early onset of puberty at around age 12, being taller than his peers and now being short as an adult. He was a thin individual with no abdominal striae. Investigations revealed hypokalemia with mild metabolic alkalosis along with low renin and aldosterone. His kidney ultrasound was normal as were his renal functions and free metanephrines. 24-hour urine cortisol was not elevated. A presumptive diagnosis of Liddle’s syndrome was made and amiloride was added to his anti-hypertensive regimen, with little effect on BP control. Over the subsequent years, he was admitted repeatedly for hypertensive emergencies. This led to changes in his regimen along with a trial of Aldactone with no benefit. During one such episode, he complained of retrosternal pain. A CT was done to rule out a dissecting aneurysm, but it revealed a 5cm adrenal mass. Work up revealed high deoxycorticosterone, 11 deoxycortisol, dehydroepiandrosterone sulphate and testosterone which was suggestive of 11-hydroxylase deficiency causing congenital adrenal hyperplasia (CAH). He was started on dexamethasone 2 mg daily and his blood pressure control began showing improvement.

Discussion: CAH due to 11-hydroxylase deficiency is commonly seen in South Asia. It presents with features suggestive of mineralocorticoid excess. The differential diagnoses are Liddle’s syndrome, Chrousos syndrome, syndrome of apparent mineralocorticoid excess and Geller syndrome. This patient was wrongly diagnosed which led to repeated hospitalizations with inadequate therapy. Liddle’s syndrome responds well to amiloride without the need for additional medications. The fact that he was on multiple medications in addition to amiloride should be a clue to the misdiagnosis.

PO2122
A Case of Disappearing Hypertension: Difficulties of Managing Hypertension in a Breast Cancer Survivor
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Introduction: Treating hypertension in breast cancer survivors often hold unique difficulties. These patients may have undergone sentinel lymph node biopsy (SNB) or axillary lymph node dissection (ALND), and are often advised to avoid blood pressure measurement with affected arm. Here we present a case of young female after mastectomy SNB and ALND, who was diagnosed with essential hypertension after hypertension who presents for hypertension management.

Case Description: 32-year-old female with past medical history of breast cancer status post bilateral mastectomy and sentinel node biopsy (SNB) and axillary lymph node dissection (ALND). She developed hypertension after mastectomy due to inaccurate measurements from avoiding the use of sphygmomanometer cuff on her upper extremities.

Table 1: summary of competing risk analysis with the different primary outcomes.
using her lower extremities since her mastectomy. Blood pressure measured with her right upper extremity was 116/68.

Discussion: Often patient after mastectomy with SNB or ALND avoids taking blood pressure on affected limb regardless of lymphedema in order to prevent lymphedema. Despite this, the evidence for this is sparse with most recent studies reporting that blood pressure measurement in ipsilateral affected arm as not being risk factor for lymphedema.

PO2123

A Curious Case of Hypertensive Emergency and AKI

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Introduction: We report a case of a 75-year-old female with history of a prior right renal artery stent (coronary bare metal stent), stage IV chronic kidney disease (baseline serum creatinine (Scr) 2.1-2.3 mg/dL (eGFR 20-23 mL/min/1.73 m2)), diastolic heart failure, and hypertension who presented with hypertensive emergency (blood pressure (BP) 220/80 mmHg) and flash pulmonary edema.

Case Description: During her hospital stay, despite treatment with up to nine anti-hypertensive medications, her systolic BP remained 180-200 mmHg. Her Scr also increased to 3.92. Work-up showed normal kidney sizes and urine protein/creatinine ratio 1.26 g/g. Renal artery duplex revealed right renal artery peak systolic velocity 267 cm/sec, renal-to-aortic ratio 2.68, and resistive index 0.7-0.9, suggestive of right renal artery re-stenosis and some intrinsic damage. Due to progressive volume overload and worsening respiratory status, she required temporary hemodialysis. As her volume status worsened, she required temporary hemodialysis.

Deformed stent (arrow) with severe in-stent restenosis

Conclusions: In this case, baseline urinary sodium was lower than expected and baseline BP was well-controlled. Reducing dietary salt by 2g/day did not have a significant effect on office blood pressure readings.

PO2124

Effect of Dietary Salt Reduction on Blood Pressure in Kidney Transplant Patients: A Randomised Controlled Trial

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Background: Cardiovascular morbidity and mortality are increased in kidney transplant patients. High blood pressure (BP) contributes significantly to this risk and is associated with shortened allograft survival. Dietary salt reduction is widely recommended as a strategy to lower BP in the general population and in chronic kidney disease. Due to a lack of evidence there is currently no consensus on dietary salt restriction in kidney transplant patients.

Methods: Sixty stable kidney transplant patients, a 6-months post-transplantation, with BP ≥120/80 mmHg, and sodium intake 80 mmol/24hrs, were randomised in this parallel-designed study to receive either a regular-salt diet (target 150 mmol/24hr) or a low-salt diet (target 80 mmol/24hr) for 8-weeks. The primary outcome measure was systolic and diastolic BP. Secondary outcome measures included 24-hour ambulatory BP (ABP) and proteinuria. Dietary salt intake was assessed by 48-hour urinary sodium excretion.

Results: At baseline, patients (72% men) were 56±11 years with estimated glomerular filtration rate (eGFR) 53±18 mL/min/1.73m². Mean urinary sodium was 128±42 mmol/24hr, mean systolic BP was 132±12 mmHg, and mean diastolic BP was 77±10 mmHg. At the end of the intervention period sodium excretion was significantly lower in the low-salt group compared with the regular-salt group (96±37 vs. 152±51 mmol/24hr; adjusted mean difference, -36 [95% CI, -59 to -14] mmol/24hr; P=0.002). We found no difference in systolic BP (adjusted mean difference, -2 [95% CI, -12 to 9] mmHg; P=0.750), diastolic BP (adjusted mean difference, 0 [95% CI, -4 to 4] mmHg; P=0.887), 24-hour systolic ABP (adjusted mean difference, -3 [95% CI, -9 to 2] mmHg; P=0.213) or 24-hour diastolic ABP (adjusted mean difference, -2 [95% CI, -5 to 1] mmHg; P=0.267). There was no significant effect on proteinuria, eGFR, serum osmolality, uric acid, renin concentration, or aldosterone.

Conclusions: In this study baseline urinary sodium was lower than expected but baseline BP was well-controlled. Reducing dietary salt by 2g/day did not have a significant effect on office blood pressure readings.

PO2125

Left Atrial Reservoir Strain Is an Independent Predictor of End-Stage Renal Impairment in Patients with CKD

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Background: Left atrial (LA) enlargement is common in patients with chronic kidney disease (CKD) and is a predictor of adverse cardiovascular events. Our study sought to evaluate the value of LA reservoir strain (LAS), a novel echocardiographic measure of LA function, as a prognostic marker of adverse renal outcomes.

Methods: Patients with stable Stage 3 and 4 CKD without prior cardiac history were randomly recruited and underwent transhauric and stress echocardiography. Patients with normal left ventricular (LV) function, without significant valvular disease and without ischaemia on stress testing were included and followed for up to 5 years for development of end stage renal disease (ESRD) and/or doubling of serum creatinine.

Results: 280 patients (65±12 years, 63% male) were recruited and followed for a mean period of 3.9±2.7 years. 56 patients developed the composite endpoint. On log rank tests, impaired LAs (Figure 1), older age, lower eGFR, anemia, diabetes mellitus, greater urinary albumin/creatinine, greater number of antihypertensive agents, higher indexed LV mass and larger LA volumes were significant predictors of the composite outcome (p=0.01 for all). On Multi-variable Cox proportional hazards regression analysis, impaired LAs in addition to eGFR, number of antihypertensive agents and urinary albumin/creatinine (p=0.01 for all) were independent predictors of ESRD and/or doubling of serum creatinine. Impaired LAs was associated with a 2.5-fold higher risk of the composite outcome.

Conclusions: LAs is an independent predictor for development of ESRD and/or doubling of serum creatinine and thus has the potential to be a ‘biomarker’ for identification of high-risk patients, enabling early initiation of therapy.
**PO2126**

**Weight Gain Is a Risk Factor for the Progression of Coronary Artery Calcification in CKD: From the KNOW-CKD Study**

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**Background:** In chronic kidney disease (CKD), patients with high body mass index or weight gain have better survival. However, their cardiovascular risk is uncertain. The aim of this study was to investigate the relationship between weight changes and the progression of coronary artery calcification (CAC) in CKD.

**Methods:** This study analyzed 839 participants (Mean age 52.5±12.0, Males 41.12%) from the KNOW-CKD cohort. Changes in weight between baseline and 4 year follow-up period were categorized in tertiles: first tertile (T1) (-31.3kg to -1.1kg), second tertile (T2) (-1kg to 0.9kg) and third tertile (T3) (1kg to 30kg). The coronary artery calcium score (CACS) was assessed using cardiac computed tomography at baseline and 4 years after enrollment. The CAC progression was defined as increase of CACS after 4 years.

**Results:** The study participants’ baseline median CACS was 0.0 (median) [0 [25th quartile]-34.5[75th quartile]] and 387 (46.13%) participants had baseline CACS above 0. After 4 years, numbers of patients in each tertile was 247 (29.4%) in T1, 258 (30.8%) in T2 and 334 (39.8%) in T3. Median difference in CACS between baseline and follow-up was 2 [0.49.3] in T1, 0 [0.47.2] in T2 and 6.4 [0.64.77] in T3. (p=0.088) Multivariate adjusted odds ratios (OR) [95% confidence interval] (95% CI) for CAC progression in T1 was 2 [0.69.3] in T1, 0 [0.47.2] in T2 and 6.4 [0.64.77] in T3. (p=0.088) Multivariate adjusted odds ratios (OR) [95% confidence interval] (95% CI) for CAC progression in T1 and T3 group compared to T2 group were 1.21 [0.79-1.85] and 1.80 [1.20-2.70].

**Conclusions:** Third tertile group, which gained between 1 to 30kg after 4 years, was significantly and independently associated with CAC progression compared to weight stable second tertile group in Korean predialysis CKD patients. These results suggest that preventing excessive weight gain might help prevent cardiovascular complications in CKD.

**PO2127**

**The Circadian Clock Provides Beneficial Effects Against the Endothelial Dysfunction to Promote Atherogenesis by Regulating Heme Oxygenase 1 Expression**

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**Background:** The circadian clock is a molecular mechanism that confers 24 hour variations in gene expression and function to regulate number of physiological functions in humans. Disruption of the clock is associated with pathological remodeling in the arterial structure and vascular stiffness. Chronic circadian clock disruption is also associated with dysfunction in endothelial signaling and responses. Heme oxygenase-1 (HO-1) is an intracellular enzyme which catalyzes the oxidation of heme to generate ferrous iron, carbon monoxide, and biliverdin, which is subsequently converted to bilirubin. These products have anti-inflammatory, anti-apoptotic and anti-thrombotic properties. In this study, we observed if the deletion of Bmal1, a critical component of the circadian clock, can influence HO-1 which play an important part in the protection of vascular diseases.

**Methods:** Congenic 12- to 16-week-old male, wild-type and Bmal1-KO littermate mice were generated from heterozygote breedings to be used for these studies. We also knocked down Bmal1 to evaluate the protein levels of HO-1 expression in the knocked down cells.

**Results:** Endothelial function was reduced in aorta from Bmal1-KO mice. In aorta from Bmal1 KO mice, there was a reduction in HO-1 expression in mice with a dysfunctional circadian rhythm. Moreover, Bmal1 KO mice display pre-mature aging to have a dramatic proatherosclerotic phenotype. This phenotype is linked to changes in the regulation of key risk factors for cardiovascular disease. These include HO-1 which is significantly reduced in Bmal1 KO mice. We also confirmed that HO-1 levels follow a circadian pattern and this pattern was absent in Bmal1 KO mice.

**Conclusions:** These findings indicate that circadian clock provides beneficial effects against the endothelial dysfunction to promote atherogenesis by regulating HO-1 expression. This study establishes a mechanistic connection between Bmal1 and cardiovascular phenotype.

**Funding:** Government Support - Non-U.S.
Macrophage Neutrophil Gelatinase-Associated Lipocalin Has a Critical Role in Aldosterone-Induced Renal Fibrosis via the CCL5/L4 Pathway

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**Background:** Neutrophil Gelatinase-Associated Lipocalin (NGAL) (or lipocalin 2) is a metalloelastocortin. Boosted in the cardiovascular system. NGAL is also described as an acute renal lesion biomarker and NGAL serum concentration is associated with the severity of renal damages patients with a chronic kidney disease (CKD). Lipocalin2 (Lcn2) gene inhibition in a CKD model mouse predicts from proteinuria and renal lesions. We hypothesized that NGAL produced from macrophages promotes expression of chemotractant molecules involved in renal lesions induced by mineralocorticoid excess.

**Methods:** The role of Lcn2 was analyzed using full Lcn2 knockout mice (NGAL KO) challenged with uni-Nephrectomy, Aldosterone 200 mg/kg/day, Salt 1% (NAS model) during 6 weeks. Assessment of CCL5/L4 in kidney fibrosis were studied using maritavice administration (50 mg/kg in chow diet) or by injections of anti-L4 antibody (600 mg/kg).

**Results:** NAS induced a significant increase in the expression (relative values, means±SEM, compared to 1 in the control samples, p<0.05) of extracellular matrix proteins such as collagen I (2.35±0.33), a-SMA (2.04±0.44) and fibronectin (3.20±0.42) in the kidney of WT mice associated with interstitial kidney fibrosis (6.49±0.70). This is fully prevented by Lcn2 deletion. Expression of macrophages markers F4/80, CD80 and CD68 was increased (5.11±0.46, 4.84±0.19 and 5.22±0.45 respectively) in WT NAS mice and partly prevented in Lcn2 KO mice. Macroplages isolated from Lcn2 KO or WT mice were co-treated with aldosterone (10µM) and NaCl (40mM). In WT macrophages, expression of Lcn2 (2.81±0.30) and the CCL5 chemokine (2.84±0.32) was increased. The increase of CCL5 was blunted in Lcn2 KO macrophages. Similarly, to Lcn2 inactivation, CCL5 receptor blockade improved renal fibrosis and reduced high levels of TGF2 (CD4+) cell markers induced by NAS. Neutralization of IL4, a Th2 cytokine, in NAS mice injected with anti-IL4 antibody blunted kidney fibrosis and overexpression of profibrotic proteins such as collagen I, α-SMA and fibronectin.

**Conclusions:** NGAL produced by macrophages plays a critical role in renal interstitial fibrosis through the CCL5/L4 pathway in mice exposed to mineralocorticoid excess.

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**PO2130**

Water Intake and Blood Pressure in Children: Results from the SPA Project

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**Background:** Sodium (Na) intake is involved in the development of hypertension (HPT), to reduce Na is important in the treatment of HPT, but the increase in renal Na excretion might also be a potential preventive and/or therapeutic opportunity. The SPA Project studied blood pressure (BP) in relation to water (H2O) and Na intake with the working hypothesis that increased water intake can improve renal Na handling.

**Methods:** 339 healthy, non-overweight children (166 girls), 5.7 years old (IQR: 5.3-6.2) were characterized for: BP (using standardized multiple office BP measurement), Na and water intake (by means of urinary Na and creatinine from 4 samples taken in 4 different days). After categorizing subjects as low/high Na and low/high water intake (based on median value), BP was compared.

**Results:** Among children with higher Na intake, those introducing more water, showed a significantly (p<0.001) lower BP (both systolic and diastolic) compared to those who drink less (figure). This difference was not observed among children with lower Na intake.

**Conclusions:** Our findings support the hypothesis that an increased water intake, reduces BP by increasing renal excretion. We speculate that this simple, highly acceptable, inexpensive and harmless measure might play a role in preventing and minimizing the epidemics of HPT and related morbidities.
expressed as % total gated kidney cells: Sham = 6.6±0.3%. ORX significantly decreased renal tissue vs. sham in renal necrosis in H&E staining was not significantly altered vs. sham despite having the lowest BP (ORX = 4±0.45; HCTZ/Ren = 5±3.0±0.3; p<0.003). To begin to gain insight into the mechanisms mediating maturation-induced increases in necrosis, RIP3 and HMGB1 protein expression were measured in 5 and 15 wk old male SHR. Expression of RIP3-1 (α = 0.001; n=5-6) and HMGB1-1 (α =0.006 vs. 0.7±0.1; P=0.005; n=5-6) were greater in 15 wk old SHR.

Conclusions: In conclusion, these data suggest that male sex hormones contribute to maturation induced increase in renal necrosis in male SHR to a greater extent than maturation-induced increases in BP. Future work will determine the relative contributions of RIP3 and HMGB1 to renal necrosis in adult male SHR.

Funding: Other NIH Support - American heart association

PO2133

SIRP α Interacts with the IGF-1 Receptor in CKD-Induced Cardiomyopathy

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Background: A major consequence of chronic kidney disease (CKD) is associated cardiomyopathy. Even at early stages of CKD with near normal GFR, and normal blood pressure, left ventricular hypertrophy (LVH) is present, which suggests an unidentified trigger unrelated to pressure overload. We now find that elevations of signal regulatory protein alpha (SIRP α), a substrate for tyrosine phosphatases, in cardiac muscle adversely influences insulin signaling via interactions with the insulin-like growth factor-1 receptor (IGF-1R) in CKD.

Methods: SIRP α fixed (control) vs. muscle-specific (mSIRP α) KO mice were subjected to subtotal nephrectomy. The binding affinity between IGF-1R immunoprecipitated lysates and purified recombinant SIRP α was determined based on the association rate (ka) and the dissociation rate (kds) using biosensor bio-layer interferometry (BLI, Octet RED384 systems). Finally, SIRP α vs. GFP plasmids were transferred to immortalized mouse cardiomyocytes (C2C12 6-mice group), transfection was performed as mentioned above.

Results: Control mice with CKD displayed reduced levels of tyrosine phosphorylation of IGF-1R in cardiac muscle. However, in mSIRP α KO mice with CKD there was no downregulation of IGF-1R phosphorylation despite the presence of CKD. Next, we examined the interactions of these proteins by immunoprecipitation analysis. SIRP α proteins were immunoprecipitated and immunoblotted with the IGF-1R confirming interactions. IGF-1R-SIRP α interactions were further validated using the BLI to assess protein quantities and characterization of kinetics. Specifically, IGF-1R was immunoprecipitated from cardiac muscle and the binding kinetics of Fc-tagged recombinant SIRP α (sSIRP α) to the IGF-1R was identified via BLI. We concluded that sSIRP α was bound to immunoprecipitated IGF-1R with a kD of 147 uM, which further validate their interactions. Lastly, SIRP α plasmids were transfected into myocytes, which led to an upregulation of SIRP α and impaired activation of insulin signaling mediators (IGF-1R and pAKT) plus worsening muscle fibrosis when compared to control transfected cells.

Conclusions: SIRP α interacts with IGF-1R reducing receptor activities, confirming its role in regulating insulin/IGF-1 intracellular signaling in cardiac muscle, exacerbating cardiac muscle functions in CKD.

Funding: Veterans Affairs Support

PO2134

Increases in Renal CD81 and NCC Are Associated with Lipopolysaccharide-Induced Preeclampsia

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Background: CD81, a member of the tetraspan superfamily, is an important component in the pathogenesis of pregnancy hypertension while the status of renal salt transport proteins plays an important role in blood pressure (BP) regulation.

Methods: In order to explore whether there is a connection between the two in the process of preeclampsia, we studied the interaction of CD81 and Na+−Cl− cotransporter (NCC) in vivo and in vitro.

Results: Our model of pregnancy hypertension was built by injecting a small amount of lipopolysaccharide (LPS, 0.5μg/kg in 2ml saline) into the tail vein of pregnant rats on GD 5. On GD 18, BPs (SBP :99.9±4.9 vs 116.9±4.1 1SBP :85.2±2.7 vs 94.4±1.2 mmHg, n=7/group) and urine protein (1185a±35.0 vs 1350a±15.0, μg/day, n=4/group) were higher in LPS rats relative to vehicle rats while renal protein abundance of CD81 (186.8±17.20, μg of protein, n=4/group, same as below) and NCC (278.0±53) was increased. The interaction of CD81 and NCC was found in the co-immunoprecipitation complexes from rat kidney homogenates with the antibodies against CD81 or NCC. In order to further explore the relationship between increased levels of CD81 in treated mice and hypertension in vivo, future studies will use LPS for 24h to construct an in vitro experimental model. The cell viability, detected by CCK-8, was not affected at all concentrations of LPS (0, 1, 10, 20, 30, μg/ml). The toxicity of LPS, detected by LDH release studies, was increased at concentrations of 20 (108.0 ± 3.4, μg/ml) and 30 (115.5±3.3) respectively but not altered at the lower concentrations. Relative to vehicle, LPS at concentration of 10μg /ml increased the protein abundance of CD81 (161.5 ±22.2, n=6/group) and TfN-α (207.5 ±2.7) but did not change the protein abundance of MCP-1. The protein abundance of NCC (193.5 ± 27.6) was increased remarkably while α1-NKA was also increased slightly (134.3 ± 4.51). The mRNA expression of CD81 mRNA was decreased at LPS (10μg/ml) of NCC (115.5±3.3) of vehicle (n=6/group), 10 (134.2±10.54,20 (148.0±8.61,30 (139.1±20.9) respectively.

Conclusions: Our findings in vivo and in vitro suggest that LPS can cause an increase in protein abundance and mRNA expression of CD81 and up-regulate NCC in renal distal convoluted tubules, which can contribute to an increase in blood pressure in pregnancy rats.

PO2135

Neurogenic Tachykinin Mechanisms in Experimental Nephritis of Rats

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Background: We demonstrated earlier that renal afferent pathways combine very likely “classical” neural signal transduction to the central nervous system and a substance P (SP) dependent mechanism to control sympathetic activity. SP content of afferent sensory neurons is known to mediate neurogenic inflammation upon release. We tested the hypothesis that alterations in SP dependent mechanisms of renal innervation contribute to experimental nephritis.

Methods: Nephritis was induced by Ox-7 antibodies in rats, six days later instrumented for recording of blood pressure (BP), heart rate (HR), drug administration; intrarenal administration (IRA) of the TRPV1 agonist capsaicin to stimulate afferent renal nerve pathways containing SP and implantation of electrodes for renal sympathetic nerve activity and recording of sympathetic nerve activity, renal expression of chemokines and markers of sclerosis.

Conclusions: Hence, SP promoted renal inflammation by weakening sympathoinhibitory mechanisms while at the same time substance SP released intrarenally from afferent nerve fibers aggravated immunological processes i.e. by the recruitment of DCs.

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PO2136

Renoprotective Effect of KLF2 on Glomerular Endothelial Dysfunction in Hypertensive Nephropathy

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Background: KLF2 plays a role in maintaining normal vascular integrity by proinflammatory, anti-thrombotic, anti-angiogenic effects in endothelial cells. Endothelial dysfunction is associated with hypertension, and is a predictor of atherosclerosis development and cardiovascular events. Also, it is commonly observed in chronic kidney disease (CKD). The association between glomerular endothelial cell damage in diabetic nephropathy of KLF2 has been studied, but not in hypertensive nephropathy. Here, we present a role of KLF2 in hypertensive nephropathy.

Methods: Human primary glomerular endothelial cells were harvested and cultured under various duration, pressure condition by a rotational force device for mimic hypertensive nephropathy. We established the appropriate culture environment by confirming the pressure and survival rate applied to endothelial cells according to rotational force device which regulate the mRNA expression of smooth muscle actin (αSMA), KLF2 and αSMA. To induce hypertensive nephropathy in rat, 5/6 nephrectomy was done and kidney injury marker, blood pressure, KLF2 expression were evaluated. We evaluated the KLF2 expression in hypertensive nephropathy patients’ biopsied kidney tissue.

Results: The survival rate of human primary glomerular endothelial cells was maintained at a pressure of up to 4mmHg and decreased from above. After the application of 4mmHg pressure for 48hr in human primary glomerular endothelial cells, expression of KLF2 mRNA was decreased, while αSMA mRNA was increased and KLF4 mRNA was similar compared to control. 5/6 nephrectomy in rats resulted in increased blood pressure, decreased kidney function, as well as decreased KLF2 expression of glomerular endothelial cells. In addition, the expression of KLF2 in biopsied kidney tissue of hypertensive nephropathy patients was lower than that of normal kidney tissue.

Conclusions: We found that KLF2 expression of glomerular endothelial cells was reduced in both in vivo and in vitro models of hypertensive nephropathy. These findings suggest a new role for KLF2 in hypertensive nephropathy, which may be the basis for the development of new therapeutics.

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PO2137

Substance P: Differential Influences on Action Potential Production in Afferent Neurons of the Kidney?
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Background: Afferent nerve fibers of the kidney play a role in controlling sympathetic activity in hypertension and cardiovascular diseases. Proinflammatory substances influence the action potential production of these neurons. Therefore, we tested the hypothesis that proinflammatory substance P (SP) released from afferent nerves inhibits the action potential production in neurons with renal afferents.

Methods: Cultured dorsal root ganglion neurons (DRG TH1-L2) of rats with renal afferents were investigated in current clamp mode to assess action potential generation during both current injections and TRPV1 stimulation with protons (pH 6) with and without exposure to SP (0.5 μmol) or CGRP (0.5 μmol). Neuronal classification as tonic (high AP generation upon stimulation) and phasic (AP ≤ 5 upon stimulation). Additional experiments were performed in voltage clamp mode to fully assess electrophysiological properties of the neurons.

Results: Renal neurons were stimulated with current injection (14,4±1,5 APs/600ms, mean±SE) and protons (9,6±1,9 APs/160ms with pH6). The co-stimulation of renal neurons with injections and SP decreased the number of action potentials in tonic neurons (15,2±1,1 APs/600ms vs. 10,1±1,6 APs/600ms, p<0.05, mean±SE), however superfusion of renal neurons with both protons (pH 6) and SP increased (9,6±1,9 APs/600ms vs. 16,9±2,3 APs/600, p<0.05, mean±SE). Additional experiments with the SB-366 containing co-culture abolished. Co-stimulation with CGRP was without significant effect under any circumstances.

Conclusions: Neuronal SP influences action potential production in renal neurons in a very complex way: Both inhibition and specific increases in action potentials via a TRPV1-dependent mechanism in acid-sensitive renal neurons could be demonstrated. Afferent nerve fibers are likely to respond very specific in different conditions while influencing sympathetic nerve activity and putatively renal physiology or pathology (proinflammatory actions of SP).

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PO2138

Tonic Inhibition of Sodium Reabsorption by Na/K-ATPase in the Renal Proximal Tubule
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Background: In the renal proximal tubule (PT), Na/K-ATPase (NKA) is exclusively located in the basolateral domain. Through its classic ATP-dependent ion-pumping function, NKA generates the Na+-gradient that drives apical Na+ reabsorption, mostly through Na/H+ exchanger (NHE3). Accordingly, activation of NKA-mediated ion transport decreases natriuresis through activation of basolateral (NKA) and apical Na+ reabsorption (NHE3). In contrast, activation of the more recently discovered Na+/H+ cotransporter (NBCe1A) content. Rescue with wild-type but not Src signaling-null (FEN or NPFF treatment [1 mM/30 min], n=4). The increased co-immunoprecipitation (coIP) between renal NPF22 and D1R, enabling the D1R to limit NPF22 effects. A normal (145±μM) to low (90 μM) NaCl raised both promoter activity (~2.5 fold, n=3), mRNA and protein expression (n=4; 8-9 hr). A normal to high (175 μM) Na concentration reduced promoter activity (~0.5 fold), mRNA and protein expression of NPF22 (0-8 hr). The increased co IP between prophyptensive NPF22 and antihypertensive D1R, resulted in an increased receptor antagonism to cAMP response and Na transport (vs FEN or NPFF treatment [1 mM/30 min], n=4).

Results: We found a "Sodium Response Element" (NaRE), homolog of "Dehydration Responsive Element" ("TACCGACAT") in Arabidopsis thaliana genome, at the NPF22 promoter. We measured NPF22 promoter activity to test NaRE response to Na. The NPF22 promoter responded to low (4±0.05 fold increase) and high (0.5±0.5 fold decrease) Na with wild type NaRE, but not in the absence of NaRE (mutant NPF22). Using a selective NaRE blocker, (antigen RNA) on mouse kidneys, showed no increased NPF22 response to low Na intake (<0.4 G Na/day) but a decreased systolic blood pressure due to the low Na diet (65±6.6 mm Hg vs. 83±3.1, n=4).

Conclusions: Our data identified NaRE and novel transcriptional and posttranslational mechanisms by which mammalian genes respond to sodium. Funding: NIDDK Support, Other NIH Support - NHLBI

PO2140

Age-Dependent Regulation of the NCC and the Development of Salt-Sensitive Hypertension
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Background: The prevalence of hypertension (HTN) increases with age, and age-dependent HTN is associated with increased sympathetic tone and blood pressure (BP). Dietary sodium intake is a major risk factor for HTN as excessive dietary sodium intake leads to increases in BP in individuals that demonstrate the salt sensitivity of BP to evoke salt sensitive HTN (SSH). We have previously demonstrated excessive release of norepinephrine upregulates the activity of the renal sodium chloride cotransporter (NCC) to promote sodium reabsorption and salt sensitive hypertension. However, the regulation of the NCC with age remain unclear. Thus, we tested the hypotheses that 1) upregulation of NCC contributes to age-dependent HTN, and 2) aged rats develop SSH.

Methods: Three different age groups (3, 8, 16 month old (MOJ)) of male Sprague-Dawley (SD) rats were fed a normal salt (NS; 0.6% NaCl) or HS (4% NaCl) diet for 21 days respectively. On day 21, basal MAP and NCC activity (peak natriuresis to IV hypertonic NaCl infusion) were measured. The expression of total NCC, phosphorylated NCC, with-nosyl- [K] kinases (WNK1), WNK4, STE20/SPS1-related proline-alanine-rich protein kinase (SPAK), oxidative stress responsive kinase 1 (OxSR1), and phosphorylated SPAK/OxSR1 were assessed via immunoblotting (N=6/gp).

Results: Male SD rats develop age-dependent HTN with increased NCC activity and expression, and increased WNK1 expression. Aged male SD rats developed SSH, impaired dietary salt evoked suppression of NCC activity, phosphorylation, and the expression of kinases SPAK and OxSR1.

Conclusions: These data suggest that the NCC contributes to the development of age-dependent HTN. Moreover, dysregulation of the NCC may play a pivotal role in the development of age-dependent SSH.

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Ang II infusion caused a greater rise in MAP (+30 ± 3 mmHg; P < 0.005) and RVR (+190 ± 50 mmHg; P < 0.05). CVR remained quite unresponsive (-7 ± 4%; NS).

Conclusions: Low basal RVR and CVR depend on PG-dependent NO generation. Whereas CVR is entirely protected from vasoconstriction with Ang II, the increase in RVR with Ang II is moderated by PG-dependent NO generation. Thus, PGs and NO exert distinct action in the renal and cerebral vasculature.

PO2143
The Intrarenal RAS Upregulates SGLT2 Expression and SGLT2 Inhibitors Attenuate Angiotensin-II Induced Hypertensive Kidney Injury in Mice
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Background: Clinical trials have shown that SGLT2 inhibitors (SGLT2i) improve both cardiac and renal outcome in several diseases. However, the mechanisms underlying regulation of SGLT2 gene expression remain unclear. Here, we studied whether the intrarenal renin-angiotensin-system (RAS) modulates SGLT2 expression and SGLT2i efficacy.

Methods: We analyzed the association between RAS-related genes and SGLT2 gene expression in the tubulointerstitial compartment of the kidneys of adult non-diabetic patients in the Nephrotic Syndrome Study Network (NEPTUNE). We compared SGLT2 expression in transgenic mice overexpressing angiotensinogen (Agt) in their renal proximal tubular cells (RPTCs/Agt-Tg) vs RAS blockers, and wild-type (WT) mice. We administered angiotensin II (AngII, 1000 ng/kg/min subcutaneously) in WT mice a canagliflozin (Cana, 15mg/kg/day in drinking water for 4 weeks). We also studied human immortalized RPTCs (HK2) as an in vitro model.

Results: In human kidney samples (N=183 patients), SGLT2 mRNA was significantly correlated with AGT (r=0.55, p<0.001), Remin (r=0.46, p<0.001), ACE (r=0.47, p<0.001), and ATIR (r=0.28, p<0.001), but not with AT2R. SGLT2-immunopositive staining was higher in RPTCs of Agt-Tg mice than in WT mice and this was attenuated by losartan treatment. Ang II infusion in WT mice significantly increased blood pressure, which was not reversed by Cana co-treatment. Ang II caused glomerulosclerosis, tubulointerstitial fibrosis, and albuminuria, which were all attenuated by Cana. Fractional glucose excretion was significantly higher in Ang II+Can-Ta than Wt+Can. In vitro, Ang II dose-dependently stimulated SGLT2 mRNA in HK2 cells, and these were inhibited by losartan.

Conclusions: Our data demonstrate that the intrarenal RAS upregulates SGLT2 expression and show that SGLT2i attenuate AngII-induced kidney injury independent of blood pressure.

Funding: Government Support - Non-U.S.

PO2144
Loss of Soluble (Pro)renin Receptor Attenuates DOCA-Salt Hypertension
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Background: Cleavage of the extra-cellular domain of the (pro)renin receptor (PRR) yields a soluble fragment (sPRR), which may be involved in mediating hypertension. We recently developed a mouse model with mutation in the cleavage site of the PRR using CRISPR/Cas9 such that sPRR is not generated and showed that absence of sPRR attenuated angiotensin-II induced hypertension and kidney damage. In this study, we examined if sPRR attenuated blood pressure (BP) in angiotensin-II independent hypertension using deoxycorticosterone acetate (DOCA)-salt treatment.

Methods: Mutant sPRR mice and littermate controls were treated with DOCA (50 mg/kg) and high Na+ diet for 3 weeks. BP was monitored by radio-telemetry and metabolic balance studies performed on Day 17-18 of DOCA-salt treatment. Only male mice were studied as the PRR gene is on the X-chromosome.

Results: Compared to control male sPRR mice, fed markedly lower plasma sPRR levels (control: 21.5 ± 2.5 vs mutant 0.2 ± 0.3 ng/ml) and baseline BP (systolic control: 122 ± 3 vs mutant 114 ± 3; diastolic control: 94 ± 5 vs mutant 82 ± 3 mm Hg). BP remained low in mutant sPRR mice relative to controls following 12 days of DOCA-salt treatment (systolic control: 141 ± 2 vs mutant 132 ± 5; diastolic control: 110 ± 4 vs mutant 95 ± 5 mm Hg). Mutant sPRR mice had lower body weight but similar food intake and urinary albumin excretion compared to controls (Table 1). Mutant mice had lower urine volume, water intake and urinary K* but not Na* excretion. No differences in renal histology were noted between control and mutant sPRR mice.

Conclusions: Loss of sPRR attenuates DOCA-salt mediated hypertension. The mechanisms by which sPRR might regulate BP and water/Na* homeostasis in DOCA-salt hypertension are currently being investigated.

Funding: Private Foundation Support
Effect of Dietary Magnesium Supplementation on Tubulointerstitial 
Damages in Angiotensin II-Induced Hypertensive Rats

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Background: Recently, it has been epidemiologically suggested that Mg deficiency promotes progressive renal damage, and conversely, it has been reported that Mg load to Cyclosporine A-induced renal damage models attenuates renal impairment. This study aimed to investigate the ameliorating effect of high Mg diet on the renal impairment by use of hypertensive nephrosclerosis model.

Methods: Eight-week-old Sprague-Dawley rats were subjected to continuous infusion of Angiotensin II by subcutaneously placed osmotic minipumps for 2 weeks (435 ng/kg/min) and then housed for 6 weeks. The food for animals was normal Mg diet (NMD); 4% NaCl+0.05% Mg or high Mg diet (HMD); 4% NaCl+0.5% Mg. PicroSirius Red staining was used to assess fibrosis, immunostaining of Claudin-16, which is known to be down-regulated in the renal interstitial damage was also performed.

Results: No significant difference in mean blood pressure was seen between two groups (NMD: 97.8±6.7 mmHg vs HMD: 94.2±6.9 mmHg, n=4), and serum Mg was elevated in HMD group (NMD: 1.5±0.1 mg/dL vs HMD: 2.4±0.1 mg/dL, n=4). Analysis of PicroSirius Red staining positive area by semi-quantification showed that positive area in outer medullary region was significantly reduced in HMD group (NMD: 1.6±0.1 vs HMD: 1.1±0.1, n=4). Positive area of claudin-16 immunostaining in HMD group was greater than NMD (NMD: 1.5±0.3 vs HMD: 1.7±0.7, n=4).

Conclusions: Hypertensive nephrosclerosis is one of the major causes of end-stage renal failure, and its suppression is important. It was confirmed that the outermedullary fibrosis was inhibited by high Mg diet, while there was no change in the blood pressure, indicating that anti-fibrotic effect of high Mg diet seemed to be an independent mechanism from the blood pressure. We report the fact that claudin-16 expression is reduced and Mg excretion is increased in the interstitial fibrosis model (Shimizu, Magnesium Res 2018). These results suggest that high Mg diet has an inhibitory effect on fibrogenesis through suppressing the increased Mg-excretion.
Inhibition of Mineralocorticoid Receptor Ameliorates Salt-Sensitive Hypertension After Ischemic-Reperfusion Injury in Rats

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Background: The transition from acute kidney injury (AKI) to chronic kidney diseases a major pathway for progression to end-stage kidney disease. Although hypertensive nephropathy is reported to be associated with the clinical progression of chronic kidney disease, the mechanism by which AKI induces hypertension remains elusive. Previous studies have demonstrated that salt-sensitive hypertension occurs in rats after ischemic reperfusion injury; treatment with a renin-angiotensin model of AKI, and that during hypertension play an important role in the development of salt-sensitive hypertension. Herein, we investigated the role of the mineralocorticoid receptor (MR) in the progression of IRI-induced salt-sensitive hypertension in rats.

Methods: Seven days after right nephrectomy, IRI was induced by clamping of the left renal artery for 45 min in 6-week-old male Sprague-Dawley rats. Rats were sacrificed at 7 days after IRI, and expression of MR examined. IRI rats were also given drinking water with 1% sodium chloride (IRI/NaCl), or were implanted with an osmotic mini-pump to infuse aldosterone (IRI/Aldo). Exsudase (3 mg/kg/day; a non-steroidal MR antagonist [MRa],) or vehicle were administered in IRI/NaCl and IRI/Aldo rats for 6 weeks. Blood pressure and urinary protein level were measured weekly during the study period. Protein expression in renal tissues was examined by immunoblotting and/or immunohistochemistry.

Results: MR expression was increased at 7 days after IRI. Further blood pressure and urinary protein excretion increased in IRI/NaCl and IRI/Aldo rats over the 6-week observation period, whereas these effects were negated by MRA administration. Similarly, MRA ameliorated the expression of the β-epithelial sodium channel (ENaC), γ-ENaC, and fibrotic markers, but not α-ENaC or NaCl cotransporter channel in both IRI/NaCl and IRI/Aldo rats.

Conclusions: Upregulation of MR, β-ENaC, and γ-ENaC may play a pivotal role in the development of salt-sensitive hypertension in rats after IRI.

PO2150 The Effect of Epidermal Growth Factor Inhibition on Salt Sensitivity in Mice

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Background: Every year in the United States, more than 3 million adults are determined to have high blood pressure. Studies have shown that the epidermal growth factor (EGF) decreases the open probability of the epithelial-Na+ channel (ENaC) along the apical surface of the kidney cortical collecting duct (CCD). Yet, it is unknown whether EGF influences renal Na+ transport via the Na+-Cl- cotransporter (NCC). Our laboratory determined to have high blood pressure. Studies have shown that the epidermal growth factor (EGF) influences renal Na+ transport via the Na+-Cl- cotransporter (NCC). Our laboratory determined EGF to be involved in the development of salt-sensitive hypertension.

Methods: Using radio-telemetry in five male mice ages 7 weeks old, we collected the systolic blood pressure (SBP) measurements over 24 hours daily for two weeks. These animals received a low salt (LS) diet (0.4% Na+ chow) for 6 days and high salt (HS) diet (4% Na+ chow) for 8 days. Overall, the period of two weeks, only the experimental (E) group (n=3) received geltin in (an EGF receptor tyrosine kinase inhibitor) at a regimen of 100 mg/kg/d given orally while the control (C) group (n=2) received a placebo.

Results: The results for the change in awake-SBP while receiving diet (0.4% Na+ chow) for 6 days and high salt (HS) diet (4% Na+ chow), showed the experimental (E) group had a greater increase in SBP in response to a higher dietary Na+ intake (E group: 7.70 ± 0.17 vs. control (C) group: 3.11 ± 0.29 mmHg, p<0.001). The delta for the difference in BP change when increasing dietary Na+ intake was greater for the E group of mice (delta = 7.40 mmHg, p<0.001).

Conclusions: Therefore, our data strongly suggests that inhibition of EGF increases the salt sensitivity. This may be due to upregulation of the EGF ligands act as tonic inhibitors of tubular sodium reabsorption. Future experiments will explore the involvement of EGF effects of inhibition on NCC, ENaC and sodium excretion.

Funding: NIDDK Support, Veterans Affairs Support

PO2153 The Effect of Epidermal Growth Factor Inhibition on Diurnal Variation of Blood Pressure in Mice

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Background: There are 78 million adults in the United States who have hypertension (HTN). HTN is a serious medical condition that serves as risk factor for cardiovascular disease (CVD) and chronic kidney disease (CKD). Blood pressure (BP) normally declines about 10% during sleep and this is called “dipping”. Studies have demonstrated that an augmented decline in nocturnal BP (“non-dipping”) is associated with increased cardiovascular risks. Investigations by our group and others have demonstrated an effect of the epidermal growth factor (EGF) on sodium transport proteins and BP. However, an association between EGF and “dipping” has not been described.

Methods: Using radio-telemetry in five male mice ages 7 weeks old, we collected the systolic blood pressure (SBP) measurements over 24 hours daily for two weeks. These animals received a low salt (LS) diet (0.4% Na+ chow) for 6 days and high salt (HS) diet (4% Na+ chow) for 8 days. Only the experimental (E) group (n=3) received geltin in (an EGF receptor tyrosine kinase inhibitor) at a regimen of 100 mg/kg/d given orally while the control (C) group (n=2) received a placebo. The change in SBP was evaluated during rest (9am-9pm) which are morning hours versus awake (9pm-9am) during evening hours since mice are nocturnal.

Results: The results showed the E group had less of a decrease in their SBP during the day compared to the control group (E group: -7.3 ± 0.18 vs. C group: -13.5 ± 0.01 mmHg, p<0.001). Here the delta is 6.1 mmHg, p<0.001, which shows that the C group maintained a greater decrease in their SBP compared to the E group.

Conclusions: Overall, our results suggest that inhibition of EGF leads to decreased dipping in SBP regardless of the dietary Na intake and this effect is greater with a high dietary Na intake. Therefore, our data is the first to suggest that EGF may play a role in the nocturnal dipping of BP, which could have potential implications for managing HTN-related cardiovascular disease.

Funding: NIDDK Support, Veterans Affairs Support

PO2154 The Klotho Deficiency and Not the FGF-23 Rise Is Associated with Heart Failure with Reduced Left Ventricular Ejection Fraction in Patients with Preserved Kidney Function

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Background: The FGF23-Klotho axis is increasingly implicated in the pathophysiology of heart failure, especially during advanced chronic kidney disease (CKD). Our objective is to study the association between this FGF23-Klotho axis and heart failure (HF) in patients with preserved kidney function. This topic is less studied in medical literature.

Methods: This is a cross-sectional study of the FGF23 assessment, Klotho and the phosphocalcic axis in 70 patients with normal renal function. These patients had echocardiographic exploration which made it possible to distribute them in two groups: Group HF: LVEF (Left Ventricular Ejection Fraction)<55% (n = 18); Group NoHF: LVEF ≥55% (n = 52). Heart failure(HF) was exclusively of ischemic origin.

Results: These were 36 women and 34 men, average age 58 ± 10 years with an estimated glomerular filtration rate (eGFR) at an average of 92 ml / min / 1.73m2. No difference in eGFR between the two groups. Klotho was far lower with a statistically significant difference in Group HF. FGF23 was higher in Group HF but the difference was not statistically significant. PTH (parathyroid hormone) was statistically higher in Group HF and calcium was statistically lower in Group HF. Phosphatemia and vitamin D were not associated with heart failure.

Conclusions: Although the sample studied is not large, Klotho but not FGF23 is strongly associated with systolic heart failure. This and other results will be further discussed.

PO2158 Aetiological Subtypes of Transient Ischaemic Attack and Ischaemic Stroke in CKD: A Population-Based Study


Background: Chronic kidney disease (CKD) is strongly associated with stroke risk but the mechanisms underlying this association are unclear, and might be informed by subtype-specific analyses. However, few studies have reported stroke subtypes in CKD according to established classification systems such as the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria. We therefore aimed to determine which transient ischaemic attack (TIA) and ischaemic stroke subtypes using the TOAST classification occur most frequently in patients with CKD.

Methods: In a population-based study of all TIA and stroke (Oxford Vascular Study; 2002-2017), all ischaemic events were classified by TOAST subtypes (cardioembolism, large artery disease, small vessel disease, undetermined, multiple, other aetiology, or undetermined and not investigated). Logistic regression was used to describe the relationship between CKD (defined as an estimated glomerular filtration rate [eGFR] < 60 ml / min / 1.73m2) and TIA/stroke subtypes adjusted for age, sex, and hypertension, and then stratified by age and eGFR category.

Results: Among 3175 patients with TIA (n=1167), ischaemic stroke (n=1802), and intracerebral haemorrhage (n=209), 1267 (40%) had CKD. Although there was a greater prevalence of cardioembolic events (31.8 vs. 21.2%; p<0.001) in patients with CKD, this association was lost after adjustment for age, sex, and hypertension (Adjusted
Identification of Novel Biomarkers and Pathways for Coronary Artery Calcification in Non-Diabetic Patients on Hemodialysis Using Metabolomic Profiling
Wei Chen,1 Jessica Fitzpatrick,2 Stephen M. Sozio,3 Bernard G. Jaar,3 Michelle M. Estrella,4 Dario F. Rioscios-Bernal,5 Tongtong Wu,6 Yuning Ou,7 Irwin J. Kurland,8 Ruth F. Dubin,9 Yabin Chen,10 Rulan S. Parakh,10 David A. Bushinsky,11 Nicholas Sibiga,12 PACE13 Montefiore Medical Center, Bronx, NY;14 Hospital for Sick Children, Toronto, ON, Canada;15 Johns Hopkins University, Baltimore, MD;16 San Francisco VA Medical Center, San Francisco, CA;17 University of California San Francisco, San Francisco, CA;18 University of Rochester Medical Center, Rochester, NY;19 Yeshiva University Albert Einstein College of Medicine, Bronx, NY;20 University of Alabama at Birmingham, Birmingham, AL.

Background: A better understanding of pathophysiology involving coronary artery calcification (CAC) in hemodialysis (HD) patients will help to develop new therapies. We sought to identify the differences in metabolomics profiles between HD patients with and without CAC.

Methods: This is a case-control study nested within a cohort of 568 incident HD patients from the Predictors of Arrhythmic and Cardiovascular Risk in ESRD (PACE) study. Cases were non-diabetics with a CAC score >100 (n=51), and controls were non-diabetics with a CAC score of 0 (n=48). We measured 452 serum metabolites in each participant using liquid chromatography-mass spectrometry. Metabolites and pathway scores were compared using Mann–Whitney U tests, partial least squares-discriminant analyses, and pathway enrichment analyses. Multiple logistic regression was used to examine associations between metabolites and pathways with CAC.

Results: Cases had a median CAC score of 466 (IQR 246–981). Compared to controls, cases were older (64 ± 13 vs. 42 ± 13 years) and were less likely to be African American (51% vs. 94%). We identified three metabolites in bile acid synthesis (chenodeoxycholic, deoxycholic, and glycolithocholic acids) and one metabolic pathway (arginine/proline metabolism) that were associated with CAC. After adjusting for demographics, higher levels of chenodeoxycholic, deoxycholic, and glycolithocholic acids were associated with higher odds of having CAC. Comparing the third with the first tertile of each bile acid, the adjusted OR (95% CI) was 6.34 (1.12–36.06), 6.73 (1.20–37.82), and 8.53 (1.50–46.16), respectively. Using the first principal component (PC1) score, arginine/proline metabolism was associated with CAC after adjusting for demographics [OR: 1.38 (95% CI: 1.06-3.15) per 1 unit higher in PC1 score], and the association remained significant after adjusting for additional covariates.

Conclusions: Among HD patients without diabetes mellitus, chenodeoxycholic, deoxycholic, and glycolithocholic acids may be potential biomarkers for CAC, and arginine/proline metabolism may emerge as a new pathway in the pathogenesis of CAC.

Funding: NIDDK Support, Other NIH Support.

Poster PO2154

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Poster PO2155

NaRE: A Novel “Salt Response Element” in the NPPFR2 Gene Promoter and Antagonist of the D1 Dopamine Receptor
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Background: the neuromedin F receptor FF2 (NPPFR2) is one of two receptors for NPPF and is endowed with pro-hypertensive and anti-natriuretic activities. We looked for regulatory elements in the NPPFR2 gene promoter and how it interacts with an anti-hypertensive and natriuretic protein, the dopamine type receptor D (D). R.

Methods: Human renal proximal tubule cells (hRPTCs) treated with low NaCl (90 mM) increased mRNA (2.3±0.4-fold) and protein (1.5±4% vs. 100±4%) levels of the salt-retaining NPPFR2, whereas treating the cells with high NaCl concentration (170 mM) decreased the mRNA (0.7±0.05-fold) and protein (±0.54%, P=0.05 levels).

Results: Promoter analysis of the mouse and human NPPFR2 genes for regulatory elements identified a single 8-bp region, aptly called “NaRE” for Na Response Element, at -2.3 kb upstream of +1 position. This is 75% identical to the “Dehydration Responsive Element” (“TACCGCAT”) in the Rld2 gene of Arabidopsis thaliana which is a cis-acting element which responds to dehydration, low temperature, and salinity.

In the presence of the wild-type NaRE, the NPPFR2 promoter responded well to both low (4.1±0.5-fold increase) and high (0.52±0.5-fold decrease) NaCl concentrations, but not in the absence of NaRE in a mutant NPPFR2 promoter construct. Antigene RNA to block NaRE expression in the kidneys of C57BL/6 mice resulted in the inability of the mice to respond to a low sodium diet (<90° g sodium/day) and reduced further the decreased systolic blood pressure caused by the low sodium diet (65±0.6 mm Hg vs. 83±1.3, P<0.05). We then studied a mechanism by which NPPFR2 dynamically interacts with the D1R. NPPFR2 and D1R co-immunoprecipitated and colocalized in hRPTCs. Knocking out the mouse kidney, NPPF and the D1R:D1R agonist fenoldopam had antagonistic effects on CAMP production (2.5±1.0 pmol/min for fenoldopam vs. 1.2±0.2 for vehicle). We then studied a mechanism by which NPPFR2 and D1R, thus increasing the ability of NPPFR2 to antagonize the D1R effects.

Conclusions: Our data are the first to identify NaRE and demonstrate novel transcriptional and post-translational mechanisms by which mammalian genes respond to sodium.

Funding: NIDDK Support

Poster PO2156

Discovery and Characterization of Small-Molecule Potentiators of K, 4.1, 5.1
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Background: Heterotetratricopeptide (K) and K4.1 (KCNJ10 and Kir5.1) open channel in response to sodium, potassium, and water balance by the distal convoluted tubule of the renal tubule. Loss-of-function mutations in KCNJ10 lead to EAST syndrome, which is characterized by renal salt wasting and neurological dysfunction.

Methods: We established a monoclonal HEK-293 cell line that stably expresses human Kir4.1 and Kir5.1 from a bicistronic vector, and developed and validated a fluorescent-based transduction assay of KCNJ10 and Kir5.1 channel function in 384-well format. This assay was used to screen small-molecules from the Vanderbilt Chemistry Institute Library and confirmed with whole-cell electrophysiology.

Results: To date, we have screened more than 60,000 compounds using this assay and identified 420 putative inhibitors and 354 putative potentiators of Kir4.1-K5.1. Forty-five of these potentiators increase Kir4.1-5.1-mediated transduction flux by greater than 50% and are selective for Kir4/5.1 over homomeric Kir4.1 channels. Fourteen (14) potentiators are active at low single micromolar concentrations with EC50 values less than 5 μM, while six (6) compounds appear to be highly efficacious and increase Kir4/5.1-mediated transduction flux by more than 100%. Importantly, we have also verified with patch clamp electrophysiology the activity of one of the first-in-class activator of Kir4.1-5.1, termed VU206. In thallium flux assays, VU206 potentiates thallium flux dose-dependently with an EC50 of 1.9 μM and maximal efficacy of -50% above baseline between 10-30 μM. In whole-cell patch clamp experiments, VU206 led to maximal activation of whole-cell currents at 10 μM, complementing the thallium assay. Analysis of current-voltage relationships showed robust activation at both negative and positive test potentials without a depolarizing shift in the reversal potential suggesting VU206 potentiates Kir4.1-5.1 activity without affecting ion selectivity.

Conclusions: Findings from this study provide a novel pharmacological tool for exploring renal Kir4.1-5.1 channel integrative physiology and therapeutic potential of Kir4/5.1 potentiators for the treatment of EAST syndrome.

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Poster PO2157

Improvement in Albuminuria and Hypertension in Renin Transgenic Mice by a Novel Filterable Form of Angiotensin-Converting-Enzyme 2 with Prolonged Half-Life
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Background: ACE2 is a monocarboxypeptidase that converts angiotensin (Ang) II to Ang 1-7. Its large molecular size precludes it from being filtered by the kidneys. We have developed a novel filterable form of ACE2 (ACE2-ABD) which is characterized by a prolonged half-life while maintaining full enzymatic activity. The protein is filterable and re-absorbable by the proximal tubule, thereby providing increased kidney ACE2 activity

Methods: Short soluble mouse(m) and human(h) ACE2 variants were fused with Albumin-Binding Domain(ABD). In vivo pharmacokinetic was determined after i.v. and i.p. injection followed by repeated measurement of plasma ACE2 activity. Subsequently, m and h ACE2-ABD(2 mg/kg) were injected every 2-3 days t.p. to Ren TgMK mice. The kidney included urinary albumin and blood pressure was monitored.

Results: Administration of 619-ABD to ACE2KO mice resulted in detectability of urinary ACE2 activity which at the baseline was not detectable. Blocking proximal tubule (PT) reabsorption with L-lysine, further increased urinary ACE2 activity suggesting that the ABD-tagged ACE2 undergoes glomerular filtration and is taken up by PT. In WT mice, augmentation of plasma ACE2 activity could still be shown a week after administration. In Ren TgMK mice, both m and h ACE2-ABD markedly reduced SBP and ACR(Figure).

Conclusions: A shorter soluble ACE2 variant fused with ABD exhibits a prolonged half-life and reduces SBP and ACR.

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as well as circulating plasma ACE2 activity. Its efficacy was documented by reduced BP and ACR in Ren TgMK, a hypertensive model due to RAS activation. Thus, this novel ACE2 variant with extended half-life offers potential for treatment of kidney disease and hypertension.

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PO2158

Fibroblast Growth Factor 23 Induces Ventricular Arrhythmias and Prolongs QTc Interval in Mice In Vivo Mediated Through FGF Receptor 4

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Background: Sudden cardiac death and arrhythmias are leading causes of mortality in those with compromised renal function, such as in chronic kidney disease (CKD). Fibroblast growth factor 23 (FGF23) is a phosphaturic hormone released by osteocytes, which becomes markedly elevated in CKD. Previously, we found that FGF23 increases intracellular Ca2+ in cardiomyocytes and alters contractility in mouse ventricles ex vivo via stimulation of FGF receptor 4 (FGF4R). Since FGF23 could disrupt Ca2+ homeostasis, we hypothesized that FGF23 at pathological levels would alter depolarization/repolarization of the heart and induce arrhythmias in vivo via a mechanism involving FGF4R.

Methods: To assess our hypothesis, CD-1 male mice (3 months old) were anesthetized and electrocardiogram (ECG) needle electrodes were inserted into the limbs. The jugular vein was cannulated for infusion of vehicle or FGF23 (9ng/ml total blood volume) with or without pretreatment with an FGF4R-specific blocking antibody (anti-FGFR4; U3 Pharma). Lead II ECG and arrhythmias were monitored at baseline and then for 30 minutes post injection.

Results: FGF23 induced premature ventricular contractions (PVCs) in 5 out of 11 mice (P=0.038 vs vehicle) with an average maximal rate of PVCs in these mice of 10.2 ± 5.2 PVCs/minute (P=0.01 vs vehicle). Vehicle (n=9) and FGF23+anti-FGFR4 treated (n=8) mice did not exhibit PVCs. Treatment with Isoproterenol (0.1mg/kg) after FGF23 further augmented arrhythmias to a maximal rate of 25.0 ± 21.1 PVC/minute (P=0.05 vs vehicle) and 2 out of 8 mice displayed ventricular tachycardia. Upon examination of ECG intervals, FGF23 prolonged QTc within 30 minutes (P<0.05, n=8) compared to vehicle treatment (n=9), whereas no effect was found for PR interval or QRS duration.

Conclusions: We conclude that FGF23/FGF4R signaling in the heart may contribute to ventricular arrhythmogenesis and repolarization disturbances commonly observed in patients with CKD and may be an important therapeutic target to reduce cardiac mortality in CKD.

PO2159

Use of Immune Checkpoint Inhibitors in ESKD


Background: Use of immune checkpoint inhibitors (ICI) in ESKD patients is limited. We describe our single-center experience of ICI use in ESKD patients and summarize the current literature.

Methods: Using an analytics database, we identified all patients with at least one of a single ESKD diagnosis code who received ICI therapy at our health system. Charts were reviewed manually to confirm that patients were on HD or PD during the ICI therapy. Clinical details such as demographics, comorbidities, cancer type, immune-related adverse events (irAEs), cancer disease status, and patient survival were reviewed. Further literature search was performed for all published cases of ICI use in ESKD patients and was summarized as part of the methods.

Results: In total, 8 patients with ESKD were initiated on ICI. A variety of malignancies were identified. Four patients received pembrolizumab, two received nivolumab, one received both ipilimumab and nivolumab, and the last received PD-1 inhibitor atezolizumab. Eight patients were receiving anemia therapy. The mean duration on dialysis (dialysis vintage) prior to ICI therapy was 15.8 months (range: 3-60 months). Two patients had an immunotherapy-related adverse event. In both cases, the physicians discontinued the offending ICI agent and started the patients on systemic steroid therapy. Both patients subsequently recovered without adverse event.

Conclusions: Based on our series and previously published literature review, the rate of adverse events appear similar to non-ESKD patients (15-25%). ESKD may not be a contraindication to the use of ICI therapy.
and nivolumab). The incidence of AKI of any duration was 36.6% (333 of 910 patients), while the incidence of AKI (defined as ≥3 days or longer or not re-measured) occurred in 31.0% of patients (282 of 910). The incidence of presumed CPI-induced AKI was 3.2% (29/910). A total of 25.2% (71/282) of sustained AKI patients had at least one concurrent immune-related adverse effect (irAE), compared to 55.2% (16/29) of presumed CPI-induced AKI. CPI-induced AKI occurred on average 88.2 days (standard deviation 80.6) after starting the CPI, with several AKI events occurring within 60 days after stopping the CPI.

Conclusions: AKI secondary to CPI is a common side effect of CPI. In our population, it occurred at an incidence of 3.2% and sometimes occurred even after the last dose of CPI. The etiology of AKI in almost all cases of biopsy-proven CPI-induced AKI is acute interstitial nephritis. The risk appears to be increased if a patient has already developed an irAE.

Funding: Private Foundation Support

PO2162
Checkpoint Inhibitor-Related Renal Vasculitis and Use of Rituximab
Harish Shanthanu,PO2162

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Background: The percentage of cancer patients eligible for checkpoint inhibitor (CPI) therapy has increased rapidly over the past few years and approaches 45%. As a result, more cases of CPI-related nephrotoxicity, including those with vasculitis, are being reported. To elucidate the clinical presentation of CPI-associated vasculitis with kidney involvement and its possible mechanisms, treatment options, and prognosis, we describe the cases from a comprehensive cancer center and reviewed the literature for similar cases.

Methods: We retrospectively reviewed the charts of all cancer patients from 2014 to 2020 who were diagnosed with CPI-related nephrotoxicity and underwent a kidney biopsy.

Results: We identified 5 cases of vasculitis with kidney involvement: 3 patients were diagnosed with renal vasculitis, 1 case with ANCA vasculitis, and 1 case with Immunoglobulin A (IgA) vasculitis. Of these cases, 4 patients were receiving nivolumab, and 1 patient was receiving tremelimumab. All patients had microscopic hematuria, four out of five had negative anti-neutrophil cytoplasmic antibodies (ANCA) serology, one patient had concurrent lung involvement and positive ANCA serology, and all had severe acute kidney injury with creatinine >4.50 mg/dL upon diagnosis. All patients were treated by discontinuing CPI and initiating corticosteroids and rituximab. Three patients received plasmapheresis. Two of these required renal replacement therapy (RRT) including the patient with lung involvement. All patients after rituximab had partial or complete renal response. Two patients died within 8 months of diagnosis due to malignancy progression. None of the patients had a relapse of vasculitis.

Conclusions: We demonstrated that CPI can be associated with different types of vasculitis with kidney involvement that are predominantly ANCA negative and manifest as severe acute kidney injury. Despite the lack of strong evidence, treatment similar to treatment of primary ANCA vasculitis with corticosteroids and rituximab is well tolerated with acceptable outcomes.

Funding: Other NIH Support - National Institutes of Health through Cancer Center Support Grant

PO2163
AKI and Immune-Related Adverse Events (irAEs) in Patients with Genitourinary Cancers Receiving Immune Checkpoint Inhibitors (ICIs)
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Background: Hyponatremia due to endocrinopathies such as adrenal insufficiency and hypothyroidism has been reported in patients receiving immune checkpoint inhibitors. Other electrolyte abnormalities such as hypocalcemia and hypokalemia have also been associated with the use of these agents. We study the incidence and predictors of electrolyte abnormalities in cancer patients receiving immune checkpoint inhibitors.

Methods: Patients who received immune checkpoint inhibitors at Massachusetts General Hospital Cancer Center between 2011 and 2018 were included. Incidence of electrolyte abnormalities were determined in the first 12 months after drug initiation and graded for severity by using Common Terminology for Cancer Adverse Events criteria.

Results: We analyzed 2458 patients started on checkpoint inhibitors in our cancer center. Average age was 64 (SD 13) years, 58% were male and 90% were White. In the first 12 months follow-up, 62% experienced hyponatremia, 27% had hypokalemia, 26% had hyperkalemia, 49% had hypophosphatemia and 9% had hypocalcemia. Grade 3 or 4 hyponatremia was seen in 136 patients (6%) and occurred 164 days (SD 100) after checkpoint inhibitor initiation; only 9 cases of grade 3 or 4 hypokalemia were due to endocrinopathies. CTLA4 inhibitors were associated with a higher risk of grade 3 or 4 hypokalemia and hypophosphatemia. Patients with gastrointestinal malignancies experienced the highest risk of grade 3 or 4 electrolyte abnormalities.

Conclusions: Electrolyte abnormalities are common in cancer patients receiving immune checkpoint inhibitors. Endocrinopathies leading to severe hyponatremia are rare (<0.5%).

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2165

Immune Checkpoint Inhibitor-Associated Glomerular Disease: A Systematic Review and Meta-Analysis
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Background: Immune checkpoint inhibitors (ICI) are increasingly used to treat several cancers. Kidney immune-related adverse events (IRAE) are now well-recognized, with purported incidence of 2-5%. The majority of initial data related to kidney IRAE has focused on acute interstitial nephritis (AIN). Recently various glomerular diseases have been reported; however, there is minimal data on the types and relative frequencies of glomerular diseases associated with ICI, their treatment, and outcomes.

Methods: We performed a systematic review and meta-analysis of all biopsy-proven published cases/series of glomerular pathology associated with ICI therapy. We searched the MEDLINE, EMBASE and Cochrane Central databases from inception to February 2020. We abstracted patient-level data, including demographics, cancer and ICI therapy details, and characteristics of kidney injury. We performed exploratory univariate logistic regressions for predictors of end stage kidney disease (ESKD) or death.

Results: After screening, 27 manuscripts with 45 cases of biopsy-confirmed ICI-associated glomerular disease were identified. Several types of lesions were observed, with the most frequent being pauci-immune glomerulonephritis and renal vasculitis (27%), minimal change disease (MCD) (20%), and C3 glomerulonephritis (11%). Concomitant AIN was reported among 41% of cases. The majority of patients had ICI discontinued (88%), and nearly all received corticosteroids (98%). Complete or partial remission of proteinuria was achieved in 45% and 38%, respectively. Most patients had full (31%) or partial (42%) recovery from AKI although 19% required dialysis and approximately one-third of patients died. In exploratory univariate logistic regression for predictors of end stage kidney disease (ESKD) or death.

Conclusions: Glomerular diseases associated with ICI are not uncommon. Pauci-immune glomerulonephritis, MCD and C3GN are the most frequently reported lesions. ICI-associated glomerular disease may be associated with poor kidney and mortality outcomes. Oncologists and nephrologists need to be aware of glomerular pathologies associated with ICI treatment.

PO2166

Statin Use, Renal Cell Carcinoma, and Combination Immunotherapy: Increase Risk of Checkpoint Inhibitor-Induced Nephritis: A Single-Center Database Study
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Background: Immune checkpoint inhibitors (ICI) are associated with improved cancer outcomes, however immune related adverse events (irAE) develop and are poorly understood. Renal irAE (RirAE) are less common but may jeopardize effective cancer therapy, and no reliable risk factors for RirAE have been identified. Concomitant medications have been shown to play a role in response to ICI but the impact on toxicity is unknown. We report risk factors and clinical outcomes of patients who develop RirAE.

Methods: We queried a patient database with advanced cancer treated with ICI between 2010 and 2017 at Ohio State Univ for pts who developed AKI (defined as a doubling of creatinine after initiation of ICI). irAEs were reviewed by nephrologist and oncologist. Overall survival (OS) was calculated from date of initiation of ICI to death from any cause or date of last follow-up. Associations between irAE incidence and categorical outcomes were studied using chi-square or Fisher’s exact test. The Wilcoxon test was used for continuous outcomes. Survival outcomes were studied using log-rank test or cox regression model.

Results: Of 1,091 pts treated with ICI, 160 (14.7%) developed AKI of any cause and 30 (2.74%) developed RirAE. PPI use (p=0.032), renal cell carcinoma (RCC) diagnosis (p=0.009) and line of therapy (p=0.033) were all associated with development of AKI, and RCC, BMI, and line of therapy remained significant in multivariate analysis[OD1]. Overall survival (OS) was 12.2 months in absence of AKI vs 10.7 months with AKI (p=0.0125). Statin use (p=0.007) and RCC diagnosis (p=0.012) were significantly associated with RirAE with a trend to higher rates in combination immunotherapy (p=0.064). These three variables were also significant in multivariate analysis. OS was not different in the RIrAE group (10.8 months) vs no RIrAE group (11.8 months).

Conclusions: Patients undergoing ICI therapy can develop AKI as well as RirAE. However, outcomes are worse for AKI. Survival for pts who develop RirAE does not appear to differ from patients without RIrAE. AKI and RIrAE share an independent risk factor in RCC. However, statin use and combination ICI therapy appear to be unique risk factors for RIrAE. Further studies are needed to verify the finding regarding statin use, a drug with widespread use.

PO2167

A Potential Mechanism of Distal Renal Tubular Acidosis in Patients Treated with Immune Checkpoint Inhibitors
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Background: The main cause of acute kidney injury in patients on immune checkpoint inhibitors (ICI) is acute interstitial nephritis (AIN). However, as their use continues to increase, we observe other renal manifestations being described. Distal renal tubular acidosis (dRTA) has been described, but the mechanism is not clear to date. We hypothesized that an alteration of H+-ATPase or anion exchanger (AE-1) in alpha intercalated cells (α-IC) in collecting duct is affected.

Methods: We present two patients with AIN and dRTA secondary to ICI: Patient #1 with metastatic adenocarcinoma of lung and patient #2 with metastatic melanoma, both treated with anti-PD1-antibodies (pembrolizumab/nivolumab). They had prominent electrolyte abnormalities consistent with dRTA (Figure 1A). Kidney biopsy was performed in each patient which showed diffuse AIN with negative routine immunofluorescence (IF) staining. Both patients had received PPI in addition to ICI therapy and had improvement in their kidney function following steroid therapy and with discontinuation of the drugs. In order to investigate the potential mechanism for developing dRTA, the kidney biopsy frozen sections from patients1 and 2 were further stained by indirect IF for acid base transporters in α-IC (α4 and B1) subunits of the vacuolar H+-ATPase (V-ATPase) and the AE1. In order to quantify the staining, data were normalized to a T0 allograft biopsy as control.

Results: α-IC cell markers were decreased in both patients compared to the control as shown in Figure 1B. Quantification of AE1, B1-V-ATPase and A4-V-ATPase were all reduced compared to control biopsy, however, staining for other markers of α-IC (c-kit) were not reduced. This suggests a more targeted reduction in V-ATPase subunits that may be immune-mediated.

Conclusions: The reduction in staining for V-ATPase subunit could be related to damage from AIN, however, an immune-mediated process that reduces the expression of V-ATPase in α-IC is likely. Comparing staining of V-ATPase in α-IC in patients with AIN secondary to ICI with and without dRTA in the future will be useful.

Funding: NIDDK Support
PO2168
Clinical Features of AKI in Patients Receiving Tisagenlecleucel (CAR-T Therapy)
Meghan Lee,1 Ian A. Strohbehn,2 Harish Shanthanu Seethapathy,1 Nifusha Rusibamalya,1 Keagan S. Casey,2 Shruti Gupta,2 David E. Leaf,2 Matthew Frigault,1 Meghan E. Sise.1 Massachusetts General Hospital, Boston, MA; 2Brigham and Women’s Hospital, Boston, MA.

Background: CAR-T therapy uses genetically engineered T cells to target tumor antigens. Some CAR-Ts can lead to cytokine release syndrome (CRS), neurotoxicity, and in severe cases, AKI. Prior series demonstrated 20% incidence of AKI after axicabtagene ciloleucel (Yescarta), a CD28 costimulatory domain CAR-T. Tisagenlecleucel (Kymriah) is a 41BB CAR-T that targets CD19 on B cells but has delayed toxicities, slower expansion kinetics, longer persistence, and is associated with lower rates of severe CRS. We determined incidence and clinical features of AKI in patients receiving tisagenlecleucel.

Methods: We performed a retrospective review of adults with diffuse large B cell lymphoma treated with tisagenlecleucel at our institution between Jan 2019–Apr 2020. Baseline demographics, laboratory data, and clinical outcomes were obtained from electronic health records. The primary outcome, AKI, was defined as a ≥1.5-fold rise in creatinine from pre-CAR-T baseline and staged using KDIGO criteria.

Results: Overall, 37 patients received tisagenlecleucel: average age was 60 (SD 18), 65% male, 86% white. CRS occurred in 51% (no severe CRS); neurotoxicity occurred in 24%. Thirteen (35%) required steroids, 8 (22%) received tocilizumab, and 8 (22%) received anakinra to treat CRS/neurotoxicity. AKI occurred in 2 (5%) patients; both had stage 3 AKI. One had acute tubular necrosis due to septic shock starting post-infusion day 1. The other had AKI with new-onset nephrotic range proteinuria (5-6g/g) concurrent with a hemophagocytic lymphohistiocytosis-like syndrome beginning day +8. The patient was also receiving amphotericin and acyclovir. Both patients with AKI died (days 4 and 28, respectively). Among patients without AKI, the 30-day mortality was 8.6%. Clinically significant electrolyte disorders were also common (Table).

Conclusions: Compared to prior reports, we found lower rates of CRS and AKI in patients receiving tisagenlecleucel. We report a case of new-onset nephrotic-range proteinuria and AKI following CAR-T.

PO2169
Dabrafenib-Induced Acute Interstitial Nephritis (AIN) and AKI in Patients with Cancer
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Background: BRAF inhibitors (vemurafenib, dabrafenib, encorafenib) commonly used to treat BRAFmutant cancers have been associated with AKI. Cases of acute and chronic tubular injury and AIN have been reported with dabrafenib. We aimed to define the incidence and clinical features of AKI in patients on dabrafenib.

Methods: We conducted a retrospective cohort of patients receiving dabrafenib from 2010-2018 in a large healthcare system. Baseline comorbidities and medication use was determined by chart review. The primary outcome was AKI (≥1.5-fold increase in baseline creatinine) within 12 months. AKI etiology was reviewed by 2 nephrologists. Multivariable modeling was used to determine predictors of AKI.

Results: Overall, 199 patients were included; mean age was 59 (SD 16) years, 56% were male, and 94% were white. 96% received trametinib (a MEK inhibitor) concurrently. Mean baseline creatinine was 0.9 (SD 0.2) mg/dL, 20 (10%) had baseline CKD (eGFR < 60 mL/min/1.73m2), and 42 patients (21%) experienced AKI at a mean of 141 (SD 116) days after starting dabrafenib. In multivariable modeling, only baseline liver disease predicted AKI. Etiology and stage of AKI are shown in Fig 1A; clear alternative causes for AKI were found in 32 of 42 cases. Ten patients (5% of total cohort, 24% of AKI) experienced AKI attributed to dabrafenib-induced cytokine release syndrome (CRS); all experienced fever, chills, gastrointestinal distress (nausea/vomiting/diarrhea) +/- rash and transaminitis within 4-6 weeks of starting dabrafenib. The majority improved with intravenous hydration and discontinuation of the drug. One patient with persisting AKI underwent kidney biopsy demonstrating granulomatous AIN (Fig 1B); he was treated with intravenous solumedrol and a prednisone taper for two weeks with full resolution of AKI.

Conclusions: AKI is common in patients on Dabrafenib (21%). A febrile systemic response or CRS after dabrafenib may explain up to 24% of AKI; we report another case of AIN after dabrafenib.

Funding: NIDDK Support

PO2170
Temporal Trends of Palliative Care Use Among Hospitalized Patients with Metastatic Renal Cell Carcinoma
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Background: Patients with metastatic renal cell carcinoma have a poor prognosis and they may suffer from hypercalcemia, venous thromboembolism, anorexia-cachexia syndrome. Little is known about the trends in the utilization of palliative care in this patient subset.

Methods: We conducted a retrospective cohort study using data from 2004 to 2014, which were extracted from the National Inpatient Sample. ICD-9-CM was used to identify all diagnosis variables. We compared the baseline demographics. We assessed the annual trend over time in palliative care utilization rates. Statistical analysis was performed using STATA 16.0. We considered a two-tailed P value of <0.05 as statistically significant.

Results: We identified 181,199 hospitalizations with metastatic renal cell carcinoma from 2004 through 2014, of which 16,390 (9.0%) involved palliative care services. Inpatient palliative care utilization increased from 2.8% in 2004 to 16.3% in 2014 (p<0.001). Compared with patients discharged from non-teaching hospitals, we noticed a significantly higher rate of palliative care utilization in patients discharged from teaching hospitals [aOR 1.46; 95% CI 1.29 to 1.65]. There were higher odds of receiving palliative care in patients with private insurance [aOR 1.26; 95% CI 1.11 to 1.42]. We also observed lower odds of receiving palliative care in Hispanic patients [aOR 0.83; 95% CI 0.70 to 0.98, p=0.03].

Conclusions: The rate of inpatient palliative care use in metastatic renal cell carcinoma patients sharply increased between 2004 and 2014. Our findings demonstrated improving adherence to the National comprehensive cancer network (NCCN) guidelines, which is highly encouraging. Patients from teaching hospitals and using private insurance and were more likely to receive palliative care.

PO2171
AKI Secondary to Multiple Myeloma: Complications of Treatment with High Cut-Off Filters

Background: Acute kidney injury is a frequent complication of MM that can affect 18 to 50% of patients and more than 10% end up needing dialysis. One of the drawbacks associated with the technique is attributed to the albumin loss. The other complications are related with the dialysis technique itself, especially infections.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2172 Acute Myeloid Leukemia Worsens Sepsis-Induced AKI Takayuki Tsui, Naoko Tsui, Tetsushi Yamashita, Xuzhen Hu, Peter S. Yuen, Robert A. Star. Renal Diagnostics and Therapeutics Unit National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD.

Methods: We performed extensive mouse experiments to assess the potential contributory role of leukemia to sepsis-induced AKI. In brief, leukemia cells bearing recombinant IL-6 were injected into NSG (null) mice. After engraftment 2 weeks later, these mice were subjected to cecal ligation and puncture (CLP) to induce sepsis. The total number of mice was 104. The main observation was that 80% of mice developed AKI, which is significantly higher than the control group (20%).

Results: The results of our experiments showed that leukemia cells bearing recombinant IL-6 significantly worsened sepsis-induced AKI. The mean BUN and LDH levels were significantly higher in the leukemia group compared to the control group. The AKI severity was also significantly higher in the leukemia group.

Conclusions: These results suggest that leukemia cells can contribute to sepsis-induced AKI. Further studies are needed to investigate the mechanisms of this contribution.
Selinexor-Associated Hyponatremia: Single-Center Real-World Data
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Introduction: Hyponatremia is a commonly reported side effect in recent clinical trials evaluating the efficacy and safety of selinexor in treatment of refractory multiple myeloma (MM). With incidence ranging 7-47%, the hyponatremia was reported to be generally asymptomatic, transient, and highly responsive to medication dose reduction and sodium. The etiology for hyponatremia is not yet completely understood and speculated to be multifactorial, hypovolemia, diuretics, deprivation, and diuretics that included thiazides. Cancer related pain was observed in both groups but the hyponatremic group was on higher dose selinexor and more likely to have more gastrointestinal side effects, sepsis, hypotension. Nephrology was consulted on only 4 out of 13 patients. These 4 patients had pre-existing hyponatremia with serum sodium < 130 meq/l and high urine sodium concentration that along with euvolemia favored SIAD diagnosis in 3 out these 4 patients.

Conclusions: Our observations suggest that hyponatremia is multifactorial, as the patients had history of hyponatremia, and selinexor side effects (hypovolemia, nausea and possible unidentified factor) may contribute to hyponatremia. It is possibly dose dependent, more likely to occur with patients who had gastro-intestinal side effects, sepsis and hypotension. We recommend discontinuation of medications associated with hyponatremia prior to starting/during selinexor therapy, obtaining basic hyponatremia investigations, and early referral to nephrology to prevent potential serious symptoms.

Antiemetic Drugs and the Risk of Cisplatin-Induced AKI
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Background: Cisplatin (CIS) is an effective first line therapy for a variety of cancers. Acute kidney injury (AKI) is a common side effect of CIS seen in up to 30% of patients (Latcha et al CJASN, 2016). AKI results from the selective uptake and accumulation of CIS in proximal tubules. CIS is a highly emetogenic and fluid loss can also contribute to AKI. We retrospectively reviewed the medical records of all relapsed MM patients at our hospital between January 2014 and Dec 31, 2016 (n=6,889) were reviewed. The association between use of anti-emetics and development of AKI (50% increase in serum creatinine (sCr)) was evaluated. Inclusion criteria were adults, baseline sCr, CIS dose and administration of anti-emetics. AKI developed after CIS in 1,666 (24.2 %) patients. Of patients without AKI (n=5223), patients who received any antiemetic represented 45.4% whereas AKI alone was 13.6%. Risk factors for AKI included chemotherapy (odds ratio [OR]=3.245,P=0.002), robotic technique (OR=2.437,P=0.029) and operation time (OR=1.005,P=0.012). Of 150 patients without CKD history, CKD developed in 62.5% of patients with AKD,33.3% with AKI alone and 30.6% withNKD during the 30 months follow up (p=0.013). K-M analysis showed AKD patients had the highest CKD incidence(Fig.1). Cox model also identified AKD (HR=2.224,p<0.012) but not AKI alone, was independent risk factor predicting CKD, along with age.

Conclusions: The incidence of AKD was higher than AKI alone after microinvasive Radical RC and 111 for laparoscopic RC. The incidence of AKD was 14.7% whereas AKI alone was 13.6%. Risk factors for AKD included chemotherapy, male gender, black race, and cumulative CIS dose were associated with higher risk for AKD (P<0.001). After adjusting for these variables, use of any antiemetics was protective for AKI (OR 0.84, 95% CI: 0.75, 0.94; P = 0.003). The Surveillance, Epidemiology and End Results (SEER) database was used to identify all adult patients (≥18 years) diagnosed with ccRCC and sRCC between 2000 and 2017. Variables included age, sex, ethnicity, laterality, staging, histological grade, and nephrectomy. Overall survival was estimated using the Kaplan–Meier method, and compared using the Log–Rank test. Multivariable covariate-adjust Cox models were used for adjusted survival analyses.

Background: Acute kidney disease (AKI) proposed in 2012 by KDIGO is getting more and more attention for its vital role in acute kidney injury (AKI) to chronic kidney disease (CKD) transition. However, no study has explored the incidence, risk factors of AKD and its impact on new-onset CKD after microinvasive radical cystectomy (RC).

Methods: The medical records of 308 patients at our hospital between January 2014 and May 2019 were reviewed. We excluded 29 patients from the study due to missing sCr preoperatively or postoperatively. AKD was diagnosed as a ≥25% decrease in eGFR or >50% increase in sCr between 7-90 days after surgery. AKI alone was defined by the 2012 KDIGO classification but failed to meet AKD criteria after 7 days. No kidney disease (NKD) was defined if patients didn’t meet either criteria. Logistic regression model was used to explore risk factors of AKD, while its significance for CKD was assessed using Kaplan–Meier analysis and Cox model.

Results: We evaluated 279 bladder cancer patients, including 168 for Robotic-assisted Laparoscopic RC and 111 for Laparoscopic RC. The incidence of AKD was 14.7% whereas AKI alone was 13.6%. Risk factors for AKD included chemotherapy (odds ratio [OR]=3.245,P=0.002), robotic technique (OR=2.437,P=0.029) and operation time (OR=1.005,P=0.012). Of 150 patients without CKD history, CKD developed in 62.5% of patients with AKD,33.3% with AKI alone and 30.6% with NKD during the 30 months follow up (p=0.013). K-M analysis showed AKD patients had the highest CKD incidence(Fig.1). Cox model also identified AKD (HR=2.224,p<0.012) but not AKI alone, was independent risk factor predicting CKD, along with age.

Conclusions: The incidence of AKD was higher than AKI alone after microinvasive Radical RC and 111 for laparoscopic RC. The incidence of AKD was 14.7% whereas AKI alone was 13.6%. Risk factors for AKD included chemotherapy, male gender, black race, and cumulative CIS dose were associated with higher risk for AKD (P<0.001). After adjusting for these variables, use of any antiemetics was protective for AKI (OR 0.84, 95% CI: 0.75, 0.94; P = 0.003). The Surveillance, Epidemiology and End Results (SEER) database was used to identify all adult patients (≥18 years) diagnosed with ccRCC and sRCC between 2000 and 2017. Variables included age, sex, ethnicity, laterality, staging, histological grade, and nephrectomy. Overall survival was estimated using the Kaplan–Meier method, and compared using the Log–Rank test. Multivariable covariate-adjust Cox models were used for adjusted survival analyses.

Results: A retrospective cohort study of 20248 patients (19398 ccRCC, 850 sRCC) with overall survival rate of 38% (40% ccRCC and 16.2%sRCC). Although the two subtypes share similar demographic characteristics, including mean age (66.8±13.7 for ccRCC vs 62.9±12 for sRCC), and female-ratio (1.77 to 2.1), survival analysis using Kaplan–Meier showed a significant worse prognosis for sRCC after adjusting for covariates.

Conclusions: The Surveillance, Epidemiology and End Results (SEER) database was used to identify all adult patients (≥18 years) diagnosed with ccRCC and sRCC between 2000 and 2017. Variables included age, sex, ethnicity, laterality, staging, histological grade, and nephrectomy. Overall survival was estimated using the Kaplan–Meier method, and compared using the Log–Rank test. Multivariable covariate-adjust Cox models were used for adjusted survival analyses.
regression analysis, advanced stage, high histological grade, and older age 65+years (HR 1.002, 95%CI [1.001-1.00]) P < 0.001) were associated with worse outcomes. Patients with cancer-related death had significantly shorter survival time in both RCCs (P<0.001). Nephrectomy was associated with better survival outcomes (HR 0.486 [0.459-0.514], P < 0.001).

Conclusions: sRCC had worse prognosis. Advanced stage, high histological grade, and older age are the most important predictors of survival in both subtypes of RCC. Although caucasian male patients were more affected in sRCC, gender and ethnicity have no impact on survival. Nephrectomy imparts better survival benefits in both subtypes.

PO2179
Acid-Base Biomarkers and Cancer Mortality
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Background: Acidosis in the tumor microenvironment is associated with cancer progression in animal models. We explored the association of serum bicarbonate and anion gap – measures of acid-base balance – with cancer mortality in community-dwelling adults.

Methods: We conducted a prospective cohort study using the National Health and Nutrition Examination Survey (NHANES), a nationally representative cross-sectional survey of the US non-institutionalized population. Anion gap (mEq/L) was calculated as serum sodium (mmol/L) – (serum chloride (mmol/L) + serum bicarbonate (mmol/L)). We used weighted Cox proportional hazards models to assess the associations between serum bicarbonate and anion gap with cancer-specific mortality, as recorded by the National Death Index. Multivariable models were adjusted for demographics data, BMI, smoking status, diabetes, systolic blood pressure, cardiovascular disease history, ACEi/ARB, diuretics, HIV drugs, metformin, serum albumin, total cholesterol, total protein, total calorie intake, hemoglobin, cancer diagnosis, cGFR and urine albumin to creatinine ratio.

Results: This study included total 39,137 participants [mean (SD) age, 46.83(19.25) years, 20,162(46.3%) females, 18,119 (46.3%) white]. During 4,433,277 person-years of follow up, 964 (2.46%) participants died secondary to cancer. A history of cancer at the time of enrollment was reported in 3186 (8.8%). Table 1 shows the associations between serum bicarbonate and anion gap in tertiles with cancer-related mortality. In analyses restricted to those with a history of cancer, results were 78% increased risk for cancer mortality in highest tertile compared to lowest tertile [HR 1.78; 95% CI (1.11,2.87)].

Conclusions: Increased anion gap may be a risk factor for cancer mortality. The reasons driving this association deserve further examination.

Risk of cancer mortality according to bicarbonate and anion gap as tertiles (method weighted survey cox regression)

PO2180
In-Hospital and 1-Year Mortality Among Patients with AKI and Haematological Malignancies
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Background: Patients with haematological malignancies (HIM) are at high risk for acute kidney injury (AKI), which is associated with high morbidity and mortality. The aim of this study was to identify the prognostic factors for in-hospital mortality and one-year mortality in this population.

Methods: We conducted a single centre, retrospective, observational cohort study of 101 in-hospital patients with AKI and HIM between 1 January 2015 and 31 December 2019. We recorded essential demographic, clinical and laboratory data at baseline, 1 and 12 months. We classified AKI according to the KDIGO definition. Cox proportional hazard model was applied to investigate the one-year mortality, and logistic regression analysis was used to assess the in-hospital mortality.

Results: The study population included 64 males and 37 females, with a mean age of 58.7 ± 16.8 years. Multiple myeloma was present in 30.7% (n=31) of the patients, followed by non-Hodgkin lymphoma (LNH) in 27.7% (n=28). 51.5% (n=52) were admitted to intensive care unit (ICU). 60.4% (n=61) needed renal support therapy (RST). Basal GFR, one-month GFR and one-year GFR were, respectively, 65.7 ± 28.9 mL/min/1.73m², 57.1 ± 28.5 mL/min/1.73m² and 54.9 ± 28.1 mL/min/1.73m². Mean length of in-hospital stay was 18 days (IQR 1-88). In-hospital death was 52.5% and after one year only 26 patients were alive. In multivariate analysis, the independent predictors for in-hospital mortality were invasive mechanical ventilation (IMV) (OR 49.53; 95% CI 19.17 – 267.57; p<0.001) and sepsis (OR 5.09; 95% CI 1.18 – 21.89; p=0.029). The C-statistic was 0.93 (95% CI: 0.87 – 0.98), indicating that the equation had a great discriminatory power. The independent predictors for one-year mortality were LNH (HR 2.78; 95% CI 1.53 – 5.05; p=0.001), cancer progression (HR 2.91; 95% CI 1.56 – 5.41; p=0.001) and IMV (HR 5.79; 95% CI:3.30 – 10.15; p<0.001). Elevated levels of albumin at the time of AKI conferred a better prognosis (HR 0.65; 95% CI 0.42 – 0.95; p=0.027).

Conclusions: Our model showed that HM patients with AKI are at high risk of sepsis and IMV, and resulting in elevated in-hospital death. Elevated levels of albumin at the time of AKI correlated with a better one-year survival, while LNH, cancer progression and IMV were risk factors for death.

PO2181
Renal Recovery after AKI After Hematopoietic Stem Cell Transplantation: A Systematic Review and Meta-Analysis
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Background: Patients with the recovery of renal function after an episode of acute kidney injury (AKI) have better outcomes compared to those without recovery. The current systematic review is conducted to assess the rates of kidney function recovery among patients with AKI or severe AKI requiring RRT within 100 days after hematopoietic stem cell transplantation (HSCT).

Methods: Ovid MEDLINE, EMBASE, and the Cochrane Databases were systemically searched from database inception through August 2019 to identify studies reporting the rates of recovery from AKI after HSCT. Random-effects and generic inverse variance method of DerSimonian-Laird were used to combine the effect estimates obtained from individual studies.

Results: A total of 458 patients from 8 cohort studies with AKI after HSCT were enrolled. Overall, the pooled estimated rates of AKI recovery among patients with AKI and severe AKI requiring RRT within 100 days were 58% (95%CI: 37%-78%) and 10% (95%CI: 2%-4%), respectively. Among patients with AKI recovery, the pooled estimated rates of complete and partial AKI recovery were 60% (95%CI: 39%-78%) and 29% (95%CI: 10%-61%), respectively. There was no clear correlation between study year and the rate of AKI recovery (p =0.26).

Conclusions: The rate of recovery from AKI after HSCT depends on the severity of AKI. While recovery is common, complete recovery is reported in about two-thirds of all AKI patients. The rate of recovery among those with AKI requiring RRT is substantially lower.

Table 2. Forest plots of the involved studies assessing renal recovery rates from AKI after HSCT

PO2182
Renal Outcomes After Autologous Stem Cell Transplantation for AL Amyloidosis
Naresh Bumm, Michael Ozga, Isabelle Ayoub, Salem Almaani, Nidhi Sharma, Yvonne A. Efebera, Samir V. Parikh. The Ohio State University, Columbus, OH.

Background: Renal involvement in AL Amyloidosis is common and results in end-stage kidney disease (ESKD) in 30% of cases within 3 years of diagnosis. Newer therapeutic regimens directed at the plasma cell clone including high-dose melphalan with autologous stem cell transplantation (ASCT) are associated with improved survival but effect on renal outcome is not well established. We evaluated renal outcomes for patients who underwent ASCT and achieved a complete (CR) or very good partial (VGPR) hematologic response.
Methods: We performed a retrospective analysis of 50 AL Amyloidosis patients who underwent ASCT. Patients with renal involvement who achieved a hemodynamic response were included. Renal response was defined prior to transplant, according to consensus guidelines, as partial response (PR, > 30% decrease in proteinuria) or stable disease (SD, ≤ 30% proteinuria reduction). Primary endpoints were progression free survival (PFS) and overall survival (OS). PFS and OS were defined as the time from transplant to day of progression or death, respectively. Kaplan-Meier survival function estimated the PFS and OS. The log-rank test tested the equality of survivor functions between different groups of patients.

Results: Following ASCT, 16 patients (32%) achieved hematological VPCR/CR after ASCT. All had renal involvement. Baseline and 1-year post-transplant proteinuria and serum creatinine (SC) levels are shown in the Table. In the group of pts achieving VPCR/CR as hematological response PFS and OS were similar for patients having PR and SD as renal response (p=0.89 and p=0.44, respectively). No patients required hemodialysis. Median follow up for PFS was 4.1 years and for OS was 5.6 years (PR) and 11.9 years (SD).

Conclusions: Hematological response is important in AL amyloidosis and survival improves similarly with VPCR and CR. In patients with renal involvement, this study shows similar outcomes to patients who achieved a PR or SD as renal response prior to ASCT. However, our study has a small sample size and we would recommend a larger study.

RENAL RESPONSE METRICS PRE AND POST ASCT

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<tr>
<th>AT DIAGNOSIS</th>
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<td><strong>Partial Response</strong> (pr)</td>
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<td>35 (7.5%)</td>
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Median Serum Creatinine prior to ASCT in PR group was 1.2 mg/dl and 2.0 mg/dl in SD group.

PO2183

High-Dose Methotrexate (HDMTX) and Nephrotoxicity: Effect on Subsequent Dosing

Background: HDMTX is an important part of various chemotherapeutic protocols due to its central nervous system penetration. A key complication of HDMTX is nephrotoxicity as this leads to delayed MTX excretion and further morbidity. Nephrotoxicity in a previous cycle of HDMTX leads to an increased risk of future toxicity. Our aim was to establish how nephrotoxicity affected clinical decision making with regards to future dosing.

Methods: A retrospective review of the electronic medical record was performed to identify patients who developed nephrotoxicity post HDMTX from 1/1/02 to 12/31/18. A retrospective review was performed to identify patients who went on to receive subsequent doses of HDMTX. We stratified the effect of nephrotoxicity by grade of AKI, according to the acute kidney injury network criteria, on resumption of MTX. In those who received a subsequent dose, we assessed whether a dose reduction had an impact on rate of Nephrotoxicity. Analysis was performed in Minitab.

Results: We identified 670 episodes of nephrotoxicity which equated to an overall incidence rate of 19% of total cycles. The majority were AKI grade 1 (79.7%). Higher grade AKI were significantly less likely to receive a future dose (p=0.001), with 71.3% of AKI N1, 59.2% of AKI N2, and 21.2% of AKI N3. Other factors associate with future dosing included elevated 48-hour MTX trough (p=0.001), admission to ICU (p=0.001), and prolonged Hospital LOS (p=0.009). 449 patients received a future dose of Methotrexate with 152 (33.9%) receiving a dose reduction. The overall incidence of AKI with subsequent dosing was 33.85%. The incidence of AKI in subsequent dosing was 55.3% with no dose reduction compared to 30.3% with a dose reduction (p=0.29) (see table 1 for breakdown).

Conclusions: Nephrotoxicity had an important impact on subsequent dosing, especially with higher grade AKI. Previous AKI infers a higher rate of nephrotoxicity in future dosing with no significant reduction in incidence with reduction in MTX dose. Given the retrospective nature of the data and the many complexities to dosing calculation, this should be further explored with a prospective study.

Effect on dose reduction on subsequent AKI

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PO2184

Nephrology and Hematology Referral Trends in CKD Patients with Monoclonal Gammapathy and Factors Associated with Deferring Kidney Biopsy
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Background: Many patients with CKD are managed by their primary care providers (PCP). The presence of monoclonal gammapathy (MG) in the setting of CKD raises the possibility of monoclonal gammapathy of renal significance (MGRS) which would require a nephrology or hematology referral. However, rate and factors that affect specialty referral in patients with MG remains unknown. Moreover, factors for deferring a kidney biopsy are also unknown.

Methods: We retrospectively identified adult CKD patients with MG at our center from 2017-2018. Baseline characteristics and laboratories studies were compared between nephrology/hematology referral group (RG) vs. no referral group (NRG). We also assessed the rate of kidney biopsy and the reasons for not pursuing a biopsy in the referral group.

Results: We identified 596 CKD patients with MG. Of these, 416 (69.8%) were seen by nephrology/hematology (380 (92.2%) were not referred to either. Of the 180, 32% were followed by their PCP (n=57), 30% by cardiologist (n=54), and 19% by neurologist (n=35). Demographics were similar between the two groups. Patients in the NRG were more likely to have coronary artery disease, dementia, active or metastatic cancer. In multivariate analysis, 24-hr urinary protein (OR: 1.36 (1.01, 2.09)), abnormal FLC (OR 2.46 (1.29, 4.93)), and serum creatinine (OR 2.38 (1.37, 4.59)) were strong independent predictors for referral. Of 416 patients in RG, 62 (15%) patients underwent a kidney biopsy and 26 had an MGRS lesion. There were no differences in the comorbidities between the patients that were biopsied vs. those that were not. The main reason for deferring biopsy was lack of awareness of CKD or MG (42, 40%) and low suspicion for MGRS (130, 37%). In 62 patients, biopsy was not pursued as it was unlikely to change management (majority had amyloidosis). Other reasons included watchful waiting and patient’s frailty.

Conclusions: Up to 30% of CKD patients with MG are not referred to a specialist. Co-morbidities lower the rate of referral whereas impaired kidney function and higher M-spike & FLC increase referral. However, once patients are referred, the comorbidities had no impact on who underwent biopsy. Most common reason for not pursuing a biopsy was lack of awareness that patient had CKD or MG.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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PO2186

Daratumumab for Management of Bortezomib-Resistant Monoclonal Gammapathy of Renal Significance

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Background: The management of monoclonal gammapathy of renal significance (MGRS) is challenging. In our center, MGRS patients are initially treated with a bortezomib-based regimen. Patients who do not respond have very limited therapeutic options. Daratumumab is an anti-CD38 monoclonal antibody that is being increasingly used in patients with multiple myeloma with a favorable adverse effect profile, and represents a potential therapeutic option for patients with MGRS.

Methods: Retrospective review of the use of daratumumab in management of patients with bortezomib-resistant MGRS.

Results: Five patients were treated with daratumumab after receiving a variety of immunomodulatory therapies (Table 1). All received bortezomib with no response. One patient had a dramatic improvement in proteinuria with a stable renal function. One patient had resolution of glomerular monoclonal protein deposits but had persistent proteinuria due to significant damage to the glomerular basement membrane. One patient suffered from an acute kidney injury due to acute tubular necrosis (noted on biopsy) and became dialysis dependent. Two patients were started on daratumumab recently and had limited follow up, however both demonstrated a reduction in proteinuria. Daratumumab was well-tolerated and no patients required hospitalization due to adverse effects.

Conclusions: Our experience in using daratumumab for management of bortezomib-resistant MGRS suggests good tolerability and short-term response rates.

PO2188

Immune Checkpoint Inhibitor-Induced p-ANCA Multigranulocytosis

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Introduction: Use of immune checkpoint inhibitors (ICIs) has led to improved mortality in melanoma, lung cancer, and lymphoma. ICIs augment immunologic reaction against tumor cells via blockade of cytotoxic T-lymphocyte antigen-4 (CTLA-4), programmed cell death-protein 1 (PD-1), or programmed death-ligand 1 (PD-L1). Renal complications from ICIs are uncommon but can involve development of glomerular diseases and interstitial nephritis. Below we present a case of p-ANCA vasculitis in a patient on ICI therapy.

Case Description: A 52-year-old female with adenocarcinoma of the right lung (T2N2) s/p right lower lobectomy, cisplatin/vinorelbine, radiation therapy, and durvalumab was hospitalized for evaluation of new onset oral blisters, fevers, hemoptysis, skin lesions, and acute kidney injury. Her creatinine rose to 3.2 mg/dl (baseline of 0.5 mg/dl). Urinalysis revealed >180 RBCs and 17 WBCs per high power field with a urine protein to creatinine ratio (UPCR) of 2.63 g/g. ANCA titers were positive for PR-3 antibody of 4.6 units. Patient underwent renal biopsy, which revealed evidence of renal vasculitis involving all glomeruli and crescents in 4 out of 20 glomeruli. There was concern for endocarditis with vegetation seen on echocardiogram; however, with negative blood cultures the etiology was attributed to autoimmunity (vasculitis) rather than infection. The patient was aggressively treated for ANCA vasculitis with pulse steroids, plasmapheresis, and rituximab (1g given 2 weeks apart). She had a dramatic improvement in her skin lesions, hemoptysis, cardiac and renal function. Two months following her last rituximab infusion, she has not had further hematuria, her UPCR remains < 0.5 g/day, and creatinine is stable at 1.2 mg/dl. PET/CT continues to demonstrate clinical remission of her underlying cancer.

Discussion: With the dramatic cancer responses seen in patients receiving immune checkpoint therapy, there has also increased understanding associated toxicities. Although reports of ANCA positive vasculitis from ICI has been reported; this case is unique due to the multigranulocytic involvement of her vasculitis including the heart valves. Aggressive treatment with steroids, plasmapheresis, and rituximab has proven effective due to hindering her tumor response.

PO2187

Diffuse Background Monoclonal Light Chain Staining in Kidney Biopsies, Without Electron Dense Deposits: Is It Relevant?

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Background: Pathologic diagnosis of monoclonal gammapathy (MgG)-associated kidney disease requires specific morphologic and immunofluorescence (IF) findings with deposits on electron microscopy. We have encountered kidney biopsies showing only diffuse “background” monoclonal light chain staining the renal parenchyma, without characteristic lesions of MgG-associated kidney disease or organized/non-organized deposits on ultrastructural examination. Such staining is either overlooked if weak, or can be over-diagnosed as MgG-associated kidney disease if strong, causing dilemma over the need for immediate clone-directed therapy. We performed a clinic-pathologic study to better understand its significance.

Methods: Database search over 12-year period revealed such 32 cases. Clinical and laboratory data was retrieved along with a mean follow-up of 13 months.

Results: Out of the 32 patients, 15 (47%) had active myeloma by hematologic criteria (despite absence of myeloma casts on kidney biopsy) warranting immediate clone-directed therapy; but 11 (34%) did not have/develop myeloma defining events till the (despite absence of myeloma casts on kidney biopsy) warranting immediate clone-directed therapy. But it is important to note that there is a subset of patients that do not have active myeloma despite the strong background staining. Care must be taken to avoid inadvertent immediate clone-directed therapy in these patients, but periodic monitoring with hematologic and renal parameters to watch for possible malignant transformation is important.

Conclusions: It is important to recognize and document this isolated background monoclonal light chain staining in the biopsy report, but by itself, should not be classified as MgG-associated kidney disease. It does warrant a thorough hematologic work-up. It can help to unmask (previously unsuspected) underlying active myeloma which many patients. But it is important to note that there is a subset of patients that do not have active myeloma despite the strong background staining. Care must be taken to avoid inadvertent immediate clone-directed therapy in these patients, but periodic monitoring with hematologic and renal parameters to watch for possible malignant transformation is important.

PO2189

IgA Nephropathy in the Setting of Dual Immune Checkpoint Inhibitor Use

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Introduction: Acute kidney injury (AKI) is a recognized side effect of immune checkpoint inhibitors (ICIs), with acute tubulointerstitial nephritis (AIN) as the most common pathologic finding. Risk of AKI is higher with use of proton pump inhibitors (PPIs) and dual ICI use. Glomerular disease with ICI is infrequently found on kidney biopsy. We report a case of concomitant IgA nephropathy and AIN associated with dual ICI blockade.

Case Description: 62-year-old male with metastatic sarcoma recently initiated on ipilimumab and nivolumab presented with dark colored urine for 2 days. He was recently hospitalized for neutropenic fevers with a negative infectious work up. On admission his blood pressure was 181/94 and he was afebrile. Physical exam was notable for new bilateral lower extremity edema, and no rash present. His creatinine was 2.2mg/dl (0.6-1.3), with a baseline creatinine of 0.8mg/dl. He started a PPI one month ago and denied NSAID use. Laboratory findings showed eosinophilia 7.7% (0.0-4.9) and urine protein was 5085mg. His serum complement levels were normal. Kidney biopsy showed 1.6mg/dl after 1 week, with plan for outpatient steroid taper. At 10mg prednisone daily, his creatinine improved to 2.7mg/dl, though he developed several steroid related side effects. Due to inability to tolerate higher doses of steroids, mycophenolate was added to his treatment regimen while undergoing steroid taper.

Discussion: This case underscores the importance of considering acute glomerulonephritis as a cause for AKI in patients recently started on ICI therapy. Risk of AKI in this patient was higher given use of PPI and dual ICI therapy. This case is unique as the renal biopsy showed both AIN and IgA nephropathy. These findings had important implications for the treatment plan since the patient was unable to successfully stop prednisone and required a second immunosuppressive agent.
PO2190
Hypercalcaemia Associated with Immune Checkpoint Inhibitors
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Introduction: Immune checkpoint inhibitors revolutionized treatment of many cancers with marked improvement in prognosis. They target CTLA-4, PD-1/PD-L1 pathways. However immune related adverse events complicate their use. Here we present the early onset case of hypercalcaemia as a result of immune checkpoint inhibitors.

Case Description: A 68-year old man with metastatic renal cell carcinoma underwent right nephrectomy followed by immunotherapy with ipilimumab and nivolumab. Two weeks after his second cycle of immunotherapy, he presented with inflammatory arthritis and pruritus. Work up was significant for sCa 12.8 mg/dL and Scr 3.6 mg/dL. Hypercalcaemia was suspected to be malignancy related from bone metastasis or humoral stimulation. He received fluids, calcium and Zoledronic acid. Further investigations showed a suppressed iPTH 6.3 pg/ml, normal PTP, low TSH 0.04 uIU/ml, free T4 1.91, normal T3 < 1.8, normal 25-HC, low calcium 8.9 mg/dl and normal phosphorus 3.8 mg/dl. No monoclonal proteins were detected in serum. CRP and interleukin 6 were elevated to 80 mg/dl and 176 pg/ml respectively. PET scan showed diffuse hypermetabolic lymph nodes in mediastinum, neck, and abdomen. Transbronchial needle aspiration was negative for malignancy. Inflammatory arthritis, pruritus, hyperlymphocytosis, nonmalignant diffuse lymphadenopathy, and 1.25 dihydroxyvitamin D induced hypercalcaemia are suggestive of immune related adverse effects rather than disease progression. Patient was started on prednisone 1mg/kg/d. Hypercalcaemia, AKI, pruritis and inflammatory arthritis resolved. Repeat 1.25 dihydroxy vitamin D and CRP levels were back to normal.

Discussion: Hypercalcaemia related to checkpoint inhibitors was previously described in setting of increased PTHrP. Our patient had hypercalcaemia directly related to immunotherapy likely through increased alpha hydroxylase.

PO2191
Double Trouble with Pembrolizumab: Immune Checkpoint Inhibitor-Induced Type I Renal Tubular Acidosis and Secondary Adrenal Insufficiency
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Introduction: Pembrolizumab is a novel immune checkpoint inhibitor (ICI) that targets programmed cell death protein (PD-1) signaling. Checkpoint inhibitor associated nephrotoxicity is an immune-mediated process that can manifest with a variety of clinical presentations. Here, we report a unique case of Pembrolizumab induced distal renal tubular acidosis (RTA) and secondary adrenal insufficiency (AI) which was successfully treated with steroids.

Case Description: A 72-year-old male with a history of stage IIC malignant melanoma, who had recently completed 3 cycles of therapy with Pembrolizumab was admitted with generalized fatigue, weakness, and anorexia. Initial work up was notable for severe hyperatenorpea, and a non-anion gap metabolic acidosis (NAGA): (Na: 120 mmol/L, Cl: 89 mmol/L, K: 3.8 mmol/L, HCO3: 20 mmol/L and creatinine 0.67mg/dL). Serum aldosterone was 11 pg/dL, serum ACTH 1.4 pg/mL and DHEA 12 ng/dl. Other pituitary hormones including LH, FSH, ACTH, TSH, PRL, and prolactin were within normal limits. Serum cortisol was 22 ng/dL (normal 12-24 ng/dL), CRH stimulation test demonstrated a serum cortisol response of 30 mcg/dL at 30 minutes and 58 mcg/dL at 60 minutes. No monoclonal proteins were detected in serum. CRP and interleukin 6 were elevated to 80 mg/dl and 176 pg/ml respectively. PET scan showed diffuse hypermetabolic lymph nodes in mediastinum, neck, and abdomen. Transbronchial needle aspiration was negative for malignancy. Inflammatory arthritis, pruritis, hyperlymphocytosis, nonmalignant diffuse lymphadenopathy, and 1.25 dihydroxyvitamin D induced hypercalcaemia are suggestive of immune related adverse effects rather than disease progression. Patient was started on prednisone 1mg/kg/d. Hypercalcaemia, AKI, pruritis and inflammatory arthritis resolved. Repeat 1.25 dihydroxy vitamin D and CRP levels were back to normal.

Discussion: Hypercalcaemia related to checkpoint inhibitors was previously described in setting of increased PTHrP. Our patient had hypercalcaemia directly related to immunotherapy likely through increased alpha hydroxylase.

PO2193
Immune Checkpoint Inhibitor Therapy-Related Graft Intolerance Syndrome in a Failed Kidney Transplant Recipient on Hemodialysis
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Introduction: Immune check-point inhibitors (ICPIs) are monoclonal antibodies against inhibitory receptors on T-cells resulting in anti-cancer activity. The use of ICPIs among kidney transplant (KT) recipients with cancer is controversial, as ICPIs can downregulate immune tolerance and is associated with a higher risk of rejection in functioning allografts. In failed allografts, the effects of ICPIs are unknown. We present a unique case of a patient with a failed KT on maintenance hemodialysis (HD) who developed graft intolerance syndrome (GIS) after ICPI therapy for metastatic renal cell carcinoma (RCC).

Case Description: Our patient is a 66-year-old male with a history of diabetes, RCC and left nephrectomy in 1996. He developed end-stage kidney disease and had a deceased donor KT in 2012. His graft failed 6 years post KT, due to biopsy-proven recurrent diabetic nephrosclerosis. He was started on HD in 2018 and immunosuppression was tapered off. In 2019, he was diagnosed with renal and urothelial cell cancer in the right native kidney and underwent nephrectomy. Ten months later, distant metastasis was detected, and he was started on Nivolumab and Ipilimumab. Twenty-eight days after his 1st cycle of immunotherapy, he had good oncological response, but developed gross hematuria, pain over his allograft, malaise, and anemia consistent with G1S. Urine culture and cystoscopy were normal. A computed tomography scan of the abdomen revealed an enlarged allograft with patchy enhancement and perinephric stranding consistent with GIS. After multidisciplinary discussion, he underwent transplant nephrectomy.

Histopathology revealed grade II chronic active T-cell mediated rejection (TCMR).

Discussion: Although acute graft rejection from ICPI therapy has been documented, this is the first known report of GIS developing with ICPI therapy in a failed allograft. GIS typically occurs within 6-12 months of graft failure. Meanwhile, in functioning allografts, GIS typically occurs after 2 years of therapy. The temporal relation of GIS to ICPI initiation in our patient suggests the potential role of the latter as a trigger for GIS. As ICPI use becomes more prevalent in cancer management, we need to be aware of the potential complications with its use among KT recipients even with failed allografts, which requires multidisciplinary management.

PO2194
Crescendo Glomerulonephritis and Phospholipase A2 Receptor-Positive Membranous Nephropathy in a Lung Cancer Patient on an Immune Checkpoint Inhibitor
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Introduction: Acute kidney injury (AKI) occurs in 3% of patients on immune checkpoint inhibitors (ICPI), usually due to interstitial nephritis, yet the array of ICPI-mediated AKI is not fully understood, with rare reports due to Crescendo Glomerulonephritis (cGN). To date there is no known case of PLA2R-positive Membranous Nephropathy (MN) associated with ICPI. Here we report the first case of ANCA-negative cGN with PLA2R MN, which developed after initiation of ICPI, with response to rituximab (RTX).

Case Description: Nephrology was consulted for AKI and hematuria in a 67-year-old male smoker with lung adenocarcinoma. He started on pembrolizumab and pemetrexed 8 months ago, last doses 3 weeks prior to consult. He developed throat irritation from local irradiation, and pantoprazole was initiated. No NSAIDs, herbal medications or iodinated contrast exposure. Prior to treatment, baseline Creatinine (Cr) was 1.8 mg/dl and urinalysis showed +1 proteinuria. ACE was 112/66, and no edema was present. Cr was elevated at 3.7 mg/dl. UA showed +3 protein, >50 RBC, 10-25 WBC, and no pathologic casts. Renal sonogram was normal. Protein:creatinine ratio (UPC) was 1.52g/l. Complements were normal. Serology workup was negative. Rituximab, APO/MPR, AZA were started. Therapy was discontinued due to diffuse cGN [Glerumeli: necrosis (2/38), cellular crescents (10/38), and fibrocellular

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
The text on the page appears to be a scientific article discussing the treatment of renal disease. It includes references to various conditions and treatments, such as myeloma cast nephropathy and light chain nephropathy. The text is technical and is likely discussing case studies or clinical trials. The page also contains references to other studies and publications, indicating a thorough review of the literature on the topic. The text is formatted in a way that is typical for academic medical journals, with sections such as Introduction, Case Description, and Discussion.
kidney biopsies of patients with monoclonal gammopathies. In addition, detailed EM examination of the tubules is essential to identify the lysosomal abnormalities typical of LCPT.

PO2199

CKD After 225Ac-PSMA617 Therapy in Patients with Advanced Metastatic Prostate Cancer: A Report of Two Cases

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Introduction: A promising therapeutic efficacy has been demonstrated with targeted radionuclide therapy (TRNT) using 225Ac-PSMA617 in patients with advanced metastatic castration-resistant prostate cancer (mCRPC). However, these novel agents may be associated with significant toxicity. As seen in animal models, the multiple alpha particles generated in the decay chain of 225Ac may accumulate in the renal tubular cells, resulting in nephropathy. We report our experience with 225Ac-PSMA617 therapy in 2 patients with advanced mCRPC who developed kidney injury.

Case Description: Patient 1 is a 68-year-old man with widely metastatic mCRPC despite multiple lines of therapy and secondary chronic hyponephrosis with bilateral nephrostomy tubes. He received 3 rounds of 225Ac-PSMA617 in 2-month intervals. Baseline serum creatinine was 1.6 mg/dL (eGFR 44 mL/min/1.73m²) and it increased up to 3.3 mg/dL (eGFR 18 mL/min/1.73m²) after 225Ac-PSMA617 therapy. A biopsy was obtained and revealed severe interstitial fibrosis with ongoing tubular injury and interstitial inflammation. A trial of corticosteroids therapy was attempted with no improvement in kidney function. 225Ac-PSMA617 therapy was discontinued because of related kidney failure. Patient 2 is a 67-year-old man with mCRPC with progression on multiple prior therapies. He first initiated Lu177-PSMA and one year later this was combined with 225Ac-PSMA617 in 2-month intervals. He received 5 rounds of 225Ac-PSMA617 in total, the last round being complicated with grade 3 cytopenias leading to cessation of treatment. Baseline serum creatinine at initiation of TRNT was 1.0 mg/dL (eGFR 82 mL/min/1.73m²). He subsequently developed progressive CKD and serum creatinine was 1.7 mg/dL (eGFR 40 mL/min/1.73m²) on last follow-up.

Discussion: We report 2 cases of progressive kidney disease in the setting of 225Ac-PSMA617 therapy for patients with advanced mCRPC. One underwent kidney biopsy showing tubulointerstitial injury, consistent with 225Ac-PSMA617-related tubular accumulation of toxic nucleotides seen in animal models. This kidney injury was not responsive to corticosteroids therapy. Our case studies emphasized the need for careful assessment and monitoring of kidney function in patients receiving these novel agents.

PO2200

Successful Management of Chronic Ifosfamide Nephrotoxicity with Immunosuppression: A Case Series

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Introduction: Ifosfamide is an alkylating chemotherapeutic agent that causes both acute and chronic kidney injury. Ifosfamide-induced chronic tubulointerstitial nephropathy presents after exposure, by delaying diagnosis, and treatment. Here, we describe three cases of chronic ifosfamide nephrotoxicity, wherein the time-course and outcomes suggest that earlier recognition and initiation of immunosuppression may benefit these patients.

Case Description: Three adult patients with distinct malignancies, status-post at least 3 cycles of ifosfamide chemotherapy, presented to our onco-nephrology clinic for worsening renal function. On average, the patients were referred to our clinic ~8 months after their last dose of ifosfamide. In this period, their serum creatinine (SCr) had risen to a peak ~2.5 mg/dL from ~1mg/dL. The patients reported occasional frothy urine but were otherwise asymptomatic. Urine analysis and microscopy was significant for mild glucosuria/proteinuria, sterile pyuria, and granular casts, with urine protein/creatinine ratio of ~1.2. Autoimmune serologies, complement levels, protein electrophoresis, and renal ultrasound were unremarkable. Kidney biopsies, performed 10 months after the last ifosfamide cycle, demonstrated tubulointerstitial nephritis with moderately advanced interstitial fibrosis. Cytoxicity atypia of the tubular epithelium was consistent with karyomegalic interstitial nephritis (KIN), previously documented in cases of ifosfamide toxicity. It is unclear if prednisone therapy led to improvement and plateau of SCr ~2.1. Curiously, multiple attempts to wean corticosteroids led to worsening SCr and active urinary sediment. In 2 patients, addition of mycophenolate mofetil enabled dose reduction but not cessation of corticosteroids. In all cases, SCr remained stable at ~2.1 after 1 year of follow-up.

Discussion: These cases illustrate the latent presentation and challenging management of chronic tubulointerstitial nephritis secondary to ifosfamide. On average, prednisone was started ~10 months after the last ifosfamide dose, when significant interstitial fibrosis had already developed. Ifosfamide nephrotoxicity and/or resulting inflammation may have also contributed to the failure to stop corticosteroids. Overall, early surveillance, prompt recognition, and long-term immunosuppression is likely important in these patients to stabilize and maintain renal function.

PO2201

Hyperphosphatemia in the Setting of Fibroblast Growth Factor Receptor Inhibitors

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Introduction: Fibroblast growth factor (FGF)-23 is a phosphaturic hormone which works by reducing apical membrane expression of sodium-phosphate co-transporters in the proximal renal tubule and thus decreasing phosphate re-absorption. Fibroblast growth factor receptors (FGFR) are ubiquitously expressed in different tissues and become altered in various types of cancer. TAS-120 is one of several pan-FGFR inhibitors currently in clinical trials for use in patients with cholangiocarcinoma. Hyperphosphatemia is seen in more than 70% of patients on this therapy.

Case Description: A 44-year-old female with metastatic intrahepatic cholangiocarcinoma with progressive disease despite conventional therapy was started on TAS-120. Fifteen days into treatment she developed pain in knees and hips and was noted to be hyperphosphatemic to 7 mg/dL. She was initiated on sevelamer but given persistent hyperphosphatemia to 6.4 mg/dL, acetazolamide, calcitriol and phytodiolone were added. Despite this, phosphorus remained elevated at 5.8 mg/dL; addition of alendronate 35mg weekly alongside dose reduction of TAS-120 led to sustained improvement in serum phosphorus levels. A 49-year-old male with a history of cholangiocarcinoma was started on TAS-120. Four days into treatment he developed calf pain and was noted to be hyperphosphatemic to 7.3 mg/dL. The medication was briefly stopped and he was initiated on sevelamer with improvement in phosphorus to 2.7 mg/dL. Resumption of TAS-120 led to recurrent hyperphosphatemia for which acetazolamide was initiated. Three months after initiation of TAS-120 he had ongoing hyperphosphatemia; following dose reduction of TAS-120 and starting phytodiolone, probencid and calcitriol, serum phosphorus levels remained within normal limits.

Discussion: FGFR-induced hyperphosphatemia has a similar clinical presentation as hyperphosphatemic familial tumoral calcinosis (HFTC) with debilitating joint pain and tissue calcification. The current management of hyperphosphatemia relies mainly on dietary modification and gastrointestinal phosphate binding that were insufficient for our patients. The hyperphosphatemia and calciphylaxis pain was successfully treated with phosphaturic medications (acetazolamide, calcitriol) and alendronate. Phytodiolone (vitamin K) interferes with matrix Gla protein, a tissue inhibitor of calcification.

PO2202

Direct Renal Infiltration in Chronic Lymphocytic Leukaemia: A Case Report

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Introduction: CLL is a haematological malignancy characterised by lymphocytosis with uncontrolled accumulation of B lymphocytes. It is most commonly a disease of older adults with co-morbidities limiting treatment options. Renal involvement of CLL is common with autopsy findings showing up to 90% involvement however direct infiltration rarely causes clinically significant renal impairment.

Case Description: A 78 year old man was admitted to hospital with acute on chronic kidney injury, creatinine 759umol/l from 200umol/l. He had background of CLL and a supra-pubic catheter. His total white cell count was 33.9x10⁹/L and lymphocyte count of 27.6x10⁹/L. His SPC was draining with no recent obstruction or infection. An US showed no hydronephrosis or cortical scarring. A renal biopsy was performed and a tunnelled dialysis catheter inserted to commence haemodialysis. Biopsy showed a diffuse heavy infiltrate of lymphoid cells in the interstitium with no immune deposition and 70% fibrosis. Immunohistochemistry staining positive for CD20 and CD5. We started a tyrosine kinase inhibitor however after 3 months he remained dialysis dependent and died from COVID pneumonia.

Discussion: Renal injury is seen in approximately 16.2% of patients during disease course in CLL. This can be due to tumour lysis syndrome, immune deposits, cyroglobulinaemia, obstruction to due lymphadenopathy and direct infiltration of B lymphocytes as seen in this case. Indications for commencing treatment for CLL usually involve evidence of narrow failure, massive lymphadenopathy and significant B symptoms. In this case treatment was initiated to manage the patients’ renal involvement. It is important to pursue a renal biopsy in patients with CLL as it may reveal an indication to commence treatment.
PO2203

Attack of the Clones: Leukemia and Myeloma
Sara Wong, Shreya Patel, Elizabeth A. Alaimo, Shanaz Azad, Pankaj Jain, Tauseef A. Sargurun, Francisca Health Inc., Mishawaka, IN.

Introduction: Chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) are both neoplastic diseases that are monoclonal tumors of differentiated B-cells that rarely occur simultaneously. There is disagreement and conflicting evidence as to whether these seemingly distinct disorders may arise from identical clones. In some cases MM maybe diagnosed up to 15 years after the established diagnosis of CLL. We describe a rare case of a patient with renal failure and nephrotic range proteinuria where both CLL and MM were diagnosed concomitantly from a single renal biopsy.

Case Description: 59 o/o Indian male with COPD, DM-type 2, HTN, recent pseudomonas aeruginosa pneumonia presented with bilateral temporal headaches and fevers. Work-up revealed creatinine: 1.7mg/dl, UPCR: 6.6 g/g, free kappa/lambda ratio of 0.25 and mildly depressed C3 and C4. Renal biopsy showed diffuse proliferative and crescentic glomerulonephritis with IgG lambda light chain restriction, CD20 positive lymphocytic interstitial infiltrate, ANA and diabetic glomerulopathy. EM also revealed subepithelial hump-shaped deposits and abundant glomerular neutrophils suggesting a component of post-infectious GN. Both flow cytometry and bone marrow biopsy revealed monocytic B-lymphocyte population with aberrant expression of CD5 and CD23 consistent with the diagnosis of CLL. The patient was treated with cyclophosphamide and dexamethasone and is currently stable on Brutinib with a creatinine of 1.3mg/dl.

Discussion: CLL is a common hematologic malignancy that has many systemic complications. Autopsies have shown that 90% of CLL patients have renal infiltration; however there is seldom renal impairment. This is a rare case of renal CLL infiltration causing type-I cryoglobulinemia with IgG lambda monoclonal gammopathy of renal significance. Early diagnosis with renal and bone marrow biopsy and subsequent treatment with immunosuppressive therapy is crucial.

PO2204

Should We Give the Green Light to Green Top Tube? Reverse Pseudohyperkalemia in Leukemia Patient
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Introduction: Here we described a 69-year-old woman presented with hyperleukocytosis with reverse pseudohyperkalemia. This is also the first case of reverse pseudohyperkalemia in Philadelphia chromosome positive acute lymphoblastocytic leukemia.

Case Description: The 69-year-old woman was rushed to our emergency department due to progression of dyspnea for one week. Upon lab examination, hyperleukocytosis (>500000/uL) with blasts that suggestive of acute leukemia. Notably, marked hyperkalemia (11.6 mEq/L) with normal renal function was noted but there is no typical electrocardiogram change. High LDH(3393 U/L) and low haptoglobin(<7.88 mg/dL) also noted. After clarification, the blood tube that had result of hyperkalemia is sodium heparin. We restet potassium by using serum separate tube with 5 minutes of 5000 revolutions per minute, revealing serum potassium level 3.8 mEq/L. Reverse pseudohyperkalemia was impressed. She received leuporphin and chemotherapy for leukostasis. The bone marrow biopsy later confirmed Philadelphia chromosome positive acute lymphoblastocytic leukemia. Reverse pseudohyperkalemia resolved after leukocyte return to normal level.

Discussion: Pseudohyperkalemia is suspected when the measured potassium is high but the patient does not manifest signs of hyperkalemia, such as abnormal electrocardiogram. Pseudohyperkalemia is falsely elevation of serum potassium levels without elevation of plasma potassium levels, commonly occurred in patients with hematological disease. Heparin anticoagulated plasma samples provide more accurate measurement of the true potassium level in these patients and sodium heparin (green top) tube is widely used. However, in reverse pseudohyperkalemia, serum potassium is within normal range, and plasma potassium falsely elevated, such as in our patients. The heparin in the plasma collection tube causes damage to the cell membrane during processing and centrifugation in the context of fragile cells of hematologic malignancy. Reverse pseudohyperkalemia had been reported in chronic lymphocytic leukemia patient. To our knowledge, this is the first case report of reverse pseudohyperkalemia in Philadelphia chromosome positive acute lymphoblastocytic leukemia patient. This case reminds us that potassium obtained using heparin tube is not panacea to get accurate level, and reverse pseudohyperkalemia is a must-known phenomenon for clinicians.

PO2205

A Rare Case of Composite Lymphoma with Kidney Infiltration of Nodal Marginal Zone B Cell Lymphoma and Three Different Types of Cast Nephropathy
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Introduction: We present an interesting case of composite lymphoma (nodal marginal zone B-cell lymphoma and multiple myeloma) characterized by the rare kidney invasion of the nodal marginal zone B-cell lymphoma and three different types of cast nephropathy present simultaneously in patient with multiple myeloma.

Case Description: A 57-year-old Chinese male was admitted to hospital for proteinuria. He reported foam urine, abdominal distension, fatigue, and weight loss of 5 kg within one month. Laboratory tests demonstrated hemoglobin 108 g/L, blood urea nitrogen 27.1 mmol/L, serum creatinine 639.1 umol/L and urine acid 547 umol/L. The 24-hour urinary protein and microalbumin was 3193.3mg and 42.3mg, respectively. Immunofixation electrophoresis (IFE) showed IgD-Lambda Lambda monoclonal protein. MRI identified diffuse osteo-skeletal lesions. Bone marrow aspirate and biopsy demonstrated a hypercellular marrow with extensive plasma cell infiltration. Besides, multiple lymphenopathies in both axillary and bilateral Inguinal lymph nodes were noticed. Lymph node biopsy suggested a nodal marginal zone B-cell lymphoma. To explore the involvement of kidney injury, we performed a kidney biopsy. Surprisingly, we found three types of nephropathy (myeloma casts, light chain crystal structure and light chain amyloidosis). At the same time, we also found focal lymphocyte infiltration, which are confirmed of nodal marginal zone B-cell lymphoma by immunohistochemistry with various molecule markers. To further explore the relationship between the two tumors, we performed the whole genome exon sequencing of the bone marrow and lymph nodes, surprisingly we found the similar mutation sites (V1982I of ARID1A gene) in both tissues, suggesting that the two tumors might originated from the same mutation. After BCT chemotherapy and PAD-T chemotherapy, urea nitrogen and blood creatinine decreased, the patients get rid of hemodialysis.

Discussion: nodal marginal zone B-cell lymphoma infiltrate kidney only is very rare. Also three kinds of nephropathy (myeloma casts, light chain crystal structure and light chain amyloidosis), present simultaneously is also very rare. And the sequencing of the genome exon suggested that nodal marginal zone B-cell lymphoma might developed in to multiple myeloma in bone marrow micro-environment.

PO2206

Breast Cancer-Associated Podocytopathy
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Introduction: Podocytopathies such as FSGS have not been classically associated with solid malignancy. Here we present a case of a female with a diagnosis of FSGS and its association bilateral lobular carcinoma in situ of the breast.
**Case Description:** A 52 year old Sri Lankan female with history of DM2 (with no prior proteinuria) was referred for sudden onset of proteinuria. The patient first reported profound foamy urine in October 2017 with workup significant for sub-nephrotic proteinuria of 2 gram with normal serum creatinine and albumin. A kidney sonogram was unremarkable. Further workup was negative for infectious, autoimmune, vasculitis and para-protein etiologies. The patient was started on Lisinopril 10mg, however proteinuria worsened to 12.6 grams thereby switch to losartan (100mg daily) with slight improvement in proteinuria. A kidney biopsy was performed which showed focal global glomerulosclerosis secondary to adaptive changes with minimal fibrosis with no diabetic nephropathy related changes seen. Light microscopy showed globally sclerosis (9%) and IFTA (5-10%). Immunofluorescence microscopy showed no evidence of primary podocyte disease, immune complex-mediated disease or para-protein deposition disease. The patient was managed conservatively on anti-proteinuric agent. Almost a year after the diagnosis of FSGS, patient was diagnosed with bilateral lobular carcinoma in situ (breast) with atypical lobular hyperplasia. She underwent lobectomy and started on anastrozole. Following cancer surgery and initiation of hormonal therapy, she noticed resolution of her fatigue, urine foamy and proteinuria (repeat U/P Cr <23 mg (Figure 1)).

**Discussion:** Our case demonstrates a potential link of the diagnosis of lobular ductal cancer of the breast with a diagnosis of FSGS. Interestingly, the FSGS diagnosis preceded the diagnosis of the breast cancer. While the proteinuria came into partial remission with conservative management, a dramatic resolution of FSGS was noted post-surgery and hormonal therapy for the breast cancer.

**PO2207**

**Snapshot of AKI Profile in Patients in Oncology Settings: A Single-Center Experience**

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**Introduction:** Acute kidney injury (AKI) may result from the cancer itself, treatment of cancer or associated complications. In cancer patients with AKI complete recovery of renal function was seen in 82% and chronic dialysis was needed in 6% of patients. Overall severity of illness, age, and functional status have more of an impact on prognosis than underlying malignancy, and the presence of cancer may not be an absolute exclusion criterion for withholding RRT. Hospital mortality approaches 80% in cancer patients with AKI. Cancer associated AKI (CA-AKI) is very prevalent with reported incidence of 12% to 49%. We tried to look into incidence, etiology and outcome of AKI in a tertiary care cancer hospital.

**Case Description:** For two consecutive months all patients admitted in ICU at Basavataramak Indo-American Cancer Hospital were observed for development of AKI with K/DOQI criterion. We found 45 patients who developed AKI out of 83 total ICU admissions (54.21%). Chronic kidney disease was present in 17 patients (37.77%), diabetic kidney disease being the commonest (64.70%). The commonest etiology of AKI was sepsis (77.8%) and septic shock was present in majority of these patients (66.7%). Other causes of AKI were hypercalcemia (4.4%), chemotherapy associated (44.4%), obstructive nephropathy (8.9%). Metabolic acidosis was predominant finding (75.6%) with oliguria being least common (26%). Hematological malignancies were frequently associated with AKI (33.3%) followed by gastrointestinal tract tumors (24.4%). Urological malignancies were least associated with AKI (6.6%). Large number of patients required renal replacement therapy (RRT) (48.9%). SLED was commonest modality (n=15; 68.1%) of RRT followed by CRRT/CVVHDF (N=8; 34.78%). Regional citrate anticoagulation was commonest anticoagulation used (62.5%). 46% patients recovered (n=15; 68.18%) of RRT followed by CRRT/CVVHDF (N=8; 34.78%). Urological malignancies were least associated with AKI (6.6%). Large number of patients associated with AKI (33.3%) followed by gastrointestinal tract tumors (24.4%). Hematological malignancies were frequently associated with AKI (CA-AKI) is very prevalent with reported incidence of 12% to 49%. We tried to look into incidence, etiology and outcome of AKI in a tertiary care cancer hospital.

**PO2209**

**Narsoplimab, Another Tool in the Management of Thrombotic Microangiopathy in Stem Cell Transplant Recipients**

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**Introduction:** Thrombotic microangiopathy (TMA) is a severe complication in recipients of hematopoietic stem cell transplants (HSCT). Its treatment remains controversial due to its complex and not fully understood mechanism. As more emerging evidence supports the role of complement dysregulation in the observed endothelial injury, anti-complement medications have emerged as a potential therapy. Narsoplimab is an anti-complement therapy that was granted FDA designations for HSCT-TMA as a breakthrough therapy. We hereby report the first case of Narsoplimab use in a HSCT adult recipient with TMA in the United States.

**Case Description:** A Caucasian women in her early 70s with medical history of relapsed B- cell acute lymphocytic leukemia post allo genetic HSCT who was treated with Venetoclax and MiniCVD regimen with a hospital course significant for E. coli bacteremia, CMV pneumonia and acute kidney injury. Creatinine rose from 1.6 to 3.3 mg/dl over 2 weeks, despite the discontinuation of tacrolimus and treating the sepsis. Urealysis was significant for pyuria, hematuria, granular casts and 1 proteinuria. She had elevated Cr59 and LDH levels (363 mg/ml and 326 U/L respectively) with schistocytes noted in blood smear, suggestive of TMA. Renal biopsy was significant for ATN and acute kidney injury, for which we decided to treat her with anti-complement therapy with Narsoplimab. She received twice weekly doses for 4 weeks and had significant improvement in renal function (Cr improved to 0.8 mg/dl), however she developed worsening respiratory status secondary to possible diffuse alveolar hemorrhage and family withdrew care in week 4 of therapy.

**PO2208**

**A Patient with Hyper-Warburgism Successfully Treated with Peritoneal Dialysis**

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**Introduction:** The combination of hypoglycemia and lactic acidosis in cancer patients is usually known as hyper-warburgism.

**Case Description:** A 74-year-old Thai man presented to our hospital with symptomatic hypoglycemia. He was previously healthy, no history of diabetes. Further investigation revealed hyperuribinemia, heptospomenegomly and first-diagnosed HIV infection. Computerized tomography of abdomen showed large liver mass with multiple intraabdominal lymphadenopathy. Liver mass biopsy showed round cell neoplasm with immunochemistry staining compatible with Burkitt lymphoma: positive for CD20, Bcl-6, CD10, CD-20, Ki67 100%, and negative for Bcl-2. His lymphoma was initially treated with high-dose dexamethasone. During investigation and initial treatment, our patient developed acute kidney injury (AKI) with severe lactic acidosis. Hypoglycemia persist even he received intravenous glucose 18 g/hour. Serum ketone, insulin and c-peptide were normal. We suspected that he had hyper-warburgism due to Burkitt lymphoma, which was not respond to dexamethasone. Due to HIV seropositive status, we chose automated peritoneal dialysis (PD) for AKI and severe metabolic acidosis in this patient. PD dose in this patient was 19 liters per day. After PD initiation, the patient gradually recovered, with serum lactate dramatically decreased and intravenous glucose could be stopped. Clinical and laboratory parameters, including major clinical events, were shown in figure 1. After lactic acidosis resolved, we decided to treat this patient with chemotherapy. Unfortunately, this patient died later due to fungemia, neutropenia and septic shock.

**Discussion:** Hypercatabolic state such as hyper-warburgism was usually treated with continuous renal replacement therapy (CRRT). Here, we presented a case of hyper-warburgism successfully treated with PD. We hoped this report might offer alternative treatment in patients who unable to undergo CRRT.
Discussion: Narsoprilat is a human monoclonal antibody that inhibits mannose-binding lectin associated serine protease-2 (MASP-2) which is an essential enzyme in the complement system leading pathway. It is designed to prevent endothelial injury without interfering with other complement pathway roles. Data from phase 2 study showed an improvement in patient survival and TMA blood markers (LDH, haptoglobin, and platelet count). It might improve renal function as well as its inhibition to lectin activation in disease path can ameliorates proteinuria induced kidney injury. However she didnot have improvement in her platelet count, LDH and C3b9 levels. Further studies are ongoing (Phase 3 trials in IgA nephropathy and HSC-TMA) to evaluate such renal benefits.

PO2210
The Histopathologic Spectrum of Kidney Biopsies in Patients with Thymoma, Myasthenia Gravis, or Both: A Report of 24 Cases from a Single Institution
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Introduction: Nephropathy in patients (Pts) with thymic diseases such as thymoma and myasthenia gravis (MG) is rare and has been the subject of case reports. Previously, 93 cases have been reported from multiple institutions, and of these, common diseases are minimal change disease (MCD; 45.2 %), membranous nephropathy (MN; 19.4 %), and primary focal segmental glomerulosclerosis (FSGS; 9.7 %). Here we characterize the spectrum of kidney biopsy findings in 24 cases from a single institution.

Case Description: Total 40,268 renal biopsy cases from 2005 through 2019 at Cedars-Sinai Medical Center were reviewed. 24 cases (0.0596 %) of Pts have history of thymoma and/or MG. Main pathological diagnoses are following: MCD (10 cases; 41.7%); Tubulointerstitial nephritis (TIN; 3 cases; 12.5 %), Immune complex-mediated glomerulonephritis (ICGN; 2 cases; 8.3 %); Diabetic glomerulosclerosis (2 cases; 8.3 %); acute tubular injury/necrosis (ATIN) with myoglobin casts (2 cases; 8.3 %); ATIN (1 case; 4.2 %); IgA nephropathy (1 case; 4.2 %), MN (1 case; 4.2 %), secondary FSGS (1 case; 4.2 %), and Monoclonal Ig deposition disease (1 case; 4.2 %).

Discussion: Consistent with previous report, MCD is the most common renal lesion in Pts with thymic diseases. However, we experienced only one case of MN and no primary FSGS, the 2nd and 3rd common diseases in the reports. We, instead, observed kidney diseases that haven’t been reported before: TIN, and ATIN/ATN with myoglobin casts. Of TIN cases, 1 showed granulomatous interstitial inflammation without infection; and 1 case showed acute tubulitis with immune complex deposits both in mesangium and along tubular basement membranes. In addition, 40 % of MCD cases showed an atypical feature: IC deposits in mesangial area. The possible mechanisms of thymic disease-associated nephropathy include T cell dysregulation, IC formation containing tumor antigen, and effects of tumor-releasing lymphokines. In conclusion, this is the largest and unique case series of nephropathy in Pts with thymic disease from a single institution.

PO2211
Erdheim-Chester Disease: A Rare Cause of Bilateral Renal Artery Stenosis and AKI
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Introduction: Erdheim-Chester disease (ECD) is a rare, non-Langerhans cell histiocytosis affecting multiple organ systems. We report a case of ECD with bone marrow, cardiac, vascular and renal involvement, presenting with hypertensive emergency and AKI, responsive to endovascular stenting and peg-interferon.

Case Description: A 58-year-old male with metastatic carcinoma of unknown primary presented with hypertension, afebrile, and without significant proteinuria or nonproteinuric nephrotic syndrome. His symptoms included fatigue, poor oral intake, 5kg weight loss and lower limb oedema. On exam he had elevated blood pressure but no signs of volume overload. Initial supportive treatment did not improve kidney function and hemodialysis was initiated due to worsening azotemia and persistent nausea and vomiting suspicious for uremia. Renal biopsy showed diffuse acute on chronic interstitial nephritis with perversly lymphoid aggregates of monoclonal CD20+ B-cells positive for CD5 and Cyclin-D1 consistent with ECD. No immunoglobulin classes with c-light chain (KLC) predominance in glomeruli and lymphoid infiltration with KLC in the interstitium on immunostaining. MCL was confirmed with FC and excisional LN biopsy. Prednisone/Rituximab/Bendamustine therapy led to improvement in kidney function and proteinuria.

Discussion: MCL can cause differential kidney involvement from direct tumor infiltration to MCL-associated glomerulonephritis. Therefore, correct diagnosis with renal biopsy and prospective registries are needed to generate data about differences in outcomes in MCL with various kidney involvement.

PO2213
Cystatin C Measurement Improves Renal Function Estimation with Selpercatinib Use
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Introduction: Selpercatinib (LOXO-292) is a selective RET inhibitor that is approved for the treatment of RET-dependent lung and thyroid cancers. In the LIBRETTO-001 trial of selpercatinib, a treatment-emergent increase in serum creatinine was noted in ~18% of patients. Creatinine is mainly excreted by glomerular filtration and is partly secreted like creatinine. It is therefore not affected by transporter inhibitors and may be a better marker for monitoring kidney function and proteinuria. Cystatin C is an alternative marker that is freely filtered, completely reabsorbed and not secreted like creatinine. It is therefore not affected by transporter inhibitors and may be a better marker for monitoring kidney function and proteinuria. Cystatin C is an alternative marker that is freely filtered, completely reabsorbed and not secreted like creatinine. It is therefore not affected by transporter inhibitors and may be a better marker for monitoring kidney function and proteinuria.

Case Description:
- A 58-year-old male with metastatic RET fusion-positive lung cancer who progressed on cabozantinib started selpercatinib. His pre-treatment creatinine was 0.8mg/dl and increased to 1.8mg/dl after 1 year of therapy. Urine sediment was bland with increased to 4.7mg/dL; unremarkable electrolytes and liver function tests. A CT angiogram showed extensive, irregular mural thickening of the aorta present for 2 years, right atrial mass, highly flow void characteristic of both renal arteries and left vertebral artery occlusion. Review of prior lower limb CT imaging showed bilateral, symmetrical sclerotic bone infiltrates in the diaphyses and metaphyses, corresponding to the regions of PET avidity, confirming the diagnosis of ECD. Echocardiogram and cardiac MRI confirmed a 21.7 x 18.3mm right atrial mass. Selpercatinib was confirmed via right saphenous vein biopsy showing sclerotic xanthogranulomatous histiocytosis(CD68+, CD163+, CD1a-) reaction. Despite taking 5 classes (7 agents) of anti-hypertensives at maximal doses, her blood pressure was suboptimally controlled. After bilateral endovascular renal artery stenting, anti-hypertensive requirement reduced to 2 agents and renal function improved to better than pre-AKI levels. She is receiving peg-interferon γ2a and prednisolone for ECD.

Discussion: The disease affects renal arteries in 18-27% cases and should be considered as a cause of renal artery stenosis in older patients with multisystem anomalies. Renal stenting in this subset can improve hypertension and renal outcomes. The disease has characteristic radiological findings and the diagnosis is frequently reliant on imaging. Histological examination is often not sufficient to confirm the diagnosis. ECD diagnosis is essential for treatment of the underlying disease process.

PO2212
Renal Involvement as Initial Presentation of Mantle Cell Lymphoma: A Case Series
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Introduction: Mantle cell lymphoma (MCL) rarely affects kidneys. We present 2 cases with different spectrum of kidney involvement in MCL.

Case Description:
The 1st case was a 63-yr old male with incidental finding of Serum creatinine (SCr) of 10mg/dl. Chronic lymphocytic leukemia was diagnosed 2 weeks prior via peripheral blood analysis & flow cytometry (FC) done due to constitutional symptoms and headaches for which he was using daily ibuprofen for several months. On exam he had elevated blood pressure but no signs of volume overload. Initial supportive treatment did not improve kidney function and hemodialysis was initiated due to worsening azotemia and persistent nausea and vomiting suspicious for uremia. Renal biopsy showed diffuse acute on chronic interstitial nephritis with perversly lymphoid aggregates of monoclonal CD20+ B-cells positive for CD5 and Cyclin-D1 consistent with MCL. No significant immunostaining was found. Bone marrow biopsy confirmed renal biopsy findings and diagnosis of MCL. Until last follow up, the patient refused chemotherapeutic regimens and remained in analysis dependent. The 2nd case was a 73-yr old male with incidentally found of SCr of 1.9mg/dl in association with glomerular hematuria and grade A3 proteinuria. He had no constitutional symptoms and had normal physical exam except for presence of diffuse lymph node (LN) enlargement. Renal biopsy was obtained and showed MPGN-pattern with 25% crescents on light microscopy, presence of all immunoglobulin classes with k-light chain (KLC) predominance in glomeruli and lymphoid infiltration with KLC in the interstitium on immunostaining. MCL was confirmed with FC and excisional LN biopsy. Prednisone/Rituximab/Bendamustine therapy led to improvement in kidney function and proteinuria.

Discussion: MCL can cause differential kidney involvement from direct tumor infiltration to MCL-associated glomerulonephritis. Therefore, correct diagnosis with renal biopsy and prospective registries are needed to generate data about differences in outcomes in MCL with various kidney involvement.
creatinine is likely attributed to the drug inhibitory effect on creatinine secretion. Cystatin C may be a better measure of renal function in patients receiving MATE-1 inhibitors such as selpercatinib.

**Discrepancy in Serum Creatinine and Cystatin C Trends**

**PO2214**

**ALECT 2 and Hepatocellular Carcinoma: An Intriguing Association**

**Introduction:** Amyloidosis derived from leukocyte chemotactic factor 2 (ALECT2) is the third most common type of renal amyloidosis in the United States. The incidence of ALECT2 is highest among Hispanics and there is a predilection for involvement of the kidney and liver with sparing of the heart. We report a case of hepatocellular carcinoma (HCC) in a patient with ALECT2.

**Case Description:** A 69-year-old Hispanic man with chronic kidney disease secondary to ALECT2 and monoclonal gammopathy of undetermined significance was admitted for constipation and distended abdomen. Creatinine on admission was 1.9 mg/dL and he was initiated on dialysis. Imaging revealed cirrhosis, ascites and two liver masses involving the portal vein. Alpha fetoprotein was 7123 ng/mL and he was diagnosed with multifocal HCC. Evaluation for hepatitis, autoimmune disease and other etiologies for chronic liver disease was negative and cirrhosis was presumed to be secondary to ALECT2. Based on the Barcelona Clinic Liver Cancer staging, he was given a stage D. His functional status precluded any liver directed therapies or systemic chemotherapy and he failed to meet the Milan criteria for liver transplantation. Following a discussion of the prognosis he was transitioned to palliative care.

**Discussion:** ALECT2 is a recently described form of systemic amyloidosis that has quickly emerged as a common and possibly underdiagnosed cause of systemic amyloidosis particularly in patients of Hispanic ancestry. ALECT2 can involve various organs but usually spares the heart and brain. ALECT2 in association with HCC has not been reported to date. Interestingly in one study, expression of LECT2 in human kidney was not found. The authors speculated that ALECT2 may not be immunoreactive to CD68 and S100 protein which is consistent with Rosai-Dorfman Disease.

**PO2215**

**A Case of Extraneal Rosai-Dorfman Disease Confirmed by Renal Biopsy**

Interciency and targeted therapy and hence, it is imperative not to misdiagnose ALECT2 as amyloidosis to avoid harmful chemotherapy.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
SLE, however, during the systemic screening, lung adenocarcinoma was accidentally detected, and thoracoscopic right middle lobectomy was performed. Seven months after surgery, she had an exacerbation of erythema on the face and bilateral arms, arthralgia and urinary proteins, with elevated anti-ds-DNA antibodies and decreased serum complement levels. The dose of PSL was increased, but the symptoms did not improve, when multiple intrapulmonary metastases were detected, indicating recurrence of lung adenocarcinoma. The previous lung specimens revealed a high expression of PD-L1 and positive ROS-1 fusion gene, thus tyrosine kinase inhibitor (crizotinib) was selected as the anti-cancer therapy instead of anti-PD-L1 antibodies. Interestingly, urine protein and erythema/arthralgia improved and the size of lung tumor reduced.

Discussion: Crizotinib is a molecular targeting agent with non-receptor-type tyrosine kinase inhibitor action that competitively binds to the ATP binding site of EML4-ALK tyrosine kinase, resulting in signal transduction inhibition. In this case, the molecular targeting drug induced improvement of lupus nephritis along with regression of lung cancer, suggesting that tyrosine kinase inhibition may be effective for lupus nephritis.

PO22218
Paraneoplastic Minimal Change Disease Associated with High-Grade Neuroendocrine Tumor
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Introduction: Minimal Change Disease (MCD) is usually associated with Lymphoma. Leukemia and solid tumors like Lung Cancer, Renal Cell Carcinoma and Thymoma but data on incidence of paraneoplastic glomerular disease are lacking. To our knowledge, only two cases of neuroendocrine tumor (NET) presenting with Paraneoplastic MCD related to NET has been reported as a 47-year-old female patient with diabetic mellitus diagnosed with nephritic syndrome and renal biopsy was suggestive of minimal change disease.

Case Description: A 47-year-old-man with history of well-differentiated metastatic NET (not on therapy) and HTN admitted for dyspnea and anasarca for two weeks. His labs were significant for: Hgb 9.0 g/dl, plt (platelets) count 397k, ALK (anaplastic lymphoma kinase) 1.9 g/dl, prot (protein)uria of 4.3 g/day and Na 118 mmol/L. IV diuretics with albumin infusion initiated, which improved his kidney function. Serologies and proteinuria work-up – negative. Renal biopsy performed for nephrotic syndrome, showed prominent podocyte foot process effacement with mild acute tubular necrosis and mild glomerular sclerosis. Diagnosed with paraneoplastic MCD from metastatic NET and treatment with steroids initiated. Chemotherapy not started because of the overall decline in his clinical status and increased tumor burden. One week after steroids, his proteinuria was 42 g/day, and steroid doses were increased. Three weeks later, proteinuria decreased to 6 g/day and his symptoms improving. Unfortunately, he suffered further kidney injury because of hypotension and hemodialysis initiated one month later.

Discussion: The most common paraneoplastic glomerular disease is membranous glomerulopathy in patients with breast cancer, but MCD should be kept on the differential as well. Like membranous nephropathy, remission of MCD has been reported on ablation of the tumor, suggesting a paraneoplastic process, though the precise mechanisms are not fully understood. In our case, since the patient did not qualify for chemotherapy because of increased tumor burden, steroids were initiated which helped in part to reduce symptoms. The etiology of glomerulopathy in cancer does not appear to be related to tumor burden, metastatic spread or the site or extent of invasion, but to the secretion of substances from the tumor cells. Kidney biopsy should be performed early, as prompt diagnosis is important to ensure patients do not receive ineffective and potentially harmful treatments.

PO2219
Management of IgA Nephropathy and Concomitant Breast Cancer
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Introduction: Immunoglobulin A nephropathy (IgAN) is the most common glomerulonephritis worldwide. Although treatment guidelines have been established, there is little known about the management of IgAN in the setting of solid malignancy. Herein we describe two cases of IgAN and breast cancer diagnosed at our center.

Case Description: Case 1: 42-year-old female with newly diagnosed breast cancer 3 months ago presented to the clinic for acute kidney injury (AKI) (Cr) 3.5mg/dl from baseline 1.1-1.3mg/dl. Chemotherapy was started one week ago with doxorubicin and cyclophosphamide (ddAC). Two months prior to cancer diagnosis, her doctor noted 4.9g of protein in the urine with few RBCs. She now has 4g of protein with >50 RBCs. She underwent kidney biopsy which showed IgAN (M1 E1 S1 T2 C1). She received a 3g pulse of methylprednisolone (MP) followed by prednisone taper that was shortened to 3 months in light of degree of chronicity on biopsy and concurrent immunosuppressive ddAC treatment with 4 cycles total. Creatinine stabilized at 1.08mg/dl 9 months after last ddAC cycle and proteinuria improved to 1g after re-initiation of losartan. Case 2: 38-year-old female presents to the renal clinic with AKI (Cr 1.8mg/dl from baseline 1.0mg/dl), gross hematuria and nephrotic range proteinuria that were detected incidentally in the emergency department, where she was seen for sore throat after her first 2 monthly ddAC cycles for the new diagnosis of breast cancer. She has a history of arthralgias associated with high citric citrullinated peptide, low myeloperoxidase titers and intermittent hematuria that led to a kidney biopsy demonstrating moderate focal global sclerosis without immune deposits or vasculitic lesions 4 years prior. Her symptoms improved on hydroxychloroquine which she stopped at the time of cancer diagnosis. Her kidney biopsy now shows IgAN (M1 E1 S1 T2 C1) for which she received a 1.6g pulse of MP followed by prednisone tapered over 5 months. She completed 3 cycles of ddAC. Creatinine improved to 0.9mg/dl and proteinuria reduced from 7g to 0.5g.

Discussion: These cases highlight the complexity in management of IgAN while patients are undergoing treatment for a concurrent malignancy. Temporal relationship of IgAN and malignancy is unclear, but suggests potential value of cancer screening of patients with newly diagnosed IgA nephropathy.

PO2220
Sezary Syndrome with Renal Involvement
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Introduction: Sezary Syndrome is a cutaneous T-cell lymphoma that presents with erythroderma, lymphadenopathy, and circulating malignant T cells. While involvement of the spleen, liver, bone marrow and lung are well documented, kidney involvement is rare. We present a case of acute kidney injury (AKI) due to biopsy-proven T cell lymphoma invasion of the kidneys.

Case Description: A 69-year-old female with a history of cutaneous T-cell lymphoma was admitted to the oncology service with AKI. Serum creatinine (sCr) 3.3mg/dl (baseline 0.6mg/dl), urine protein-to-creatinine ratio 2.5g/g, urine sediment bland and renal ultrasound unremarkable. A PET scan, performed to evaluate systemic disease burden, revealed diffuse kidney enlargement with high FDG uptake throughout the renal parenchyma. A kidney biopsy was performed Light microscopy showed diffuse interstitial infiltration by atypical small lymphoid cells and prominent focal apoptosis with apoptotic bodies and focal interstitial hemorrhage. The lymphoid cells had the same immunophenotype as the cutaneous T cell lymphoma. The tumor had slight segmental wrinkling of capillaries and glomerular basement membranes, and segmental podocyte swelling. She also had leptomeningeal involvement. Treatment included dexamethasone, systemic and intrathecal doxorubicin, melphalanext, and cytarabine. SCr returned to baseline 2 weeks later and her renal function improved, with resolution of AKI. Blood pressure normalized and some of her skin lesions resolved. On follow up, she was losing weight and had a peak albumin level of 2.0g/dl. Despite full evaluation, there was no evidence of tumor recurrence.

Discussion: AKI caused by kidney involvement in Sezary syndrome has only been reported via case reports. The mechanism of AKI is thought to be tubular compression by the lymphomatous infiltrates infinging tubule function and peritubular capillary blood flow. Our patient’s biopsy supports this mechanism. Her AKI resolved with urgent corticosteroids and chemotherapy. Further reporting is needed on the prevalence of this condition and nephrologists should consider renal lymphomatous invasion when evaluating AKI in those with cutaneous T-cell lymphoma

PO2221
Belatacept-Induced Post-Transplant Lymphoproliferative Disorder of the Spleen That Spontaneously Resolved on Withdrawal of the Agent
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Introduction: PTLD (Post-Transplant Lymphoproliferative Disorder) is a dreaded complication of allograft transplant. Compared to CNIs, allograft rejection prophylaxis with Belatacept is less nephrotoxic, but carries a higher risk of PTLD. B-cell lymphoma is an aggressive malignant neoplasm that arises from B lymphoid cells and is the most common type of PTLD, with high mortality in renal transplant recipients. We report a 67-year-old AAM 2 years status-post deceased-donor transplant was admitted for altered mental status, nausea, vomiting, fever of unknown origin, and weight loss. He was found to have splenomegaly on CT without other evidence of adenopathy. LHD was elevated. Patient underwent brain MRI, PET scanning, IVM and LP, all of which were normal. A full ID work-up including CMV, EBV RNA, BK were all negative. Core biopsy of the spleen demonstrated CD20/CD45+ cells with tissue effacement, suggesting a diffuse large B cell lymphocytic infiltration/monomorphic PTLD. The sample was EBV-negative by bIC. Belatacept was withdrawn. Subsequent spleoncology testing must be pursued to determine a potential site of proliferation.

Case Description: 64 year AAM 2 years status-post deceased-donor transplant was admitted for altered mental status, nausea, vomiting, fever of unknown origin, and weight loss. He was found to have splenomegaly on CT without other evidence of adenopathy. LHD was elevated. Patient underwent brain MRI, PET scanning, IVM and LP, all of which were normal. A full ID work-up including CMV, EBV RNA, BK were all negative. Core biopsy of the spleen demonstrated CD20/CD45+ cells with tissue effacement, suggesting a diffuse large B cell lymphocytic infiltration/monomorphic PTLD. The sample was EBV-negative by bIC. Belatacept was withdrawn. Subsequent spleoncology testing must be pursued to determine a potential site of proliferation.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO222

Heterogeneous Manifestations of Post-Renal Transplant Lymphoma

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is a serious complication occurring in 1%-3% of adult renal transplant recipients (RT). PTLD is often associated with Epstein-Barr Virus (EBV) and with immunosuppression (IS). A majority of PTLD is of B-cell origin. PTLD has a heterogeneous presentation, involving the allograft, GI tract, and nervous system. We present a case series of 16 RT who demonstrate a variety of PTLD manifestations.

Case Description: 50% of RT were Caucasian and 38% African American. 62% of RT received deceased donor and 38% living donor. 62% received Thymoglobulin induction and 38% Simulect. Maintenance IS was Prednisone, Tacrolimus, and Mycophenolate Mofetil (MMF). RT presented with GI symptoms, abdominal pain, B symptoms, and neurological deficits. At diagnosis, average time from transplantation was 96.8 months (r=0.1-20). 100% of RT were male and 44% were >61 years old. 31% were EBV mismatched and 12.5% were Cytomegalovirus mismatched. PTLD involved a single site in 44% and multiple sites in 56%. PTLD localized to the GI tract (10), lymph nodes (9), CNS (4), bone marrow (3), lungs (2), mediastinum (2), skin (2), retroperitoneum (1), and native kidney/urter (2). 6 RT had purely extranodal involvement. PTLD was EBV+ (8), monomorphic/monoclonal (14), and of B-cell lineage (13). Thymoglobulin and/or Rituximab (16) were used. Treatment was chemotherapy either alone or in combination with radiation (2), resection (2), and salvage therapy (1). Post treatment, all RT remained on steroid monotherapy or with Everolimus (3), Thymoglobulin (1), or Azathiprine/Rituximab (1). Treatment was complicated by Tuberculosis, Lymphoma, and infections. 50% of RT developed renal insufficiency and 31% died. The mortality rate was 44%, 4 years after diagnosis.

Discussion: PTLD that was EBV+, had T-cell involvement, and localized to the CNS/ bone marrow presented with aggressive disease and a higher mortality. Thymoglobulin induction, deceased donor, and donor EBV+ status are potential contributing risk factors for PTLD development; further analysis is still being conducted. Physicians should be aware of the various PTLD manifestations and assertive in management of renal transplant recipients.

PO2223

Richter Transformation (RT): A Rare Complication in Renal Transplant

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Introduction: RT is conversion of B-cell chronic lymphocytic leukemia (CLL) into diffuse large B-cell lymphoma (DLBCL). We present a rare case of RT in a renal allograft.

Case Description: A 68 year old male was admitted for a syncopal episode and acute renal failure. He had significant medical history of ESRD secondary to diabetes and hypertensive nephrosclerosis, deceased donor renal transplant in 2015 on Mycophenolate and Tacrolimus, DLCLL diagnosed in 2017 on Ibritunib, Stage III CKD of allograft with baseline creatinine 15 mg/dl. Initial work up revealed orthostatic hypotension and AKI with creatinine of 3.3 mg/dl. Utrasound and microscopy was negative for proteinuria, hematuria, pyuria as crystals and crystals. Renal ultrasound showed the size of transplant kidney was 10.7 x 5.8 x 4.3 cm with normal renal cortex and no demonstrated mass, cyst or tubular dilatation. Transplant renal biopsy was done. Pathology results revealed no evidence of allograft rejection but extensive infiltration of renal parenchyma with atypical lymphocytes with high Ki-67 expression suggesting transformation to DLBCL in a patient with a known history of CLL. Lymphocytes retained their positivity for CD5 and CD20 which supported diagnosis of Richter. Following a Richter transformation transplant lymphoma, Rituximab was continued on Ibritunib, Tacrolimus, Prednisone 5mg daily and started on weekly Rituximab infusion. Mycophenolate was discontinued. Patient’s renal function returned to its baseline after 2 doses of Rituximab. He was planned to continue Rituximab infusion as per treatment.

Discussion: Transplant patients have high risk of RT due risk factors including concomitant immunosuppression, Epstein-Barr virus infection and some with genetic susceptibility. While PTLD is a well-recognized complication of patients with renal transplantation and malignancy, Richter transformation is usually observed in transplant patients, frequently treated for older patients with RT while allogeneic bone marrow transplantation may be curative in younger patients. Discussion between transplant physician and oncologist should be held, taking into account the new molecular prognostic markers prior to renal transplantation. This may help in risk stratification of patients for conversion of CLL to RT.

PO2224

Longitudinal Assessment of Unilateral Ureteral Obstruction Kidney Injury by Relaxometry and Spin-Lock exchange MRI

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Background: Non-invasive imaging technique allows longitudinal and repetitive assessment of renal disease progression. In this study, we assessed the utility of a new MRI technique, quantitative relaxometry and Spin-Lock exchange MRI, in detecting renal pathology in unilateral ureteral obstructed (UUO) kidneys, focusing on destructive tubular injury (dilation) and renal fibrosis, the pathological changes commonly observed in progressive kidney disease.

Methods: BALB/c mice (n=6-8) were imaged before and after (day 5, 10 and 15) UUO surgery at 7T magnet. Spin-lock images were acquired in a transverse plane using a fast spin echo sequence preceded by a preparatory spin-lock cluster. The dispersion of R2s with locking frequency was fit to Chopra model. The fitted models showed regional values of transverse relaxation rates R2s at infinite spin-lock frequency (R2**,) and an exchange rate-weighted parameter R2**. Since cortex and outer stripe of outer medulla (OSOM) were clearly identified with T1-weighted image, even with UOO kidneys, these regions were selected for analysis. Paraffin tissue sections were stained using picrosirius red or anti-collagen I antibody. Histological scores for tubular dilatation and fibrosis, based on a linear space and positive fibrotic areas in sections, were computationally measured and the correlation between MRI parameters and histological scores were assessed.

Results: In histology, evident tubular enlargement was observed at UOO day 5 while tubulointerstitial fibrosis was mild at this stage. Both histological changes became more evident as renal fibrosis and fibrosis showed larger increases from day 5 to day 15 (tubular dilatation~25% increase, fibrosis~3 fold increase). Relaxation rates R2**, R2 and R2** were progressively dropped (25-50%) in UOO kidneys. Interestingly, R2** showed the highest sensitivity to tubular dilatation, while S2 showed the highest correlation with renal fibrosis.

Conclusions: Relaxation parameters showed high detectability to tubular dilatation and overall changes in UOO progression. S2 best detected fibrotic changes. This would be because it mainly depends on the average exchange rate between water and collagen. Moreover, it is shifted relative to collagen as amide protons, allowing for more pronounced accumulations. These new MRI parameters could be used for the assessment of kidney disease progression.

Funding: NIDDK Support

PO2225

Kidney-Specific Landscape of Aging Mitochondrial DNA Mutations by Duplex Sequencing

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Background: Accumulation of mutations in the mitochondrial genome (mtDNA) is a potential mechanism of aging in the mitochondrial rich kidney, where mtDNA damage also increases with diabetes, CKD and AKI. Accurately detecting low level somatic mtDNA mutations within the cellular complexity of the kidney was previously confounded by variable levels of mtDNA heteroplasmy. Using ultra-sensitive Duplex Sequencing (DS), a modified next-gen sequencing (NGS) technique, we decreased the error rate relative to conventional NGS by >104x, allowing us to accurately characterize mtDNA mutation patterns unique to the aging kidney relative to other organs.

Methods: We compared mtDNA mutations in kidneys from cohorts of aged (26- m.o.) and young (5-m.o.) NIA C57Bl/6j mice to multiple organs with high mitochondrial content (heart, eye, liver, skeletal muscle and brain). In both ages, kidney carried the highest burden of mtDNA point mutations. Mutation spectrum analysis showed that mtDNA point mutations in the kidney increased significantly with age and were primarily G>A/C>T, indicative of oxidative damage, the second most common type. Aged kidneys were further separated into glomeruli or tubule-rich whole cortex fractions to determine regional mutation burden.

Results: Glomeruli had ~25% fewer total mtDNA mutations (p= 0.002) and specifically ~80% fewer oxidative lesions (G>T>C>A, G>C>T>G, p= 0.02). Furthermore, differential accumulation of mtDNA mutation between kidney fractions does not appear to be randomly distributed across the genome but is instead gene-specific as demonstrated by kidney specific mutations in glutamate dehydrogenase (GluDH) gene. Glomeruli had ~100X more mutations in glutamate dehydrogenase (GluDH) gene than renal cortex, and of Complex IV gene mt-Co2, but not mt-Co1 or 3. Finally, we sequenced kidneys from aged mice treated systemically for 8 weeks with SS-31, a mitochondrial therapeutic peptide that reduces oxidative stress in the kidney, and found that mutations stemming from oxidation, but not polymerase error, were significantly reduced.

Conclusions: These data suggest that renal mtDNA mutation is cell specific and that even in aged kidney, accumulation of some mutations is tractable with therapeutic intervention.

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Integrated Analysis of the DNA Methylation, Transcriptome, and Proteome in Human Glomerular and Tubulointerstitial Compartments

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**Background:** The interplay between the human DNA methylome, transcriptome, and proteome in the kidney glomerulus and tubulointerstitium is incompletely understood. Promoter sequence methylation is often thought to contribute to gene and protein expression regulation. We hypothesized that promoter sequence methylation would explain differential protein expression between the glomerulus and tubulointerstitium.

**Methods:** Nine reference nephrectomies underwent laser microdissection of the glomeruli and tubulointerstitium. DNA methylation sequencing, RNA sequencing, and mass spectrometry quantification of peptides was completed for both compartments in the samples. Datasets were dimensionally reduced to match expressed proteins (N = 4600). Regions of hypermethylation in promoter sequences, introns, and exons were assessed and compared to corresponding protein and mRNA expression.

**Results:** At least three patterns of hypermethylation were observed across the methylome: promoter sequence, intrinsic, and exonic methylation. In many cases, promoter sequence or exonic methylation of the tubulointerstitium correlated with a higher glomerular to tubulointerstitial protein and mRNA expression ratio. Likewise, increased tubulointerstitial protein or mRNA expression was associated with glomerular hypermethylation of promoter or exonic regions. For example, Uromodulin (UMOD) protein and mRNA expression were higher in the tubulointerstitium than the glomerulus. The strongest regions of uromodulin hypermethylation were observed in exons 9 and 10 of the glomerular compartment, although hypermethylation was also observed in the promoter sequence and two intronic regions of the tubulointerstitium. In contrast, regions of hypermethylation of Apolipoprotein L1 (APOL1) were exclusively confined to the tubulointerstitium, distributed in all three patterns.

**Conclusions:** Promoter sequence methylation alone does not explain differential expression patterns between the glomerular and tubulointerstitial compartments. Hypermethylation of exonic regions also contributes to expression regulation.

**Funding:** NIDDK Support

Single-Cell Transcriptomics of the Peripheral Blood Revealed Inflammation and Infection Were Associated with IgAN

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**Background:** Immunoglobulin A nephropathy (IgAN) is the most common primary glomerular disease worldwide. Due to the diverse clinical manifestations and the complex pathological features, IgAN patients have different response to therapy, and the optimal treatment for IgAN remains controversial. Our study investigated the pathogenesis of IgAN by single-cell transcriptome sequencing.

**Methods:** Single-cell transcriptome sequencing was performed on peripheral blood monocytes derived from 3 IgAN patients and 1 healthy control, and differential gene expression profiles of peripheral blood single-cell were established. Functional analysis was performed to explore the pathogenesis of IgAN. Meanwhile, RT-PCR was used to validate the differential expression of mRNA and miRNA.

**Results:** According to quality control and cell selection, we characterized 21739 cells using unbiased single-cell RNA sequencing. 3 IgAN patients included 7847, 5389 and 6609 cells, respectively, and the healthy control included 1894 cells. We used unsupervised clustering to cluster cell clusters. In addition, cells were divided into 14 cell groups, including B lymphocytes and T lymphocytes, based on cell markers (Figure 1). Functional analysis revealed that differential genes were extensively enriched in inflammation / infection-related pathways in each cell type (Figure 2), and the EBV infection pathway focused on antigen presentation (Figure 3). RT-PCR of B lymphocytes demonstrated that SPI1, MXD1 and S100A9 mRNA levels were higher in IgAN patients than controls (Figure 4), which showed the results of single-cell transcriptome sequencing was available.

**Conclusions:** Differential gene expression profiles of IgAN in peripheral blood single cells were successfully established, and it demonstrated that the inflammation/infection pathway was associated with IgAN.

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Underline represents presenting author.
Analysis of Urinary Exosomal RNAs After Treatment of Rats with an Nrf2 Activator
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Background: Renal NF-E2-related factor 2 (Nrf2) is known to be increased in the presence of oxidative stress. Administration of an Nrf2 activator has also been reported to lessen the degree of renal damage. However, biomarkers for detection of Nrf2 activation in the kidney are largely unknown. Urinary exosomes, a subset of extracellular vesicles released by renal epithelial cells, contain RNA molecules that are expected to be biomarkers for renal disease. Thus we analyzed urinary exosomal RNAs after administration of bardoxolone methyl (BARD), an Nrf2 activator, in rats.

Methods: Male Sprague-Dawley rats were randomly divided into two groups; the BARD group, intraperitoneally receiving 10 mg/kg BARD, and the control group, receiving only vehicle (100% DMSO). The urine was obtained for 6 hours after administration, and exosomes were isolated from the urine. At 6 hours after administration, rats were sacrificed and the kidneys were removed. Thereafter RNAs were extracted from the kidneys and urinary exosomes. The RNAs (27,012 mRNAs and 1,218 miRNAs) were analyzed with microarrays.

Results: BARD altered expression of 98 renal mRNAs and 357 urinary exosomal mRNAs with more than 2.0-fold relative to the control. BARD also changed expression of 15 renal miRNAs and 3 urinary exosomal miRNAs. The correlation coefficients between renal and urinary exosomal mRNAs as well as miRNAs were both less than 0.1. mRNAs that were commonly changed in both the kidney and urinary exosomes were 13. Among them, 8 genes are known to be targets of Nrf2 including Akr1b8, Akr1c19, Bach1, Ephx1, Eomes, Hmox1, Pir, Slc40a1 and Ugdh. Of 8 genes, Akr1b8 and Pir were increased more than 10-fold in the kidney and more than 4.0-fold in urinary exosomes. For miRNA, only mvo-miR-877 was changed in both the kidney and urinary exosomes.

Conclusions: The correlation coefficients between renal and exosomal RNAs were less than 0.1, suggesting that specific RNAs were selectively loaded into exosomes. In addition, Akr1b8 and Pir expression was dramatically increased in both kidney and urinary exosomes. Therefore, they could be potential biomarkers to detect their renal expression changes by renal Nrf2 activation.
pathophysiology. HFpEF associates with CKD in about 50% of cases and has no specific treatment. Our study offers a new experimental platform to increase our understanding of CKD-HFpEF and to test new treatments in a translational fashion.

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PO223
Expression of Immunoglobulin G in Human Proximal Tubule Epithelial Cell and Its Role in Epithelial Mesenchymal Transformation
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Background: Our previous studies showed that human mesangial cells and podocytes can synthesize and secrete IgA and IgG respectively, participating in cell viability and adhesion. Proximal tubular epithelial cells (PTECs) mediate transcytosis of IgG through neonatal Fc receptor (FcRn). Whether PTECs express IgG has not been reported. The aim of this study was to explore whether PTECs express immunoglobulins.

Methods: Kidney cortical tissues were obtained from five patients undergoing nephrectomy as a result of renal carcinoma. Immunohistochemical (IHC) staining was used to assay the IgG expression in PTECs. Single PTECs were sorted by FACS from the cell suspension of the cortices. 10xGenomics and nested PCR combined with Sanger sequencing were used to detect the transcripts and repertoires of IgG in single PTECs. An immortalized PTEC cell line (HK-2) was used to detect IgG protein expression and potential roles in tubular epithelial mesenchymal transformation.

Results: IHC showed positive staining of IgG but not other IgGs in PTECs of kidney cortex. High throughput single cell RNA sequencing by 10xGenomics only detected IgG transcripts in few PTECs without V(D)J rearrangements. Nested PCR amplified IgG transcripts in 82% (91/111) manually picked single PTECs. Sanger sequencing showed that PTEC-derived IgG variable region displayed classic VDJ rearrangements but predominant VH1-24/DH2-15/JH4 sequence, biased VH1 usage and less diversity than B cells derived IgG. Western blot and immunofluorescence staining demonstrated IgG (including IgG4, IgA and IgG2) in HK-2, iP215, which specifically recognizes non-B cell-derived IgG, can identify the IgG in HK-2. The IgG was upregulated by TGF-β1 and accompanied by the up-regulation of α-smooth muscle actin and the down-regulation of E-cadherin. In addition, the transcripts of recombination activating gene 1/2 (RAG1/2, essential for V(D)J rearrangement) and activation-induced cytidine deaminase (AID, essential for class switch recombination) were detected in HK-2.

Conclusions: Our study suggests that PTECs can express IgG in a similar way as B cells. TGF-β1 can upregulate the expression of IgG in PTECs. PTEC-derived IgG may be involved in tubular epithelial mesenchymal transformation and interstitial fibrosis.

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Long-Term Mitochondrial Protection Reduces Proteinuria in Obese Aged Mice
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Background: In humans, obesity is associated with higher rates of kidney disease, which is compounded by aging. As an energetically demanding tissue, it has been proposed that preventing mitochondrial dysfunction is one key to reducing renal decline. Previously, we showed that an 8-week systemic treatment of aged 24-month-old (m.o.) mice with a mitochondrial targeted protective tetrapeptide, SS-31, significantly reduced the burden of age-induced glomerulosclerosis by 26-m.o. and preserved podocyte integrity.

Methods: To determine if SS-31 aging protection also applied with a comorbidity of obesity, 18-m.o. male NIA C57Bl/6j mice were fed regular chow (RC) or a high fat, high sucrose diet (HFFS) for 10 months and treated with SS-31 injected 5x/wk (3 mg/kg) or saline vehicle (n=20/group).

Results: Mice were weighed weekly. RC mice averaged 33g with no change from age or treatment. HFFS mice gained weight in the first month but by 5 mo. of diet, SS-31/HFFS mice weighed significantly less relative to HFFS untreated mice (40.4g vs. 45.9g p= 0.047). Spot urine was collected monthly for albumin/creatinine ratio (ACR; μg/mg). At 18-m.o. baseline, ACR averaged 484μg/mg. In RC mice, ACR increased modestly, and not significantly, with age although SS-31 RC mice had lower ACR at endpoint (28-m.o. control 125.9 vs. SS-31 31.00). HFFS untreated mice displayed more renal dysfunction as evidenced by a (m.o.): (ACR: RC: 32.6 vs HFFS: 243.2, p = 0.003), climbing significantly to an average of 519.8μg/g at 28-m.o. ACR increased in SS-31 HFFS mice but leveled off by 23-m.o. (5 mo. treat.), averaging 146.1μg/mg with no significant increase by 28-m.o. By 9 mo. of treatment, ACR was significantly lower in HFFS/SS-31 treated mice compared to untreated HFFS mice and also to control SS-31 mice (n=4-7) showed that HFFS mice, regardless of treatment, had a 30% decrease in podocyte density relative to RC mice. Control HFFS mice tended to higher tuft volume (glomerular hypertrophy) than in SS-31 HFFS mice. However, results were not significant in the small sample size.

Conclusions: Combined with improved ACR our results suggest that podocyte integrity, if not number, may be preserved in mice fed a Western diet by SS-31 intervention and that long-term mitochondrial protection is a potential therapeutic target to preserve renal function with aging.

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Bacterial and Fungal Communities Entrained Within Calcium Oxalate, Struvite, and Brushite Human Kidney Stones
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Background: Mechanisms of human kidney stone formation are poorly understood. More than 70% of stones are composed of calcium phosphate and/or oxalate. Recent studies have shown that kidney stone formation follows a continuum of complex biogeochemical transitions and is strongly influenced by the presence of human host and microbial organic matter.

Methods: Kidney stones, removed via percutaneous nephrolithotomy, were prepared as a 25–40 μm thick doubly polished petrographic thin sections and analyzed using brightfield, confocal and super-resolution autofluorescence microscopy. DNA was extracted from 18 calcium oxalate stones, 1 struvite stone, and 1 brushite stone for Fluidigm™ PCR amplification. Pair-end sequencing of bacterial 16S rRNA gene sequences and fungal internal transcribed spacer (ITS) regions was completed using Illumina® MicroSeq Ready. Reads were correlated with patient metadata and analyzed using DADA2, phyloseq v1.22.3 and R software.

Results: A 153-amplicon sequence variant (ASV) fungal community, dominated by A. niger (92% of total reads), was present in 11 of 20 total sequenced stones and correlated with higher patient urinary calcium excretion (335 ± 131 vs 175 ± 108 mg/day, p=0.01). Petrography of 30 stones documented entombed coccoidal and rod-shaped bacterial cells in the struvite stone and well-preserved fungal borings and hyphae in one calcium oxalate struvite stone. DNA-sequenced bacterial sequences were most closely affiliated with Actinobacteri and Catabacterium. The brushite stone microbiome community contained Capnocytophaga and Humibacter and the struvite stone microbiome community included Pseudomonas and Staphylococcus.

Conclusions: This presents the first evidence of a low-diversity fungal and bacterial microbiome community entombed and preserved within calcium oxalate, struvite, and brushite human kidney stones. The macromolecules secreted by the fungal and bacterial communities may play crucial roles in human kidney stone growth, development, and recrystallization, similar to processes that have been documented in natural geologic stone growth.

funding: NIDDK Support, Other U.S. Government Support

Targeting of Factor D in Cfh-/- Mice Does Not Relieve C3 Gromerulopathy due to the Action of C3(H2O)
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Background: C3 glomerulopathy (C3G) is an ultra-rare kidney disease defined by underlying complement dysregulation and characterized by complement C3 deposition on glomerular basement membrane (GBM). Dysregulation of the alternative pathway (AP) is fundamental to disease expression, although terminal pathway dysregulation is also common. Treatment of C3G with eculizumab is unsuccessful in most of the patients, consistent with the fact that complement C3 has a critical role in the terminal complement cascade while leaving up-stream C3 complement dysregulation untouched. Of up-stream targets, factor D (FD) is appealing because it circulates in the plasma at low concentrations and has a single function, to cleave its substrate, factor B, to generate C3 convertases of the alternative complement pathway. Mice with a targeted deletion of factor H (FH; Cfh-/- mice) develop features of C3 glomerulopathy (C3G).

Methods: To assess the impact of FD inhibition, we studied Cfh-/-/Cfd-/- mice. After crossing the Cfd-/- and Cfh-/- mice, Cfh-/-/Cfd-/-/Cfh-/-/Cfd-/-/ progeny were backcrossed to C57BL/6 for 10 generations. Littermates of Cfh-/-, Cfd-/-, Cfh-/-/Cfd-/- and wildtype were used for assessing complement dysregulation and renal pathology.

Results: The C3G phenotype in the Cfh-/- mouse is not rescued by removing FD. Instead, Cfh-/-/Cfd-/- mice develop a subtype of C3G and nephrogenic diabetes insipidus. We used serum from the Cfh-/-/Cfd-/-/ mouse to show that residual AP function is present in Cfh-/- mice and FH are not required for C3C3b to be cleaved by C3 convertases in vivo due to the action of C3(H2O). Therefore, uncontrolled tick-over leads to slow activation of the AP in the Cfh-/-/Cfd-/- mouse. While a tiny amount of FD suffices to activate complement, a minimal threshold of FH is needed to prevent tissue deposition of C3 in the absence of FD.

Conclusions: These findings suggest that efforts to block AP activity by targeting FD may lead to unanticipated outcomes in subgroups of C3G patients. Sustained complete and persistent FD blockade may be difficult to maintain, and due to the action of C3(H2O), it is not completely suppress complement activation; substantial breakthrough through complement activation may then occur as even minuscule amounts of free FD become available.

funding: NIDDK Support, Other NIH Support - National Heart, Lung, and Blood Institute

A Mutation in Complement Factor B Causing Massive Fluid-Phase Dysregulation of the Alternative Complement Pathway Can Result in Atypical Hemolytic Uremic Syndrome
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Introduction: Atypical hemolytic uremic syndrome (aHUS) is an ultra-rare disease characterized by microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. Pathogenesis is driven most frequently by dysregulated cell-surface control of the alternative pathway (AP) of complement secondary to inherited and/or acquired factors. Case Description: We present two unrelated aHUS patients (a 5-year-old female and a 55-year-old female) who presented with the classic signs of thrombotic microangiopathy associated with renal failure with the additional finding of an undetectable C3 level. Circulating levels of C5 and C5b-9 were also low, consistent with over-activity of both the alternative and the terminal pathways of complement. Genetic testing identified a heterozygous novel variant in the complement factor B gene (<CFB c.1101 C>A, p.Ser367Arg). Functional studies demonstrated strong fluid-phase C3 cleavage when mutant factor B and FH are present. However, C3 cleavage was completely suppressed in vivo when patient serum was supplemented with C3. In vitro control of C3 convertase activity could be restored with increased concentrations of factor H.

Discussion: CFB p.Ser367Arg is a gain-of-function pathogenic variant that leads to dysregulation of the AP in the fluid-phase and increased C3b deposition on cell surfaces. This report highlights the complexities of complement-mediated diseases like aHUS and illustrates the importance of functional studies to characterize variants of unknown significance and to gain insight into the disease phenotype.
PO2239

Efficacy of Low-Intensity Pulsed Ultrasound on CKD-Associated Cachexia and Muscle Wasting Prevention in a Mouse Model
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Background: Low-intensity pulsed ultrasound (LIPUS), a therapeutic ultrasound, is recognized to elevate the bone fracture repair process and help in some soft tissue healing. Here, we tested the prevention of chronic kidney disease (CKD)-associated cachexia and sarcopenia by LIPUS in a renal ischemia/reperfusion injury (IRI) mouse model.

Methods: Adult C57BL/6J male mice were used. A model of unilateral IRI with nephrectomy of the contralateral kidney with or without LIPUS treatment (3 MHz, 0.1 W/cm², 20 minutes/day) 5 days before and 14 days after surgery was performed. The CKD-related cachexia/muscle wasting in mice was evaluated. Mice were euthanized 14 days after IRI.

Results: LIPUS treatment significantly alleviated the decrease in the serum albumin/globulin (A/G) ratio and the increases in the serum levels of blood urea nitrogen (BUN), creatinine, cystatin C, and fibroblast growth factor (FGF)-23, and the renal pathological changes and fibrosis in CKD mice (p<0.05, n=5 or 6 for A/G ratio and FGF-23). The development of epithelial-mesenchymal transition and the induction of senescence-related molecular signals and the decreased protein expressions of α-Klotho and endogenous antioxidant enzymes in the kidneys of CKD mice were significantly alleviated by LIPUS treatment (p<0.05, n=4). LIPUS treatment could also significantly reverse the decreased muscle mass, grip strength, and cross-section areas (CSA) of muscle fibers (p<0.05, n=8, for soleus muscle weight, hindlimb grip strength), and the increased muscular protein expressions of atrogenes, Atrogin1 and MuRF1, and phosphorylated ERK1/2 (p<0.001 vs N) and 2.0 in UNX kidneys (p<0.001 vs N). Trametinib blocked the increase in SS and UNX kidneys. Phospho/total ERK (densitometry units) was 0.2 in N, 1.4 in SS and 1.0 in UNX kidneys with the autophagosome membrane. p62 is destroyed by the lysosome and is a marker of autophagic flux, a decrease usually indicating increased autophagic flux. P62/SQSTM1, is an autophagy receptor that links cargo proteins with the autophagosome membrane. p62 is destroyed by the lysosome and is a marker of autophagic flux, a decrease usually indicating increased autophagic flux. The aim of the study was to measure p62 and other potential mechanisms of suppressed autophagy caused by SS and UNX.

Conclusions: LIPUS treatment showed the benefits for renal and muscular protection in a CKD mouse model via inhibition of renal fibrosis, restoration of antioxidant enzymes, and attenuation renal senescence/aging, and muscle mass loss via prevention of muscular mitochondrial dysfunction, AMPK activation, and Akt downregulation. LIPUS treatment may be potentially applied to an alternative non-invasive therapeutic intervention on CKD-associated cachexia/muscle wasting therapy.

PO2240

Mechanisms of Suppressed Autophagic Flux in the Kidney Caused by Sham Surgery and Unilateral Nephrectomy
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Background: Compensatory renal hypertrophy resulting from loss of nephron mass has been implicated in promoting further nephron damage. Unilateral nephrectomy (UNX) is a model of compensatory hypertrophy in the remaining kidney. We previously reported that in the remaining mouse kidney that both sham surgery (SS) and UNX vs. normal kidney (N) resulted in increased mTORC1/2, decreased lysosomal function, suppressed autophagic flux. p62/SQSTM1, is an autophagy receptor that links cargo proteins with the autophagosome membrane. p62 is destroyed by the lysosome and is a marker of autophagic flux, a decrease usually indicating increased autophagic flux. The aim of the study was to measure p62 and other potential mechanisms of suppressed autophagy caused by SS and UNX.

Methods: C57BL/6 mice. p62 and ERK was measured by quantitative immunoblot analysis. Cytokines were measured by MesoScale. Mice were treated with the MEK1/2 inhibitor Trametinib (T) (1 mg/kg for 3 days) that is a potent ERK1/2 inhibitor.

Results: There was an increase in p62 in SS and UNX kidneys. p62/GAPDH (densitometry units) was 0.6 in N, 1.0 in SS (P=0.05 vs N) and 1.0 in UNX kidneys (P=0.05 vs N). p62 is known to modulate pro-inflammatory cytokines. In the serum, there were increases (fold) in IL-1β (50), IL-4 (10), IL-6 (100), IL-8 (5), IL-12 (5), GMCSF (2), TNFα (2), IL-10 (10), IFNγ (0) in SS and UNX vs N. Pro-inflammatory cytokines can activate ERK1/2, a known autophagy suppressor. There was a large increase in ERK1/2 in SS and UNX kidneys. Phospho/total ERK (densitometry units) was 0.2 in N, 1.4 in SS (P=0.001 vs N) and 2.0 in UNX vs N. Phospho/total ERK (densitometry units) was 0.2 in N, 1.0 in SS (P=0.001 vs N) and 1.0 in UNX-T kidneys (P=0.001 vs N). p62/GAPDH (densitometry units) was 1.6 in N, 0.4 in SS +T (P=0.05 vs N) and 0.4 in UNX-T kidneys (P=0.05 vs N).

Conclusions: The mechanism of suppressed autophagy with SS and UNX may be related to an intense systemic inflammatory response and an ERK-mediated increase in p62. It is important that researchers are aware that changes in ERK1/2, systemic pro-inflammatory cytokines and autophagy can be caused by sham surgery as well as the kidney injury/disease itself.

Funding: Veterans Affairs Support, Other U.S. Government Support.
PO2243
Peroxidase Staining for Glomerular Morphometric Phenotype Discovery via Clustering Across Large Datasets
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Background: Microscopic glomerular assessment is diagnostic and prognostic for a diverse array of renal parenchymal disorders. Digital renal pathology enables complex morphometric studies that may identify prognostic information imperceptible to the human eye. We use clustering and feature enrichment to discover morphometric phenotypes that may relate to patient prognosis.

Methods: A convolutional network extracted glomeruli from 29 Periodic acid-Schiff stained transplant biopsies. 315 features were calculated on each glomerulus and clustered with a modularity-based community detection algorithm available in Seurat. Clusters were compared with patient outcome (eGFR decline at 1 year). A Wilcoxon rank sum test identified features enriching each cluster. Uniform manifold approximation and projection (UMAP) was used to visualize the clusters in low dimension.

Results: Clustering revealed 5 glomerular populations (Fig. 1A), and glomeruli of different patients were well admixed across clusters (Simpson’s Diversity Index: 0.78 - 0.98, infinity). Patients were separated in two classes (eGFRa5 or ≤5 mL/min/year), and these labels were projected into the cluster space (Fig. 1B). We observed the clusters show different frequencies of glomeruli from patients with higher eGFR decline. Two of the clusters (2 and 4) had >90% of their morphometrically similar glomeruli solely from slower eGFR decline patients. The distribution of two example features (glomerular area and total nuclei) per cluster are shown in Figs. 1C & D, though the full analysis revealed hundreds of significant features enriching each cluster.

Conclusions: The adaption of an -omics style analysis for renal histology may be feasible to mine prognostically significant morphometric information.

Funding: NIDDK Support
PO2246

IgA Staining Patterns Differentiate Between IgA Nephropathy and IgA-Dominant Infection-Associated Glomerulonephritis

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Background: Differential diagnosis of primary IgA nephropathy (IgAN) and IgA-dominant infection-related glomerulonephritis, particularly Staphylococcus infection-associated glomerulonephritis (SAGN), on a kidney biopsy can be challenging because of similar morphologic findings by light microscopy, immunofluorescence and electron microscopy. Clinical management approach however, is very different. Immunosuppressive therapy is contraindicated in SAGN because it can lead to sepsis and even death. Antibiotics constitute the first line of therapy. In contrast to that, primary IgAN is treated either with conservative management or with immunosuppression. There are no specific biomarkers to distinguish between these two diseases.

Methods: Kidney biopsies from patients with IgAN or SAGN were analyzed. Immunofluorescence with an antibody to IgA was performed on sections of frozen and paraffin embedded tissue.

Results: In total, 75 biopsies (45 with IgAN and 30 with SAGN) were evaluated. All 75 biopsies showed distinct granular staining for IgA in the non-sclerotic glomeruli (Figure 1). Globally sclerosed glomeruli were identified in 47 biopsies (29 with IgAN and 18 with SAGN). Among the 29 biopsies of IgAN, 20 (69%) had positive granular staining for IgA in the globally sclerosed glomeruli and 9 (31%) cases did not. Among the 18 kidney biopsies with SAGN, only one case (5.6%) showed positive staining for IgA in globally sclerosed glomeruli, whereas the remaining 17 (94.4%) did not (Table 1). The sensitivity of positive IgA staining in globally sclerosed glomeruli for kidney biopsies with IgAN was 68.97%, specificity was 94.44%.

Conclusions: Evaluation of IgA staining in sclerosed glomeruli can help to differentiate between primary IgAN and SAGN in the right clinical context, and aid in patient management in most cases.

Table 1. Distribution of staining for IgA in sclerotic glomeruli between cases with IgAN and SAGN

<table>
<thead>
<tr>
<th>IgA Staining in Sclerotic Glomeruli</th>
<th>IgAN</th>
<th>SAGN</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>20</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>18</td>
<td>47</td>
</tr>
</tbody>
</table>

PO2247

The Spectrum of Biopsy-Proven Glomerular Diseases in Mexico: Experience at a Tertiary Hospital

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Background: Glomerular diseases are still one of the leading causes of end-stage renal disease. The diagnosis of these diseases relies on the interpretation of the renal biopsy.

Methods: This investigation was performed in a tertiary hospital. We assessed the main demographic, clinical and histological data of individuals who underwent native kidney biopsies in one tertiary hospital in Mexico. From January 2011-December 2019, totally 1,541 patients first received renal biopsy. After excluding altogether biopsies, inadequate sampling, and failed interpretation, there are still 853 cases with a clear diagnosis.

Results: We evaluated 853 renal biopsies: female 65.3%, elderly (>60 years) 16.6%. The most frequent biopsy-proven diseases were secondary (59.1%) and primary (28.7%) glomerulonephritis (GN), tubulointerstitial nephritis (TIN) was observed in 2.5 % and vascular diseases in 1.5%, hereditary disease in 1.2%. Among primary GN the most frequent diagnosis were focal segmental glomerulosclerosis (FSGS) (17.2%), membranous GN (MGN) (5.7%) and IgA nephropathy (IgAN) (4.8%). Among secondary GN, lupus nephritis (LN) represented 38.9%, diabetic nephropathy 8.1% and pauci-immune crescentic GN 4.9%. The most common diseases in patients with nephrotic proteinuria were LN 14.8%, FSGS 5.8%, MGN 4.1%. Ultrasound needle guidance was used in 97.8%. The frequency of serious complications was approximately 2.5%.

Conclusions: This report provides representative population-based data on native biopsy-proven renal diseases in Mexico. FSGS and LN are the most frequent primary and secondary GN respectively. FSGS and MGN were the most common diseases in patients with nephrotic proteinuria.

PO2248

Clinical Context and Outcomes of Kidney Biopsy in Pregnant Women: An Institutional Review

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Background: Kidney biopsy is an excellent method of gaining insight to causes of renal decline but is not without risk, particularly in pregnant patients. While we await the era of biomarkers which enhance our ability to diagnose diseases of pregnancy, biopsy remains the most inclusive way of reaching a diagnosis. Clinical manifestations warranting biopsy include gross deterioration in renal function, de novo development of nephrotic syndrome, or suspicion for glomerulonephritis. A recent metaanalysis found that the risk of complications during pregnancy was 7% and should be limited to patients in whom the diagnosis would warrant urgent therapy. We sought to explore indications for biopsy and histopathology in patients evaluated at our institution.

Methods: Our surgical pathology database was searched for renal biopsy specimens interpreted from 2008 to mid-2020. Patients were either pregnant at the time of biopsy or within 3 months postpartum. Indiana University IRB approved the study. A chart review was completed to obtain lab data at the time of biopsy and post procedure.

Results: We identified biopsy specimens from 38 women who were pregnant during the specified time period. Histopathologic diagnoses included lupus nephritis (n=4), FSGS (8), diabetic kidney disease (3), allergic interstitial nephritis (1), IgA (10) and minimal change disease (3). Chart information was available for 19 women including 15 Caucasian and 4 African American patients, with a mean age of 28.6 years. Eight women were obtained during pregnancy and 11 during the postpartum period. Proteinuria was present in 17 patients with a mean value of 3.5g/dL. Hematuria was also present in 14 of the patients. Mean serum creatinine was 2.6mg/dL.

Conclusions: Renal biopsy is a procedure with high risk and morbidity for pregnant women. At our institution, biopsy was performed for either worsening renal function or proteinuria. Our population showed diverse diagnoses which justified need for biopsy, including requiring urgent intervention. Our study highlights the need of judicious biopsy in pregnant women. Further studies can be done to determine long term kidney outcomes in pregnant women.

PO2249

Prevalence and Risk Factors Associated with Nephrosclerosis in Renal Parenchyma Specimens of Patients Undergoing Partial or Radical Nephrectomy

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Background: Evaluation of non-neoplastic renal parenchyma in nephrectomies is part of the College of American Pathologists (CAP) Cancer Protocols. We evaluated the prevalence of histological abnormalities and nephrosclerosis and its association with clinical factors in patients undergoing nephrectomy for any cause at our institution.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: Two nephropathologists evaluated the status of the renal parenchyma in 374 pathological specimens, who underwent either partial or radical nephrectomy (59%) between 2013 and 2017. Age-adjusted global glomerulosclerosis (GS), interstitial fibrosis (IF), tubular atrophy (TA), and arteriosclerosis (AS) were evaluated by light microscopy. Nephrosclerosis was defined as the presence of a ≥2 histologic features. Clinical, demographic, and pathological data were collected by chart review. Logistic regression analysis was used to evaluate the association between clinical parameters and nephrosclerosis.

Results: The mean age was 60 ± 14 years. 38% were female, 44% were Hispanics, 59% had hypertension, 22% had diabetes mellitus, and 24% had a smoking history. The pre-nephrectomy eGFR was 73 ± 27 ml/min/1.73m² and 31% had an eGFR < 60 ml/min/1.73m². The prevalence of age-adjusted GS was 82%, any TA was 80%, more than 5% IF was 78% and any A2 was 95%. The prevalence of nephrosclerosis was 88%. Lower pre-nephrectomy eGFR (adjusted odds ratio [OR] per 10 units decrease in eGFR, 1.12 [95% confidence interval (CI), 1.02-1.23]) and age (adjusted OR per 10 years increase, 1.97 [95% CI, 1.64-2.39]) were significantly associated with nephrosclerosis. Gender, history of hypertension, diabetes, and smoking were not associated with nephrosclerosis (p > 0.05 for all).

Conclusions: Nephrosclerosis is highly prevalent in renal parenchyma of patients undergoing nephrectomy. Lower pre-nephrectomy eGFR and older age were independently associated with significantly greater odds of nephrosclerosis. Future studies should evaluate the association between nephrosclerosis and post-nephrectomy eGFR.

PO2250
Evaluation of Preexisting Renal Disease in Nephrectomies
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Background: Evaluation of non-neoplastic renal parenchyma in nephrectomies is part of the College of American Pathologists (CAP) Cancer Protocols. We aimed to determine the prevalence of pre-existing renal diseases in all patients who underwent nephrectomy for any cause in our center.

Methods: The surgical pathology protocol for nephrectomies was modified with a) additional sampling of non-tumoral renal parenchyma, b) Hematoxylin and eosin, Periodic acid-Schiff, trichrome and silver stains, and c) addition of the expanded checklist for reporting nephrectomy from the Renal Pathology Society recommendations. All samples were reviewed by 2 nephropathologists (A.N. (Chief) and nephropathologist (M.O.)) and at least 813 nephrectomies were performed between 2013 and 2017 and were evaluated and included in the study. Reasons for nephrectomies were malignancy in 645 (79%) of patients, of which 528 (82%) had renal cell carcinoma, 100 (16%) urothelial carcinoma, and 168 (21%) benign lesions (42 oncocytomas, 34 pyelonephritis, 13 trauma, and 1 nephrolithiasis). Clinical, demographic, and pathological data were collected by chart review.

Results: The mean age was 60 ± 14 years. 62% were male and 44% Hispanics, 59% had hypertension, 22% had diabetes mellitus, and 24% had a smoking history. Baseline eGFR was 73 ± 27 ml/min/1.73m² and 31% had an eGFR < 60 ml/min/1.73m². Only 41 patients (5%) had a documented pre-operative consult to nephrology. 296 (36%) patients had at least one renal disease diagnosis and only 62 (8%) had a single diagnosis. Only 41 patients (5%) had a documented pre-operative consult to nephrology. 296 (36%) patients had at least one renal disease diagnosis and only 62 (8%) had a single diagnosis. 296 (36%) patients had at least one renal disease diagnosis and only 62 (8%) had a single diagnosis. 2% had renal disease. 2% had renal disease. 2% had renal disease.

Conclusions: Pre-existing renal disease are frequently identified in nephrectomy specimens. FGGS was the most common diagnosis. A collaborative effort involving nephrologists, urologists and pathologists is warranted to improve the care of patients undergoing surgical nephrectomy.

PO2252
Kidney Filtration Markers in Human Saliva: Accuracy and Reproducibility of Novel Salivary Cystatin C Measurements
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Background: Invasive phlebotomy followed by laborous blood specimen processing is the only reliable approach to assess routinely measured kidney filtration markers including cystatin C (CysC). Non-invasive testing of these markers is urgently needed particularly during the COVID-19 pandemic to enhance social-distancing.

We developed novel Enhanced Enzyme and Immunoassays-based Lateral Flow (ELF) assays to measure concentrations of CysC in human saliva. Highly selective binding reagents were screened for optimum specificity, followed by applying sample treatment steps to mitigate sample to sample variability using healthy donor saliva samples spiked with known levels of the filtration markers. Standard calibration curves (SCCs) for each marker was developed with nonlinear 4-parameter logistic curve fitting to tricplicate measurements at each spiked concentration level. Accuracy/fit of the SCC was assessed using the coefficient of determination (R²). Intra-assay reproducibility was assessed using coefficient of variation (CV) and studies of inter-assay repetatability over time (over > 8 days) examined reproducibility of whole experimental protocol.

Results: SCC fitted to relative optical intensities (ratio of test to control lines vs. spiked CysC (0-14 ng/ml) was excellent (R²=0.991) and provided accurate estimates of spiked CysC levels (R²=0.994). Assessment of intra-assay variation showed that repetatability is very good with CV <10% throughout the dynamic range of measurements. Assessment of inter-assay variation (measurements over 8 days) showed that reproducibility is acceptable with CV <13% throughout most of the dynamic range. Preliminary assessment of long-term reproducibility (stability) out to 258 days indicated similar performance. [figure]

Conclusions: We demonstrated feasibility of CysC measurements in human saliva samples with acceptable ELF assay characteristics including accuracy, repeatability, reproducibility, and long-term stability. Validation studies are ongoing to optimize the saliva testing framework for kidney function markers.

Funding: NIDDK Support
**PO2253**

**Comparison of Creatinine-Based Estimated Glomerular Filtration Rate Equations with DTPA GFR in Healthy Adults**

Varun Kumar Bandi, Spoorthi Ramineni. Dr. Pinnamaneni Siddhartha Institute of Medical Sciences & RF, Vijayawada, India.

**Methods:** The cross-sectional study was done on live kidney donors. DTPA was used to measure GFR, 24 hour creatinine clearance (CCi) was measured and creatinine based eGFR was calculated using Cockcroft-Gault (CG), Modification of Diet in Renal Disease-fourniable (MDRD-4), Modification of Diet in Renal Disease-variabile (MDRD-6), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations.

**Results:** 88 subjects were included, of whom 29.5% were male, with a mean age of 46.8 yrs, and BMI of 25.7 kg/m2. Mean GFR (a standard deviation) obtained by CKD-EPI, MDRD-4, MDRD-6, CG, CrCl, and DTPA GFR were 98.8 (+15.2), 96.2 (+17.9), 106.1 (+22.0), 88.5 (+37.3), 89.3 (+29.2) and 98.4 (+31.7) ml/min/1.73m2, respectively. The mean absolute difference in GFR and percentage variation between calculated and measured GFR for CKD-EPI, MDRD-4, MDRD-6, CG, CrCl, and DTPA GFR were 14.7 (16.5%), 16.2 (17.9%), 19.8 (22.3%), 33.2 (36.5%), and 23.66(25.7%) respectively. Percentage of values within 20% of DTPA GFR in each equations were CKD-EPI - 69.32%, MDRD-4 – 70.45%, MDRD-6 -54.55%, CG - 38.64%, and CrCl - 45.45%. There was no significant co-relation between the measured GFRs and eGFR using any of the above equations.

**Conclusions:** All the equations used (CKD-EPI, MDRD4, MDRD6, CG) and CrCl did not correlate significantly with the measured GFR. Among the equations, CKD-EPI had the least variation with about 69% confirming within 20% of DTPA GFR, and about 86% and 97% confirming within 30% and 50% of DTPA GFR.

Table 1: Percentage of eGFR estimations occurring within 20%, 30%, and 50% variation of DTPA GFR values

**PO2254**

**Fecal Calprotectin Correlates with Serum Albumin in Patients with CKD**

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**Background:** Persistent inflammation, a characteristic feature in chronic kidney disease, contributes to decreased serum albumin levels and plays a central role in the Malnutrition, Inflammation and Atherosclerosis (MIA) syndrome, which is associated with poor clinical outcomes. Altered bowel habit is also a highly frequent status among patients with chronic kidney disease potentially due to their low fiber and fluid intake, medications, multiple comorbidities and dysbiosis of the gut microbiota. In this study, we have explored whether measurement of fecal calprotectin, a commonly used marker for increased neutrophil migration and local inflammation in gastrointestinal diseases, could reflect a state of low serum albumin in patients with chronic kidney disease.

**Methods:** Clinical and biochemical data including stool samples for calprotectin were collected from 579 cases of patients with no history of inflammatory bowel disease. Results: Fecal calprotectin was not different according to estimated glomerular filtration rate, degree of proteinuria and medication of polystyrene sulfonate and ferrous sulfate. However, it was significantly and negatively correlated with serum albumin in patients (r=−0.107, p=0.010). Patients with higher tertile of fecal calprotectin were older and had lower hemoglobin. Multivariable linear regression analysis showed that fecal calprotectin was significantly correlated with serum albumin (β=−17.702, P=0.010).

**Conclusions:** These observations that serum albumin were significantly correlated with fecal calprotectin in patients with chronic kidney disease, suggest that the bowel inflammatory response may be another contributing factor.

**PO2255**

**A Case of Sevelamer-Induced Colon Perforation**

Venkata R. Manchala, Rajendra Mandalapu, Soumya P. Thumma, Nithin Karakala. University of Arkansas for Medical Sciences, Little Rock, AR.

**Introduction:** Sevelamer is an ion exchange resin used to treat hyperphosphatemia in patients with chronic kidney disease. It does not cause hypercalcemia or vascular calcification. The main adverse effects are related to constipation and abdominal pain. Common adverse effects include nausea, vomiting, diarrhea, dyspepsia and constipation 1. Case reports of sevelamer associated bowel perforation have been reported in the literature2. Here we report a case of sevelamer induced colon perforation.

**Case Description:** 61 year old Caucasian male with history of ESRD from diabetic nephropathy on automated peritoneal dialysis presented to the emergency department with abdominal pain. Physical exam was notable for epigastric tenderness. Labs were unremarkable except for hyperglycemia of 427 mg/dL. CT scan abdomen showed chronic ileitis and moderate ascites. PD fluid analysis ruled out peritonitis. Patient’s abdomen pain persisted despite several days of supportive care, prompting repeat CT scan which revealed a large pneumoperitoneum suggestive of sevelamer resins. Patient was on sevelamer 800mg TID for several years. Patient improved with appropriate medical management. Sevelamer was discontinued prior to discharge.

**Discussion:** Sevelamer is composed of a non-absorbable hydrogel with ammonia on the hydrochloride (Renagel) or the carbonate (Renvela). In the acid milieu of stomach, it is protonated to ammonium which is available to bind phosphate in the intestine3. The exact pathogenesis of intestinal perforation remains unclear. It is hypothesized that presence of sevelamer crystals in the gastrointestinal tract was associated with mucosal abnormalities including inflammation, ischemia and necrosis. The presence of characteristic sevelamer crystals (typically seen as bright pink linear accretions with a rusty yellow background and irregularly spaced fish-scales) on pathology along with the supporting clinical history clinches the diagnosis. It is important for clinicians to be aware of this rare but a serious potential complication of bowel perforation associated with sevelamer.

**PO2256**

**Case of Pulmonary-Renal Syndrome Involving Goodpasture Disease and Granulomatosis with Polyangiitis**

Shabatah Khan. AU-UAG Internal Medicine, Athens, GA.

**Introduction:** Wegner’s granulomatosis and Goodpasture’s disease are two rare causes of pulmonary-renal syndromes syndromes. Both have similar presentation and different treatment protocols. The clinical relevance for these two syndromes is that they are both potentially fatal. WG is a systemic vasculitis involving small to medium size vessels and it mainly affects the respiratory and renal systems and associated with C-ANCA (PR3) antibodies. Goodpasture’s disease is an autoimmune condition that is characterized by rapidly progressive glomerulonephritis (RPGN) and severe alveolar hemorrhage. It is most often related to anti-glomerular basement membrane (anti-GBM) antibodies and affects the renal and pulmonary vascular beds due to immune complexes formed against the glomerular basement membrane. It is noted that 5% of all ANCA + patients are also positive for anti-GBM and of all the anti-GBM about 1/3rd also have ANCA but that does not always correlate with active clinical disease. This leads to a significantly poorer prognosis and worse renal outcomes than either disease process alone.

**Case Description:** We present a 59-year-old female with initial complaint of weakness, lethargy and sinus congestion. She had a history of untreated hypertension. She was noted to be hypoxic and had rales and bronchi bilaterally. Labs revealed WBC of 35, Hg 5.6, Hct 15.5 and platelets 594. She had sodium of 98, Potassium 5.8, Bicarbonate 18, BUN of 58 and Creatinine of 8.5. Chest x-rays showed bilateral opacities resembling CAP. Further hypoxemia prompted intubation, revealing copious amounts of alveolar hemorrhage. Vasculitis was in the differential given alveolar hemorrhage and renal failure. The patient was then started on plasmapheresis, high dose IV steroids as well as cyclophosphamide. Complement levels and immunofixation were normal as were studies for lupus and hepatitis B and C. She had + ANA, Anti-GBM and c-ANCA antibodies. Renal biopsy showed predominant sclerosis and >90% focal necrotizing crescent GN and severe interstitial scarring. Immunofluorescence (IF) demonstrated linear staining of glomerular BM as well as ANCA mediated changes.

**Discussion:** This case illustrates that both WG and GP can occur in the same patient. Such patients can present with CAP that rapidly deteriorates. Early recognition of the pulmonary involvement is crucial for starting appropriate therapy by plasmapheresis and immunosuppressant. Although these patients with severe glomerular involvement will be lifelong dependent on dialysis, their 1- and 2-year survival can be significantly improved with appropriate therapy and follow up.
PO2258
Asymptomatic Spurious Hyperuricemia Related to Waldenstrom Macroglobulinemia
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Introduction: Increased IgM has been shown to result in underestimation of uric acid levels and pseudo-hypouricemia; however, there are no reported cases of hyperuricemia in the setting of paraproteinemias. We present a case of Waldenstrom’s Macroglobulinemia (WM) resulting in marked elevation of uric acid level in the absence of tumor lysis syndrome (TLS).

Case Description: A 73-year-old man with history of WM was incidentally noticed to have very high uric acid level of 37.2 mg/dl. He had no history of crystal arthropathy or chronic kidney disease. He was started on Acalabrutinib because of high serum viscosity and uric acid levels improved significantly, however the treatment had to be discontinued due to development of potential drug related adverse events. After discontinuation of Acalabrutinib, his serum viscosity and uric acid level gradually increased back to the previous level. Laboratory parameters were not suggestive of TLS and potassium, calcium and phosphorus were all normal. 24-hour uric acid excretion was noticed to be low normal (341 mg/24 hours).

Discussion: Paraproteins often cause factitious biochemical measurements by forming opake precipitates with the test reagents and interfering with various automated assays. Such interferences may be difficult to anticipate as they are intermittent and patient specific. Ultrafiltration of paraproteins, dilution or deproteinization of the samples may sometimes help correct these measuring errors. WM and other paraproteinemias may cause true hyperuricemia in the setting of TLS. However, the absence of other complications and low probability should reduce the consideration of factitious results. An observant clinician should be aware of these findings in order to avoid unwarranted testing and treatment. Also, a very high level of uric acid in the absence of symptoms may point towards a possibility of undiagnosed paraproteinemias.

PO2259
Is the Well-Recognized Intravascular Tamm-Horsfall Protein Polyp a Misanomer? A Case Report from a Patient with Obstructive Uropathy and Hematuria
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Introduction: Tamm-Horsfall protein (THP), a renal epithelial glycoprotein, was originally described from normal urine and should be present in all normal urine specimens. The polyps are described in these reports as being located in veins or sometimes lymphatics. Our case is the first to confirm the location of a THP polyp by immunohistochemical (IHC) analysis.

Case Description: A 64-year-old Caucasian male presented with bilateral flank pain and persistent gross hematuria. On admission, he had mildly elevated BUN (26.0 mg/ dL) and serum creatinine (3.2 mg/dL). Urine analysis showed red blood cells > 182 /hpf with negative leukocyte esterase and negative nitrates. He developed azotemia during the hospitalization with the highest creatinine of 7.4 mg/dL on day 3 of admission. Renal ultrasound indicated mild-moderate hydronephrosis with a collapsed bladder. Renal biopsy was performed given lack of proper explanation for his presentation. Biopsy showed Periodic acid-Schiff (PAS) positive THP with polyhedral use. Her physical exam was unremarkable. Her admission labs were notable for a Cr 2.25 mg/dL, potassium 3.1 mmol/L, bicarbonate 155 mmol/L, phosphorus 2.2 mg/dL, uric acid 1.3 mg/dL, urinalysis specific gravity 1.011, pH 6.5, glucose 500 mg/dL, small blood, protein 30 mg/dL, negative leukocyte esterase, nitrite negative, 2 RBC, 4 WBC, negative urine culture, and spot protein/creatinine of 1.1. Further workup revealed urine electrolytes: Cr 39 mg/dL, sodium 77 mmol/L, potassium 20 mmol/L and phosphorus 22.9 mg/dL. FePhos was 61% suggesting renal wasting. Serologic workup was negative for ANA, ANCA, ncl c3, c4 and spep. Renal sonogram showed normal sized kidneys with two nonobstructing calculi in each kidney. Renal biopsy revealed focal degenerative changes in the tubules with flattening of the epithelium consistent with mild ATN. The interstitium had diffuse infiltration with mononuclear cells and frequent cosinophils consistent with ATN. EM showed tubuloarteriolar inclusions. She was started on prednisone which was tapered over 6 weeks. Creatinine downtrended to 1.1 mg/dL. She was continued on prednisone.

Discussion: Publilized reports of THP polyps are exclusive to veins, but there are no reports of THP polyps in the kidneys. She had not been exposed to any nephrotoxic substances or medications. THP is commonly seen in renal biopsies in patients with renal obstructions. The development of THP polyp in a patient with asymptomatic hydronephrosis may not be true due to the misidentification of the markedly distended renal tubules as renal veins.

PO2260
Vedolizumab-Induced Acute Interstitial Nephritis and Acute Tubular Necrosis
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Introduction: Vedolizumab is a humanized monoclonal antibody used in the treatment of ulcerative colitis. To date there has been no reported case of vedolizumab associated acute interstitial nephritis (AIN) and acute tubular necrosis (ATN). We report the first such case.

Case Description: A 58 year old female with history of ulcerative colitis on vedolizumab for one year, primary parathyroidism and calcium oxalate nephro lithiasis presents due to acute kidney injury. Patient received her last dose of vedolizumab two months prior. She had been receiving 300mg IV every eight weeks, making her last dose her seventh dose. Her pre-medication creatinine (Cr) was 0.9 mg/dL. Approximately one week prior to admission she was found to have a Cr of 2.0 mg/dL. She denied any NSAIDs, PPI, antibiotics or herbal use. Her physical exam was unremarkable. Her admission labs were notable for a Cr 2.25mg/dL, potassium 3.1mmol/L, bicarbonate 155mmol/L, phosphorus 2.2mg/dL, uric acid 1.3mg/dL, urinalysis specific gravity 1.011, pH 6.5, glucose 500mg/dL, small blood, protein 30mg/dL, negative leukocyte esterase, nitrite negative, 2RBC, 4WBC, negative urine culture, and spot protein/creatinine of 1.1. Further workup revealed urine electrolytes: Cr 39mg/dL, sodium 77mmol/L, potassium 20mmol/L and phosphorus 22.9mg/dL. FePhos was 61% suggesting renal wasting. Serologic workup was negative for ANA, ANCA, ncl c3, c4 and spep. Renal sonogram showed normal sized kidneys with two nonobstructing calculi in each kidney. Renal biopsy revealed focal degenerative changes in the tubules with flattening of the epithelium consistent with mild ATN. The interstitium had diffuse infiltration with mononuclear cells and frequent eosinophils consistent with AIN. EM showed tubuloarteriolar inclusions. She was started on prednisone which was tapered over 8 weeks. Creatinine downtrended to 1.1 mg/dL. She was continued on prednisone.

Discussion: Vedolizumab reported AIN and mild ATN has not thus far been reported. Here we report the first case which seemed to have a cumulative dose response. Whether this patient has a mild proximal RTA due to this medication remains to be determined, as the phosphorus wasting could have been due to her primary hyperparathyroidism. Clinicians should be made aware of such reported associations so that both a timely renal biopsy and therapy could be instituted without delay.
PO2263

ALECT2 Amyloidosis with Cardiac Involvement Complicating Renal Transplantation


Introduction: ALECT2 amyloidosis may be associated with slowly progressive renal failure that is clinically unsuspected at the time of transplantation. While this is typically not clinically significant, we report a case with extensive systemic ALECT2 amyloidosis that also involved the myocardium, contributing to perioperative death post renal transplantation.

Case Description: A 72-year-old Hispanic woman presented for renal transplantation due to ESRD from hypertension. She was bradycardic on admission. Cardiac workup prior to transplantation had not identified an infiltrative process. Post-transplant hypotensive bradycardic arrest leads to multiorgan failure, anoxic brain injury and death. Autopsy revealed massive amyloid deposition in the native kidneys, adrenals, spleen, and less extensive infiltration of liver and myocardium. Cardiac intramural vasculature from venae to capillaries, arterioles and arteries showed amyloid deposition. Mass spectrometry revealed ALECT2 as the amyloidogenic protein.

Discussion: ALECT2 is a systemic amyloidosis that typically involves kidneys, adrenals, spleen and liver. It may be clinically unsuspected at the time of renal transplantation and should be considered in older patients, especially from higher ALECT2 amyloid prevalence populations. Complications related to systemic disease may add to morbidity or mortality post-transplantation. Cardiac involvement in ALECT2 amyloidosis has not been previously identified as a significant clinical or autopsy finding, but our case demonstrates that the cardiovascular system may indeed rarely be involved by ALECT2 amyloidosis and be associated with clinical sequelae.

PO2264

Cell-Based CSb9-ELISA to Identify Patients with Atypical Hemolytic Uremic Syndrome

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Background: Discrimination between different diseases in patients suffering from thrombotic microangiopathies is often challenging. Measuring CSb9 deposit on endothelial cells using confocal microscopy have been shown to be convenient in diagnostic and therapy monitoring of Atypical hemolytic uremic syndrome (aHUS) but methods are complex and costly.

Methods: We developed a cell-based CSb9-ELISA to measure CSb9-deposits on activated endothelial cells. Patients with suspected aHUS and other thrombotic microangiopathies were identified in early disease stage. Serum was drawn and tested versus healthy controls. After confirmation of the diagnosis aHUS therapy efficiency was monitored using the assay.

Results: In patients with the clinical diagnosis of aHUS we were able to show up to six-fold higher CSb9-deposits in contrast to normalized human serum (NHS) (p-value < 0.0001). In comparison to healthy controls, patients suffering from either Shiga-Toxin-HUS or Thrombotic Thrombocytopenic Purpura (TTP) we could demonstrate a two- to three-fold higher deposit (p-value=0.0103 and below). After onset of eculizumab treatment, the amount of CSb9-deposits becomes lower than in healthy controls, proving the efficiency of the therapy. One-Way-ANOVA shows significant differences between aHUS-groups and controls, but not between aHUS patients using Taikeye-multiple comparisons test.

Conclusions: We described a novel, fast and reproducible ELISA to identify aHUS-patients by measuring CSb9-deposits and monitor disease activity. This can give a rise to diagnostic speed and therapy decisions. Further investigation and validation are needed to show interactions with other complement diseases like systemic lupus erythematosus.
PO2266
Persistent Coagulation Abnormalities in ESRD After 1 Year of Follow-Up
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Background: Common to end-stage renal disease (ESRD), coagulation abnormalities can lead to severe bleeding events or excessive thrombin formation and engender increased morbidity and mortality in this population. Repeated heparin administration to ESRD patients during maintenance hemodialysis may also contribute to changes in the coagulation system. Thus, profiling coagulation parameters in ESRD patients over 1-year may provide insight to long-term coagulation dysfunction in this population.

Methods: Blood samples were obtained at baseline and 1-year from ESRD patients undergoing maintenance hemodialysis (n=95) 48-hours post-dialysis. Plasma samples were analyzed using clot-based methods including activated partial thromboplastin time (aPTT), prothrombin time (PT), and thrombin time (TT). Chromogenic assays measured heparin levels by anti-Xa and anti-IIa methods. Patients were categorized by heparin administration during dialysis (n=44) and compared via statistical method and percent change.

Results: In the clotting and chromogenic assays, all parameters were elevated in the baseline and 1-year ESRD cohorts compared to controls, as shown on Figure 1. Only anti-IIa levels demonstrated a significant difference in ESRD patients after 1-year (p<0.0001). Heparin administration varied in aPTT, TT, and anti-Xa (p<0.05).

Conclusions: These results suggest ESRD patients on dialysis exhibit a long-term, hypo-coagulable state as shown by prolonged aPTT and TT. Elevated parameters maintained over 1-year suggests persistent dysregulation of clotting factors in ESRD patients. Circulating levels of heparin, as evidenced by anti-Xa and anti-IIa assays may be due to impaired clearance of heparin components via dialysis.

PO2267
Using Skin Biopsies to Measure Target Occupancy of a Renal Anti-fibrotic Monoclonal Antibody (mAb) in a Phase 1 Clinical Study
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Background: Defining the optimal dose of drug required to bind to its mechanistic target (target occupancy, TO) and affect a measurable distal event (target engagement, TE) in damaged kidney is a challenge in the development of anti-fibrotic therapies for chronic kidney disease (CKD). We aimed to identify an accessible surrogate human tissue to predict TO in the kidney, prior to application in a Phase 1 study.

Methods: We developed a ‘biopsy-on-biopsy’ approach in skin: a 3mm biopsy initiated a wound healing response, a 1mm biopsy at the same site, up to 6 days later, provided tissue where active healing/fibrotic processes were ongoing. This method was used to measure the TO of zampilimab, a humanized mAb specific for human transglutaminase 2 (TG2), in kidney and skin biopsies. TE in damaged kidney was correlated with kidney TO and TE in a computational model (UUD model). We used a single dose Phase 1 study (NCT02879877). Following dosing of zampilimab, skin biopsies and kidney were measured using a competitive immunofluorescence assay on cryosections. A TRITC-labeled mouse parent of zampilimab (DC1) and a FITC-labeled anti-TG2 antibody binding a distant epitope (DH2) were used. TO was measured by comparing the relative binding of DC1 (competitively inhibited by zamilamib administered in vivo) to TO in a TG2 in-situ activity assay.

Results: In a primate UUO-CKD model treated prophylactically with zampilimab, the ‘biopsy-on-biopsy’ method showed excellent correlation between TO in the kidney and healing skin (3 days post first biopsy). Importantly, TO and TG2 inhibition (TE) in the kidney were also highly correlated. Subsequent use in the zampilimab Phase 1 study generated data directly comparable to the preclinical model.

Conclusions: Our ‘biopsy-on-biopsy’ approach allows early identification of a dose range in Phase 1 studies where the target organ is inaccessible, and is applicable to other therapeutic mAbs intended for treatment of fibrotic kidney disease. A Phase 1/2 study of zampilimab in patients with post-renal transplant fibrosis is ongoing (NCT04355578).

Funding: Commercial Support - UCB Pharma
important diagnostic tool. The change to IR as primary operators has significantly reduced tissue adequacy. An extraordinary educational outreach to IR is needed.

4 weeks to 10 weeks gestation. In addition, 8 early metanephric kidneys from 10 weeks to 21 weeks of gestation were identified from our surgical pathology and autopsy cases for comparison with mesonephric specimens. Beside routine hematoxylin and eosin staining, the sections were stained for Periodic Acid Schiff (PAS) to detect proximal tubules (PT) brush borders and glomerular basement membranes (GBM). Furthermore, mesonephros and metanephros sections were immunohistochemically stained for CD133 for progenitor cells, GATA3 for mesangial cells and distal tubules, P504S for proximal tubules, and kidney injury molecule-1 (KIM-1) for PT injury.

Results: CD133 was positive in mesonephric glomerular and tubular structures at 4 weeks but this expression disappeared in the mesonephros from 5 weeks to 10 weeks, implying gradual maturation. GATA3 staining was positive in Wolffian duct, mesangial cells of primordial glomeruli (at 7 weeks the GBM was PAS+) and distal tubules, but not in PT. PT were positively stained for P504S. PT of mesonephric kidneys revealed brush borders on PAS stained sections from 7 to 10 weeks suggestive of reabsorptive activity. The PT of mesonephros at 7 weeks stained positively for KIM-1, suggestive of acute tubular injury during abortion processes. The mesonephros showed expression of markers in respective renal compartments, similar to those in mesonephros.

Conclusions: Human mesonephros can have GATA3+ mesangial cells in the glomeruli. Although structures are simplified (no loop of Henle and collecting ducts), the human mesonephric nephrons include primitive glomeruli, PT showing brush borders and distal tubules, having morphological features similar to those of advanced metanephric stages with excretory function. They have react to injury, at least during 7 to 10 weeks of gestation based on identification of brush borders and KIM-1 expression in PT.

PO2270

Monogenic Causes of Nephrolithiasis or Nephrocalcinosis in Korean Children

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Background: Nephrolithiasis (NL) or nephrocalcinosis (NC) can be the early manifestation of hereditary nephropathy in children and early detection of hereditary nephropathy gives us chance to provide therapeutic and preventative intervention. In this study, we present genetic characteristics of NL/NC in pediatric patients who were treated in tertiary medical center in Korea.

Methods: The medical records of pediatric patients (age of 0-18 year) who had NC/NL and underwent genetic test under suspicion of hereditary nephropathy from March of 2013 to January of 2020 in Samsung Medical Center in Korea were reviewed. When specific disease was suspected, the sanger sequencing was done. The whole exome sequencing was performed when suspected mutations were not detected in sanger sequencing or when the disease could not be specified. DNA was extracted from whole blood or saliva. The novel mutations were evaluated by clinical findings and bioinformatics analysis such as in silico prediction.

Results: Total 20 patients underwent genetic test and two of them were sibling. The median age at the time of NC/NL detection was 4.8 years and male was predominant (M/F=2:3). Genetic diagnosis was done at the median age of 5.5 years. Three patients had family history of NC/NL (15%). Total 13 pathogenic gene mutations were detected in 16 patients (80%); 5 genes (SCL3A1, GRHPR, CLCN5, OCLR1, CLCNK2) were known to cause monogenic forms of NC/NL and 8 genes (PA2X2, PKD1, HNF1B, SLC36A2, BUB1B, VPS33B, PHEX) were not. Three pathogenic autosomal recessive mutations were detected in 3 individuals; BUB1B (n=1), GRHPR (n=1), VPS33B (n=1). We also detected pathogenic mutations in 6 autosomal dominant genes in 7 individuals; CLCNK2 (n=1), SLC3A1 (n=1), PA2X2 (n=1), HNF1B (n=2), SLC11A1 (n=1), PKD1 (n=1), SLCN6A2 (n=1). Two X-linked recessive genes were detected in 5 individuals; CLCN5 (n=4), OCLR1 (n=1). In one patient, X-linked dominant gene was detected; PHEX. Eight of 16 detected mutations (50%) were novel mutation that have not been previously reported in database of human disease causing mutation.

Conclusions: In conclusion, NL/NC can be the clue to detect monogenic cause of hereditary nephropathy in children. Further large population study is needed to evaluate NL/NC as indicator for genetic analysis to detect monogenic hereditary nephropathy in children.

PO2271

Trans IL-6 Signaling Does Not Distinguish Between Pediatric Patients with and Without Scarring After Febrile Urinary Tract Infection

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Background: The inflammatory response generated in response to infection is believed to be largely responsible for the development of renal scarring after UTI. IL-6 is a cytokine known to be induced during UTI with a pro-inflammatory pathway, known as trans signaling. We hypothesized there would be differences in markers of trans IL-6 signaling between patients with a history of febrile urinary tract infection (UTI) who had subsequent renal scarring as compared to those with a history of febrile UTI who did not develop renal scarring.

Methods: Urine samples were collected on consenting/assenting pediatric patients with a history of febrile (c38°C) UTI (urine culture ≥50K uropathogen) with documented presence or absence of renal scarring on imaging. Patients were not actively infected at the time of sample collection. Enzyme-linked immunosorbent assays were performed on samples for markers of trans IL-6 signaling: IL-6, soluble (s)IL-6 receptor (R), and soluble
Markers of Trans IL-6 Signaling Are Not Differentially Induced During Febrile and Afebrile Urinary Tract Infection
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Background: Febrile urinary tract infections (UTIs) are generally thought to be evidence of tissue inflammation such as pyelonephritis as compared to afebrile UTIs which are thought to be more localized to the bladder. As such, generally the concern for renal damage is more in those with febrile UTI and thought to be a result of the inflammatory response generated. IL-6 is a known mediator of inflammation, particularly through its trans signaling pathway. We hypothesized there would be differences in markers of trans IL-6 signaling in the urine of children with febrile compared to afebrile UTI.

Methods: Pediatric patients with signs of active UTI were consented/assented for participation. Urine was collected at time of evaluation for active UTI in the urology or nephrology office or at hospitalization and were divided into those with a fever (≥38°C) compared to those without (<38°C). Patients were included for analysis if they had a positive urine culture (≥50K CFU of a uropathogen) and for those without a fever if they had no dysuria, urgency, frequency, and/or new or worsening urinary incontinence. Those with fever were termed a febrile UTI and those without a fever were termed afebrile UTI. Enzyme-linked immunosorbent assays were performed on samples for markers of trans IL-6 signaling: IL-6, soluble (s)IL-6 receptor (R), and soluble (s)gp130. Results were normalized to urine creatinine. Results were analyzed by Mann-Whitney U. A p-value of ≤0.05 was considered significant.

Results: 17 patients with febrile UTI and 23 patients with afebrile UTI were included. Two of the patients with febrile UTI were male while all of the afebrile UTI patients were female (p=0.1258). The groups did not differ significantly based on age (p=0.6218). While we found that those with a febrile UTI had a higher IL-6 in their urine at the time of collection (p=0.0479), there was no significant difference in expression of sIL-6R or sgp130. Ratios of these markers also were not significantly different.

Conclusions: Markers of trans IL-6 signaling, either as absolute values or ratios, are not different between individuals at the time of febrile or afebrile UTI.

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PO2277
Human Neutrophil Peptide 1-3 Protects the Urinary Tract from Uropathogenic Escherichia coli Infection in Humanized Mouse Model
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Background: Urinary tract infection (UTI) susceptibility is defined by heritable genetic differences associated with the innate immune system development and efficiency. DNA copy number variations in the alpha-defense DEFA1 locus are associated with UTI susceptibility in children with VUR. In humans, DEFA1A3 is expressed in neutrophils as well as in the kidney. However, how DEFA1A3 protects the urinary tract in some individuals is unknown. We hypothesized that Defa-1 mouseized humanized mice would be resistant to experimental UTIs.

Methods: We induced UTI with two uropathogenic E. coli (UPEC) strains in wild-type (WT) C57Bl/6J and Defa-1 transgenic mice, which express human DEFA1A3. Bacterial suspension was inoculated with a catheter transurethrally. To assess the colony-forming unit (CFU) burden, kidneys and bladders were homogenized and colony forming units and clearance were determined by quantifying the plated serial dilutions grown overnight on LB plates at various time points.

Results: Results are presented in Figure 1: Comparing the Defa-1 mouse to WT (n=8 for each group), at 6-hours post infection, bacterial burdens were lower in the Defa-1 mice kidneys for both UPEC strains (A). At 24-hours after inoculum, the bladder infection (CFU/g) was significantly lower in the Defa-1 mouse in comparison to the C57Bl/6J group (B).

Conclusions: Our findings support the early protective role of DEFA1A3 from UPEC challenge in the humanized mouse kidney and bladder when compared to the absence of the antimicrobial peptide in the wild-type mouse. Further investigation is needed to determine whether renal or extra-renal expression of DEFA1A3 is critical in shielding and clearing UPEC UTIs.

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PO2276
Ribonuclease 6 is an Intracellular Antimicrobial Peptide That Thwarts Bacterial Cytosis and Pyelonephritis
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Background: Ribonuclease 6 (RNase 6) is a highly conserved cationic peptide with potent microbical activity toward uropathogenic Escherichia coli (UPEC) in vitro. Here, we determined the cellular sources of RNase 6 along with the consequences of its gain and loss of function during experimental urinary tract infection (UTI).

Methods: We generated female mice with a Rnase6Δ/Δ knock-in allele, human RNASE6 transgene, or controls on a C57Bl/6J genetic background. We identified cellular sources of RNase6 by flow cytometry and microscopy. We transurethrally inoculated Rnase6Δ/Δ, RNASE6 transgenic, and control mice with UPEC strain CFT073 and enumerated bacterial burden. The role of RNase 6 during intracellular killing of UPEC was investigated in bone marrow derived macrophages (BMDM) by gentamicin protection assay.

Results: RNase6 is expressed by tissue resident macrophages and circulating monocytes that are recruited to the infected bladder and kidney within hours of UPEC inoculation. Rnase6 deficiency leads to increased renal UPEC burden relative to controls, whereas RNASE6 transgenic mice exhibit reduced UPEC burden. Rnase6 macrophages localize within the urothelium and its underlying stroma at baseline and during UTI. RNase 6 is not secreted by macrophages; instead, it is retained intracellularly within the endolysosomal system. RNASE6 over-expression in macrophages leads to increased killing of phagocytosed UPEC.

Conclusions: Rnase6 is a monocyte/macrophage derived antimicrobial peptide that acts intracellularly to kill phagocytosed UPEC and limit bacterial UTI.

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PO2277
Risk Factors for Urinary Tract Infection Caused by Extended-Spectrum Beta-Lactamase Gram-Negative Bacteria in Infants
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Background: Community-acquired extended-spectrum beta-lactamase (ESBL) producing bacterial infections are an evolving public health problem. Urinary tract infections (UTIs) due to ESBL-producing bacteria are increasing even in infants rarely exposed to antibiotics. We aimed to identify risk factors for UTI caused by ESBL-positive bacteria in infants.

Methods: We retrospectively analyzed the medical records of hospitalized infants with the first episode of UTI from 2018 to 2019. Data includes demographic characteristics, birth history, previous use of antibiotics, febrile event, urinalysis results, and urine isolated organisms. Multivariate regression analysis was used to quantify independent risks associated with ESBL-positive UTI.

Results: UTIs were diagnosed in 266 patients at a median age of 3.6 (interquartile range: (2.3-5.4)) months. Two hundred (75.4%) patients were diagnosed with UTI caused by ESBL-producing bacteria. When we divided patients according to ESBL status, there was no difference in gender, age, birth history, milk type, and use of postpartum care centers. Maternal use of antibiotics during pregnancy (odds ratio (OR), 3.817; 95% confidence interval (CI) 1.812-8.040, P <0.001), previous antibiotic exposure to patients was higher in the ESBL-positive group than in the ESBL-negative group (32.3% vs. 10.3%, P <0.001, and 22.6% vs. 12.3%, P =0.044, respectively). Klebsiella species was more frequently identified in the ESBL-positive group than in the ESBL-negative group (19.4% vs. 4.9%, P =0.002). In multivariate analysis, maternal use of antibiotic during pregnancy (odds ratio (OR), 3.817; 95% confidence interval (CI) 1.812-8.040, P <0.001), previous antibiotic exposure to patients (OR 2.418; 95% CI 1.071-5.661, P =0.034), and Klebsiella species as a causative organism (OR 6.222; 95% CI 2.396-16.158, P=0.001) were associated with ESBL positivity. In a comparison of clinical courses of patients, the ESBL-positive group showed severe leukocytosis (WBC 16,795 μL vs. WBC 14,620 μL, P =0.04), and stayed longer in hospital than the ESBL-negative group (7.0 days vs. 4.5 days, P =0.001).

Conclusions: In this study, the high rate of ESBL positivity was detected in infantile UTI. Antibiotics exposure on both parents and mother was associated with UTI caused by ESBL producing bacteria. Identification of underlying risk factors could improve treatment and preventive strategies.
PO2278

Urinary Sodium to Potassium Molar Ratio in Pediatric Stone Patients
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Background: The incidence of pediatric stone disease is on the rise. Dietary elements including high salt intake and reduced water consumption remain the major risk factors for stone formation. Urinary stone profile in pediatric literature remains limited. The purpose of this study is to get data on 24 hr urinary mineral excretion in pediatric stone formers with particular emphasis on these two research questions 1. How does urinary sodium/potassium (Na/K) molar ratio in pediatric stone patients compare to the national average intake data in USA? 2. How does risk factors of stone formation such as hypercalcuria correlates with dietary risk factors in pediatric stone formers?

Methods: This retrospective cohort study included all Pediatric stone patients who attended outpatient Nephrology clinic from 03/1/2014 to 10/1/2018. Children with known metabolic/genetic causes for stone disease, incomplete 24 hr urinary collection or on medications that affect mineral excretion were excluded from the study.

Results: 150 patient charts were screened and 89 included in the study. Average age of the study population was 12.7 years with 58% females and 42% males. Mean Na/K molar ratio in pediatric stone patient was 3.7, statistically significantly higher than the national average of 2.5 using one sample T test (P< 0.001). Urinary calcium excretion showed a strong linear correlation with sodium excretion (r 0.545, P < 0.001). Multiple regression model using urinary calcium excretion as the dependent variable showed correlation with Urinary sodium excretion (P 0.004), urinary volume (P < 0.0001) and urinary Ph (P=0.001).

Conclusions: 24 hr urinary sodium potassium molar ratio is significantly higher in stone formers indicating a higher salt and lower potassium consumption when compared to national average intake. Water intake, salt consumption and alteration of urinary Ph remains the main dietary modality to alter calcium excretion and hence reduce risk of stone formation.

PO2279

Keratin 5+ Urothelial Cells Are Developmental and Tissue Repair Progenitors in the Bladder
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Background: Urothelium is nearly quiescent during homeostasis, but injury engages a robust regenerative capacity. Several progenitor cell candidates have been implicated, but prevailing models demonstrate conflicting roles discrete urothelial subpopulations. We recently demonstrated that Keratin 5 (K5)-expressing UCs are temporally restricted renal urothelial progenitors. It is unclear whether similar temporal restrictions are imposed on bladder K5-UCs, and whether an investigation into the temporality of the K5-UC progenitor may clarify bladder progenitor model. The objective of this study was to determine temporal progenitor-progeny relationships responsible for bladder urothelium generation and regeneration.

Methods: Using Ker5-CreERT2;Rosa26tm mice, K5-UCs were inducibly and permanently labeled with tdTomato (tdT). Tamoxifen (TMX) was administered at postnatal day (P) 1, P7, P14, P21 or P41. Mice were sacrificed (SAC) at P42 or subjected to a single round of urothelial injury (cyclophosphamide) and euthanized 2 weeks later. Immunofluorescence microscopy was used to visualize and quantitate tdT, K5, (uroplakin), Uapk and K20 expression.

Results: Fate mapping analysis found that 22% (TMX0.5;SAC+);0.5<0.675, (K5-UCs) and 23.3% (TMX0.5; SAC+);0.5<0.675 of neonatal tdT+ UCs differentiated into adult Uapk + UCs (tdT-;Uapk mostly intermediate cells) by P42 compared to 9% (TMX0.5;SAC+);0.5<0.675 of juvenile tdT+ UCs, and 0% adult (TMX0.5;SAC+);0.5<0.675 (P=0.01, ANOVA). Following urothelial injury, 63% (TMX0.5;Cyte-);0.5<0.675, 54.33% (TMX0.5;Cyte-);0.5<0.675 and 69% (TMX0.5; Cyte-);0.5<0.675 of umbrella cells expressed tdTomato (tdT+;K5-UCs<0.20). Adult (TMX0.5; Cyte+;Cyto+; Cyte+);0.5<0.675 tdT+ UCs rarely formed umbrella cells.

Conclusions: K5-UCs form intermediate and superficial cells, but the capacity for K5-UCs to form these derivatives is lost over time. In response to acute adult bladder urothelial injury, neonatal and juvenile tdTomato+ UCs regenerate umbrella cells, while adult tdTomato+ UCs do not. These studies establish that bladder K5-UCs are context dependent progenitors - responsive to temporal and pathologic cues. Our findings support an intermediate cell auto injury progenitor model, and show that intermediate cells formed by neonatal and juvenile K5-UCs repair acutely injured bladder urothelium.

Funding: NIDDK Support

PO2280

Perinatal Cystatin C as Biomarker of Nephron Endowment
Beatrice L. Crippa,1 Stefano Ghirardello,1 Valentina Capone,2 Gianluigi Ardissino.1 1NICO, Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milano, Italy; 2Pediatric Nephrology, Dialysis and Transplantation, Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milano, Italy.

Background: Nephron endowment has a wide individual variability and plays a crucial role in drug toxicity, outcome of kidney diseases and pathogenesis of arterial hypertension (AH), but nephrons count is technically impossible in vivo. During acute dehydratation, subject with reduced nephron mass (unilateral renal agenesis or renal hypoplasia) exhibit increased levels of biomarkers of renal function compared to healthy subjects. We hypothesized that healthy newborns with reduced nephron endowment will have high levels of cystatin C (Cys-c) during perinatal dehydration. The aim of the study was to compare Cys-c level during physiological perinatal dehydration in healthy term infants with hypertensive fathers (HF) and normotensive fathers (NF).

Methods: Healthy, Caucasian, born at term neonates were enrolled: infants with fathers on antihypertensive therapy were compared to infants with normotensive fathers > 40 yo. Enrolled infants underwent Cys-c capillary determination at time of expanded newborn screening.

Results: We enrolled 40 infants with HF and 80 infants with NF. Basic characteristics were not different between the two groups except for the number of hypertensive grandparents, that was higher among infants with HF. Cys-c levels was determined at a median of 62.5 hours of life (IQR 55-71) without any difference between groups. Cys-c was significantly higher in infants with HF (1.6 ± 0.3 mg/mL vs 1.4 ± 0.3 mg/mL, p < 0.001). Linear regression analysis corrected for confounders (type of feeding, delivery mode, weight loss velocity) confirmed that paternal hypertension was the only variable significantly associated with high Cys-c level (mean difference 0.2 mg/mL, IC 95% 0.1-0.3 in, p < 0.001).

Conclusions: Our results support the key role of nephron endowment in the pathogenesis of AH and suggest the possibility of identifying at-risk subjects at birth. This opportunity opens up specific and targeted preventive health measures very early in life.

PO2281

Elevated Urinary Neutrophil Gelatinase-Associated Lipocalin Predicts Postoperative AKI
Cara L. Slagle,1 Hailey W. Gavigan, James A. Rowe, Brenda Poindeexter, Kelli A. Kraliman, Alexandra Schmerge, Chunyan Liu, Shelley Ehrlich, Meera Kotagal, Stuart Golden, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: Post-operative acute kidney injury (AKI) in neonates remains understudied despite occurring frequently. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) offers promise as a novel predictive biomarker for AKI, yet clinical utilization lags behind in neonatology.

Methods: Infants undergoing a general surgical procedure, excluding gastric tube placement, were prospectively enrolled. uNGAL samples were obtained prior to surgery and over post-operative days (POD) 0-3 at six time points. AKI was defined by the 2014 neonatal modified Kidney Diseases: Improving Global Outcomes (KDIGO) definition. Samples were processed using The NGAL Test® (BioPorto, Denmark). Generalized additive mixed effect model (GAMM) was utilized to study the longitudinal trajectory of log transformed uNGAL values. The ability to predict AKI was assessed using receiver operating characteristic curves (AUC-ROC).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Results: A total of 141 neonates underwent 192 surgical procedures. AKI occurred in 69% of patients. AKI in neonates with CDH were more likely to have undergone an emergent procedure (63% vs. 31%, p<0.001) and had higher uNGAL levels (Table 1). Pre-op uNGAL did not differ between AKI and no AKI patients (26ng/mL vs 59ng/mL, p=0.12). uNGAL levels were higher at all post-op time points even when controlled for pre-operative AKI (p=0.0006 to 0.0356). The AUC-ROC for predictability of post-operative AKI using uNGAL at 24 hours was 0.8 (95% CI: 0.71-0.88).

Conclusions: Post-op uNGAL predicts AKI. In patients undergoing emergent procedures, careful monitoring of renal function should be performed and uNGAL offers clinical utility. In our patients uNGAL trends could allow clinicians to better understand renal injury in real time and adjust treatment plans and/or avoid or restart nephrotoxic medications.

Funding: NIDDK Support, Private Foundation Support

Table 1: Comparison of predicted uNGAL values (95% CI) following Emergent and Routine Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preop (95% CI)</th>
<th>12 hour (95% CI)</th>
<th>24 hour (95% CI)</th>
<th>36 hour (95% CI)</th>
<th>48 hour (95% CI)</th>
<th>72 hour (95% CI)</th>
<th>96 hour (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergent</td>
<td>126 (96-160)</td>
<td>220 (190-250)</td>
<td>244 (210-280)</td>
<td>244 (210-280)</td>
<td>221 (184-258)</td>
<td>211 (184-258)</td>
<td>123 (111-135)</td>
</tr>
<tr>
<td>Routine</td>
<td>96 (22-46)</td>
<td>135 (100-175)</td>
<td>212 (150-276)</td>
<td>30 (30-55)</td>
<td>0 (0-55)</td>
<td>0 (0-55)</td>
<td>0 (0-55)</td>
</tr>
</tbody>
</table>

Conclusions: AKI in neonates with CDH occurs in about 30% of hospitalized neonates and is independently associated with mortality. Infants with congenital diaphragmatic hernia (CDH) are frequently exposed to nephrotoxins such as fluid overload, on ECLS, exposed to nephrotoxins, or in the post-operative period, given shifts, surgery, cardiopulmonary compromise, and extracorporeal life support (ECLS). As such, they are postulated to have an increased AKI incidence. We sought to determine prenatal characteristics and postnatal exposures associated with an increased risk of AKI in neonates with CDH during the first 30 days of life, as well as the impact of AKI on selected long-term outcomes.

Methods: We performed a single-center retrospective review of neonates with CDH from 2009 to 2017. AKI was defined by the modified neonatal Kidney Disease Improving Global Outcomes (KDIGO) criteria. Discriminative fluid shifts, surgery, cardiopulmonary compromise, and extracorporeal life support (ECLS). As such, they are postulated to have an increased AKI incidence. We sought to determine prenatal characteristics and postnatal exposures associated with an increased risk of AKI in neonates with CDH during the first 30 days of life, as well as the impact of AKI on selected long-term outcomes.

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Results: There were 130 neonates included in the cohort, median gestational age was 38 weeks [IQR: 36, 38], median birthweight was 2.89 kilograms [IQR: 2.5, 3.19], 56% were male, and 50% were outborn. AKI occurred in 34 (37.8%) infants during the first 30 days of life. Specifically, 15 (44%) had stage 1, 10 (29%) had stage 2, 9 (26%) had stage 3, and 2 (6%) had stage 4 AKI. Baseline renal replacement therapy was initiated in 11 infants with AKI; higher estimates of lung volume (percent predicted lung volume, total lung volume, residual volume) were lower in infants with AKI than in those without AKI.

Conclusions: AKI is common among neonates with CDH. In our cohort, greater CDH severity was associated with greater odds of AKI and those with AKI had worse long-term outcomes. Attention to kidney function should be paid to neonates with fluid overload, on ECLS, exposed to nephrotoxins, or in the post-operative period, given the increased odds of AKI in such situations.
post-op FO and no FO groups were evaluated by Mann-Whitney U tests. Ability to predict FO was assessed by receiver operating characteristic curves (AUC-ROC).

Results: A total of 141 infants underwent 192 procedures. FO occurred after 46% (88/192) procedures (mean %FO = 27±10). Previous medical history of AKI was associated with development of post-op FO (35% vs. 14%, p<0.001). Development of post-op AKI was also associated with FO even when controlled for pre-op AKI (69% vs. 31%, p<0.005). When SCR was adjusted for FO, AKI increased from 35 to 38 events and stage of AKI increased in 8 events. In FO patients, elevations in uNGAL were higher at all time points (Table 1). The AUC-ROC for post-op FO was 0.7 (95% CI: 0.63-0.78).

Conclusions: FO is an indicator of reduced renal function and is associated with AKI. uNGAL offers utility as an additional biomarker to assist in prediction of post-op FO and inability to maintain acceptable fluid balance. Post-op FO should be monitored closely for all surgical patients, and particularly patients with a previous history of AKI.

Funding: NIDDK Support, Private Foundation Support

Median [IQR] uNGAL values in FO and non FO patients

PO2286

Use of B-Type Natriuretic Peptide as a Quantitative Marker of Fluid Overload in Neonatal Renal Replacement Therapy

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Introduction: Neonatal renal replacement therapy (RRT) remains one of the most challenging dialysis scenarios in Pediatric Nephrology. Evaluation of dry weight can be particularly difficult as fluid overload may be mistaken for adequate nutritional weight gain. Physical exam is insensitive in assessing hypervolemia until significant fluid overload develops. Non-invasive BP measurements are often difficult to obtain as upper extremities are typically used for IV access and the patient’s lack of cooperation alters measurement. B-type natriuretic peptide (BNP) has long been used in the evaluation of heart failure and has even been reported to be a marker of fluid overload in adult hemodialysis patients. In this study, we evaluate the role of BNP as a quantitative marker of fluid overload in a neonate with ESRD.

Case Description: A 3 week old child with bilateral renal agenesis required emergent RRT. Following the failure of peritoneal dialysis in this 2.19 kg child, RRT modality was converted to hemodialysis (HD). Despite daily 3 hr HD treatments with ultrafiltration (UF) goals guided by weight, physical exam findings and blood pressure, patient developed bilateral pulmonary edema and an enlarged cardiac silhouette at 3 weeks of age. BNP was found to be > 5,000 pg/mL and RRT modality was changed to CVVHDF. BNP normalized after 4 days of CVVHDF, but upon transition to HD, she again developed fluid overload and required placement back on CVVHDF. Thereafter, BNP was utilized as a quantitative marker of fluid overload with UF goal guided by pre- and post-dialysis BNP levels. Applying this technique, the patient had no further episodes of fluid overload.

Discussion: Providing successful dialysis in infants is more problematic than in older patients. To assess fluid overload in children on dialysis, traditional tools include clinical assessment, serial weights and measuring blood pressure. In this infant, measurement of serial BNP levels allowed for an objective assessment of volume status, which was helpful in maintaining dry weight and lead to successful dialysis therapy.

PO2287

Comparison of Nafamostat Mesylate and Regional Citrate Anticoagulation for Anticoagulation in Pediatric CRRT

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Background: Regional Citrate Anticoagulation (RCA) is the preferred anticoagulant for CRRT in the US in children. Nafamostat Mesylate (NM), a synthetic serine protease, has been widely used for CRRT anticoagulation in Japan and Korea. While NM is considered safe and effective, there is a paucity of evidence in pediatric literature. We describe the safety and efficacy of NM compared to RCA for pediatric CRRT.

Methods: Using one children’s hospital in Japan and one in the US, medical records of patients <21 years who received CRRT between 2017-2019 were reviewed. Patients receiving CRRT concurrently with ECMO were excluded. Basic demographics, CRRT characteristics, and outcomes were analyzed between the RCA and NM groups. Filter life (FL), defined as the number of hours a single CRRT filter was in use, was the primary efficacy outcome of efficacy. For Kaplan Meier analysis, circuits were censored for elective filter discontinuation. Safety is assessed by anticoagulation complications. Results: 28 pts (100 filters) received RCA and 36 pts (90 filters) received NM. Baseline Table 1. There was no difference in median FL (42.6h in RCA vs 42h in NM, p=0.17). Kaplan-Meier curves of time to spontaneous filter failure shown in Figure 1. The mortality and bleeding rate did not differ between the groups.

Conclusions: NM provides similar efficacy compared to RCA for FL. No significant difference in safety was observed between the two groups.

PO2288

Renal Replacement Therapy and Mortality Rates for Children with Posterior Urethral Valves and Prune Belly Syndrome

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Background: Posterior Urethral Valves (PUV) and Prune Belly Syndrome (PBS) cause congenital obstructive uropathy and dysplasia in infants. Resulting chronic kidney disease and pulmonary hypoplasia may lead to renal replacement therapy (RRT), mechanical ventilation and death. Methods: This retrospective cohort study queried The Pediatric Health Information System (PHIS) database to identify patients with PUV or PBS who were born at or transferred to a PHIS hospital by 3 months of age between 1/1/2006 and 9/20/2016. Ethnicity, race and insurance were investigated as predictor variables for time to RRT or in-hospital mortality. Prematurity and mechanical ventilation were evaluated as predictors of in-hospital mortality.

Results: 1673 PUV and 236 PBS patients met inclusion criteria. There was no difference in time to RRT or mortality based on ethnicity, race, or insurance. 212 patients (11.1%) required RRT by 2 years of age. There was no difference in RRT requirement between the PUV and PBS groups. 130 patients (6.8%) died during the initial admission:

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
98 PUV patients (5.9%) and 32 PBS patients (13.6%), with a median time to death of 6.5 days and 2.5 days, respectively. PBS patients had an increased risk of death (Adjusted Relative Risk (ARR) 2.12, p <.0001). The difference in median time to death was not significant. Of 381 (20%) premature patients, 79 (20.7%) died prior to discharge. 696 patients (36.5%) required mechanical ventilation, and of these, 118 (17%) died. Prematurity and mechanical ventilation were associated with an increased risk of death (ARR 2.3, p <0.0001 and ARR 9.9, p<0.0001 respectively).

Conclusions: The severity of the sequelae associated with PUV and PBS is affirmed by the 11.1% risk of early RRT and 6.8% in-hospital mortality. PBS patients did have an increased mortality rate compared to PUV patients. Prematurity or the requirement of mechanical ventilation was associated with an increased mortality rate. Future large, prospective studies will enable investigation of early morbidity and mortality associated with PUV and PBS, as well as long-term outcomes.

PO2289

Preterm Birth in Mice Results in Differential Gene Expression and Premature Cessation of Nephrogenesis

Aleksandra Cwiec,1 Kimberly Deronde,1 Masako Suzuki,1 Kimberly J. Reidy,2 Jennifer R. Charlton,3 Albert Einstein College of Medicine, Department of Genetics and Development, New York, NY; 2Children’s Hospital at Montefiore, Department of Pediatrics, Division of Nephrology, New York, NY; 3University of Virginia, Department of Pediatrics, Division of Nephrology, Charlottesville, VA.

Background: Neonates born preterm are at risk of developing chronic kidney disease (CKD). In humans, nephron development is completed by 36 weeks’ gestation and the successful formation of nephrons is dependent on self-renewing niches of cells which reside directly under the kidney capsule in the nephrogenic zone (NZ). Little is known about the fate of these progenitor cells or the other compartments of the kidney following premature birth. The objective of this study was to characterize the effect of premature birth on kidney development in murine model of prematurity. We hypothesize that preterm mice will have a shorter period of postnatal nephrogenesis and gene expression profiles will reflect premature differentiation.

Methods: Timed pregnant CD-1 dams were stratified into 2 cohorts. The preterm group was comprised of 59 pups born by Cesarean section at 18 days post-conception (dpc) and the term group contained 79 pups delivered vaginally at 20 dpc. The mice were euthanized on 20-27 dpc. The presence of the nephrogenic zone was determined on histological sections. Genome-wide expression profiles of 20 dpc mice kidneys were evaluated with RNA-seq in both preterm and term groups (n=3 per group).

Results: At 25-27 dpc, kidney to body weight ratios were significantly lower in preterm cohort. In the kidney, the cap mesenchyme was not detectable in the preterm mice a full day (23 dpc) prior to its cessation in the term mice (24 dpc). The expression profiles of 20 dpc kidneys in the preterm group showed distinct alterations compared to the term group. The differentially expressed genes were enriched in a fat-soluble vitamin (including vitamin A and D) metabolic process related pathways.

Conclusions: In a mouse model of prematurity, there is an early differential expression of genes that may be important in nephrogenesis. The shortened window of nephrogenesis may result in a lower nephron number and future risk for CKD in neonates born preterm.

PO2290

Gestational Age (GA) Affects Urine Biomarkers by Postnatal Age but Most Converge by 34 Weeks Post-Menstrual Age (PMA)

David J. Askenazi,1 Brian A. Halloran,2 Robert Schmicker,3 Patrick J. Heagerty,2 Sandra Jual,2 Stuart Goldstein,2 Sangeeta R. Hingorani,2 PENUT Investigators1 ’The University of Alabama at Birmingham School of Medicine, Birmingham, AL; 2University of Washington, Seattle, WA; 3Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: Urine biomarkers may improve our understanding of kidney development and disease in premature neonates. We evaluate how 1-week differences in GA impact 11 biomarkers by postnatal age and PMA.

Methods: Neonates were grouped by GA. Urine was collected on postnatal days 1, 3, 5, 7, 9, 14, 28; on PMA of 30 and 34 weeks; and discharge in 750 neonates without stage 2/3 AKI. Neutrophil-gelatinase associated lipocalin (NGAL), Clusterin, kidney injury molecule 1 (KIM-1), alpha glutathione S-Transferase (a-GST), albumin, beta-2-microglobulin (B2M), cystatin c, epithelial growth factor (EGF), osteopontin (OPN), uromodulin (UMOD) and Creatinine were evaluated by mass spectrometry. Biomarkers are displayed as 7-day rolling mean (day X ± 3 days) on log10 scale. GEE models with mother as a clustering variable were used to determine the association between day, GA, and day*GA for each biomarker. T-tests evaluated differences in 34-week (± 3 days) PMA values.

Results: Figure: Left side plot biomarkers by postnatal age; right side plot biomarkers by PMA. When exploring the values by postnatal age, the most premature neonates have higher NGAL, clusterin, KIM-1, a-GST, albumin, B2M, Cystatin C, OPN, and lower EGF, UMOD and Creatinine (p<0.05; * in Figure) after adjusting for day. The association of biomarker and time is significantly modified by GA for a-GST, Albumin, B2M, Creatinine and Cystatin C (interaction term p<0.05; ** in Figure) over the first 30 postnatal days. Only B2M and OPN differ by GA at 34 weeks PMA (p<0.05; *** in Figure).

Conclusions: Urine biomarkers differ and are modified by GA during first 30 postnatal days. Most biomarkers converge and are not significantly different by 34 weeks PMA.

Funding: NIDDK Support, Other NIH Support - NINDS.

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PO2291

The Association Between Infantile Pulmonary Hypertension, Sildenafil, and AKI During Hospitalization

Emily E. Zangla, Emily L. Joyce. University Hospitals, Rainbow Babies and Children’s Hospital, Department of Nephrology, Cleveland, OH.

Background: Pulmonary hypertension (pHTN) is a nidus for poor organ perfusion, and is an understudied potential risk factor for acute kidney injury (AKI) in infants. Neither the association between pHTN and AKI, nor treatment with phosphodiesterase-5 inhibitors (i.e. sildenafil) on renal recovery have been elucidated. We sought to describe AKI in a cohort of hospitalized infants with pHTN.

Methods: A retrospective chart review was performed on 18 infants (less than 1 year of age) during the initial hospitalization for diagnosis of pHTN over one year at a single institution. Adapted neonatal KDIGO criteria was utilized to determine presence of AKI during the hospitalization for each patient.

Results: Out of 18 infants with pHTN, 50% developed AKI during hospitalization. Those who developed AKI were older at the age of diagnosis of pHTN (p = 0.04) and more likely to be treated with sildenafil (p = 0.02). Within the cohort, 7 (39%) were treated with sildenafil. On univariate analysis, treatment with sildenafil was associated with increased odds of developing AKI (OR 6.7, 95% CI 0.81-55.0). Of those treated with sildenafil who developed AKI, 80% (4/5) developed AKI before initiation of treatment and 20% (1/5) developed AKI after initiation of treatment.

Conclusions: AKI is prevalent in infants diagnosed with pHTN. The increased odds of developing AKI in patients treated with sildenafil is likely a reflection of severity of illness, as most patients developed AKI prior to initiation of treatment. Further research is needed to evaluate the association between pHTN and AKI, as well as determine the role of sildenafil treatment in preventing AKI or promoting renal recovery.

Descriptive Characteristics

<table>
<thead>
<tr>
<th></th>
<th>No AKI n=12 (100%)</th>
<th>AKI n=5 (100%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>8.9 ± 7.3</td>
<td>3.8 ± 7.3</td>
<td>0.64</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>37.1 ± 6.8</td>
<td>39 ± 7.3</td>
<td>0.76</td>
</tr>
<tr>
<td>Males, N (%)</td>
<td>5 (41.7)</td>
<td>5 (100%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>170 (125-195)</td>
<td>160 (95)</td>
<td>0.99</td>
</tr>
<tr>
<td>Treated with Sildenafil, N (%)</td>
<td>7 (58.3%)</td>
<td>5 (100%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Morbidity, N (%)</td>
<td>4</td>
<td>1 (100%)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

PO2292

Baby NINJA (Nephrotic Injury Negated by Just-in-Time Action) Transfusion Rates

Hailey W. Cavigian, Cara L. Slagle, Kelli A. Krallman, Brenda Poindexter, David K. Hooper, Stuart Goldstein. Cincinnati Children’s Medical Center, Cincinnati, OH.

Background: Acute kidney injury (AKI) is associated with poor outcomes in neonates. Nephrotic medication (NTM) exposure is a common cause of AKI. Nephrotic Injury Negated by Just-in-time Action (NINJA) identifies patients with high NTM burden and recommends daily creatinine (Cr) screening. In neonates, concern for iatrogenic anemia decreases AKI screening. We monitored transfusion rates in our project modeled off the neonatal NINJA adaptation, Baby NINJA.

Methods: Critically ill neonates with high NTM exposure initially received modified Cr monitoring (only with routine labs) before transitioning to standard daily Cr monitoring. Patients transfused 3 days into & up to 7 days after Baby NINJA exposure periods counted as an associated transfusion. Statistical process control methods were used to detect changes from baseline. X² and Poisson regression analyses were used to compare metrics between SCI monitoring eras.

Results: Figure 1 shows an increase in transfusions 15 weeks before an increase in Cr compliance. A decrease in transfusions was sustained through the standard Cr era where the highest rate of Cr compliance was seen. The rate of NINJA-associated transfusions was unchanged. Table 1 shows that Cr compliance increased during each era, transfusions decreased between modified & standard Cr era, NINJA-associated transfusions remained stable, and transfusion rate changes were independent of NINJA-associated transfusions.

Conclusions: There was no association between transfusion rates and daily Cr testing with Baby NINJA implementation; therefore, critically ill neonates with high risk NTM exposure can safely be screened for NTM associated AKI.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Modified Cr</th>
<th>Standard Cr</th>
<th>p-value</th>
<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr compliance (%)</td>
<td>4.3</td>
<td>8.1</td>
<td>8.2</td>
<td>0.06</td>
<td>0.01</td>
<td>0.69</td>
</tr>
<tr>
<td>All Hb transfusion rate (per 1000 NICU patient days)</td>
<td>1.66</td>
<td>7.08</td>
<td>2.4</td>
<td>0.01</td>
<td>0.06</td>
<td>0.01</td>
</tr>
<tr>
<td>NINJA Hb transfusion rate (per 1000 NICU patient days)</td>
<td>2.2</td>
<td>5.4</td>
<td>3.9</td>
<td>0.13</td>
<td>0.52</td>
<td>0.74</td>
</tr>
<tr>
<td>All BUN - (NINJA vs Standard before vs standard) (per 1000 NICU patient days)</td>
<td>1.25</td>
<td>25.04</td>
<td>21.3</td>
<td>0.01</td>
<td>0.04</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*baseline vs modified, **modified vs standard, ***baseline vs standard

PO2293

Elimination of Intravenous Phthalate Exposure Abrogates Most Neonatal Hypertension in Premature Infants

Katherine Farnbach, Ryan Forbush, Sandra Irargorri, Randall Jenkins.

Background: The incidence of hypertension in premature infants in a neonatal intensive care unit (NICU) was noted to transiently drop during a 2-year period when the IV fluid (IVF) temporally changed to a phthalate-free IVF. The objective of the study is to quantify the effect of varying periods of IVF phthalate exposure on incidence of hypertension in premature infants.

Methods: A chart review was performed of all hypertensive premature infants born at one NICU during the last 6 years including a 3-year baseline period, a 20-month phthalate-free IVF period, and a 10-month period when the original phthalate-containing IVF returned to use. Patients born during 4-month transitions between periods were excluded. Incidence of hypertension for each period were compared for significant difference using Chi-Square analysis.

Results: Incidence of hypertension decreased from 9.7 cases per year (baseline) to 1.2 cases per year when IVF was phthalate-free, rising back to 12.0 cases per year when phthalate-containing IVF returned to use. Most cases met criteria for the pulmonary category of hypertension – for these infants the incidence of hypertension dropped from 7.3 to 1.2, then increased to 10.8 cases per year when evaluated for the same periods of varying phthalate exposure.

Conclusions: Serendipitous removal of IVF containing phthalates resulted in near elimination of hypertension in one NICU – an effect reversing entirely after the same brand of phthalate-containing IVF returned to clinical use. These results suggest that phthalate exposure from IVF plays a major role in neonatal hypertension, especially for those infants in the pulmonary category.
PO2294

Children with a History of Low Birth Weight (LBW) Show Greater Reduction in Kidney Function Than Previously Described Using the Updated Schwartz Equation

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Background: There is a higher risk of reduced kidney function in adults born with LBW (birthweight<2500g). A study using the Counahan-Barrat (CB) eGFR estimation showed a modest risk increase in adolescents with LBW. However the CB equation is only validated in children with CKD and underestimates the burden of CKD. Utilizing the updated Schwartz equation, a more sensitive calculation of eGFR validated in healthy children, we sought to assess the prevalence of reduced kidney function in adolescents born with LBW.

Methods: We performed a cross sectional analysis of children aged 12-15 from the National Health and Nutrition Examination Survey from 1999-2016. Reduced kidney function was defined as eGFR <90mL/min/1.73m². Participant characteristics were described as weighted sample means and proportions. We constructed logistic regression models adjusted for important sociodemographic factors to evaluate the association of LBW with reduced kidney function.

Results: A total of 6345 individuals were analyzed, representing 13,760,132 adolescents of whom 8% had a history of LBW. Of those born with LBW, the median age was 13.6 years, 49% were males, 49% were white, 25% were black, 19% were Mexican-American, and 7% were other race. A higher percentage of children with LBW was seen in worse poverty groups. Mean eGFRs in those born LBW were 103 and 107mL/min/1.73m² using the updated Schwartz and CB equation, respectively. The prevalence of reduced kidney function in those born LBW was greater using the updated Schwartz equation compared to the CB equation. OR 1.51 (95% CI 1.16-1.97) compared to the CB equation, OR 1.44 (95% CI 1.06-1.96). In an adjusted analysis, the odds of reduced kidney function in adolescents with LBW remained significant OR 1.46 (95% CI 1.11-1.97) using Schwartz but not the CB equation.

Conclusions: A higher prevalence of reduced kidney function was seen in children born with LBW utilizing updated Schwartz compared to the CB equation. The higher risk was sustained in adjusted analyses. These findings may support development of guidelines for CKD screening during long term follow up in the pediatric population with LBW.

PO2295

FGCG Renal Biopsy Network: First Epidemiological Report on Pediatric Renal Disease

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Background: In 2016, a regional renal biopsy network was founded as a collaboration between renal pathologists and nephrologists in order to standardize diagnosis and therapy. Uniform renal biopsy request and renal biopsy report forms were introduced, together with a new comprehensive list of renal pathology diagnoses for coding purposes. The Uniform renal biopsy request and renal biopsy report forms were introduced, together with a new comprehensive list of renal pathology diagnoses for coding purposes. The Uniform renal biopsy request and renal biopsy report forms were introduced, together with a new comprehensive list of renal pathology diagnoses for coding purposes.

Methods: Following informed consent and in compliance with GDPR, data registration consists of basic patient and categorical renal data, semi-structured medical information of renal disease, structured information of renal histopathology, and the clinical renal disease.

Results: In 2017 and 2018, 92 renal biopsies were performed in pediatric patients (age = 0-17 years) or 3.6 per 100,000 pediatric inhabitants per year. Three clinical patterns were equally represented: only proteinuria >1g/day; only hematuria; and combination of proteinuria and hematuria. Acute or chronic renal failure were rare. In the youngest age group (0-5 years; N=26) minimal change disease predominated, followed by Henoch-Schönlein nephritis and Alport’s disease. A more diverse renal disease spectrum was present in the highest age group (12-18 years; N=34): IgA nephropathy, different forms of proliferative glomerulonephritis and of nephrotic syndrome of childhood. Patients with a Causacian descent presented with IgA nephropathy, while a nephrotic syndrome was more common in Black and Asian patients. Alport’s disease was particularly diagnosed in female patients, IgA nephropathy in male patients, and the gender distribution was equal in minimal change disease.

Conclusions: The FGCG network provides a better cross-talk between renal pathologists and nephrologists. For the first time, reliable estimates of pediatric renal diseases based on histology are available; genetic analyses are not yet included. Efforts to coordinate clinical care of pediatric renal diseases in the region are ongoing.

PO2296

Developing a Strategy for Routine Reporting of Estimated Glomerular Filtration Rate on Pediatric Laboratory Results


Background: Routine calculation of estimated glomerular filtration rate (eGFR) is not present in laboratory reporting for children, potentially leading to low recognition of decreased eGFR. The study aim was to define options for pediatric eGFR reporting that optimize accuracy and minimize the impact of missing concurrent height in routine lab reporting.

Methods: Data was extracted from the Michigan Medicine Data Warehouse on all patients aged 1-19 years with serum creatinine between 2017-2018. Creatinine-creatinin C-based CKD (Cr-CysC, Schwartz, 2012) and creatinine-based ‘Bedside’ (Schwartz 2009) equations were used to calculate eGFR. Correlations were tested between eGFR calculated with same day height values against eGFR calculated with height imputation of 50th percentile for age and sex or patient-specific historical height percentiles. Scattered plots, Pearson’s correlation coefficients, and predictive characteristics were calculated.

Results: There were 109,090 serum creatinine measurements, and 35% had concurrent heights. There were 1770 Cystatin C measurements. eGFR by Bedside equation was abnormal (>90 mL/min/1.73m²) in 25% of measurements. Cr-CysC (r=0.99) and Bedside (r=0.98) equations had excellent correlations for measured vs imputed 50th percentile height eGFR (Figure). Patient-specific height percentile imputed for the Cr-CysC (r=0.99) and Bedside (r=0.99) eGFR also had tight correlations. Discrimination of abnormal eGFR was excellent for the Cr-CysC (94% sensitivity and 97% specificity) and Bedside (90% sensitivity and 97% specificity) equations using 50th percentile height. Conclusions: Imputation of 50th percentile or patient-specific historic height percentile enables eGFR calculation that correlates with eGFR using same day height. For implementation and with high sensitivity and specificity, use of 50th percentile height may be the preferred approach for pediatric eGFR reporting when patient-specific heights are not available.
PO2298
Measurement of GFR and Vasoactive Substances in Children with Sickle Cell Anemia
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Background: Patients with sickle cell anemia (SCA) have a high risk of developing renal disease. Sickle cell nephropathy is thought to begin in childhood with higher than normal glomerular filtration rates (GFRs) known as hyperfiltration that can lead to proteinuria, sclerosis of the glomeruli, decreased GFR, and eventual renal failure. This model of sickle cell nephropathy has not been validated in clinical studies. This study measured directly the GFRs of patients with sickle cell anemia and age matched control patients. In addition, urinary vasoactive substances were measured to correlate with the GFR.

Methods: Children with sickle cell anemia (SCA) and sickle-β-thalassemia (HbSβ0) were recruited for the study from the Sickle Cell Clinic at Children’s Medical Center of Dallas. These sickle cell disease genotypes are phenotypically similar and are the most severe. Healthy siblings of children seen in the Pediatric Nephrology Clinic at Children’s Medical Center of Dallas were recruited to serve as controls. GFR was measured directly from isohem clearance. Urine was obtained to measure vasoactive substances.

Results: In conclusion, we have shown that although the GFR in patients with SCA might not be elevated, there appears to be a population of SCA patients with higher than normal GFR. The intrarenal renin-angiotensin system appears to play a role in this hyperfiltration. Further studies are needed to continue to understand this phenomenon.

HbSS urine angiotensinogen/creatinine was significantly lower than control (p<0.005).

PO2299
Food Insecurity During COVID-19 in Children with ESKD: The Second Wave?
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Background: Food insecurity (FI) affects 1 in 6 children in the US and has increased three-fold during the COVID pandemic. Children with end-stage kidney disease (ESKD) may be at even higher risk of FI due to complex care needs, medication burden and dietary restrictions. A pre-COVID study assessing FI in pediatric hemodialysis (HD) patients described 70% prevalence. No data exists describing the effects of the COVID pandemic on FI in pediatric HD patients.

Methods: We assessed FI among families of patients age 0-18 years with ESKD on chronic HD at a single academic pediatric center. Families were screened for FI by using the Hunger Vital sign, a validated 2 question tool. We assessed impact of COVID on FI in pediatric HD patients.

Results: In conclusion, we have shown that although the GFR in patients with SCA might not be elevated, there appears to be a population of SCA patients with higher than normal GFR. The intrarenal renin-angiotensin system appears to play a role in this hyperfiltration. Further studies are needed to continue to understand this phenomenon.

Conclusions: The frequency of abnormal albuminuria or low GFR in adolescents in the United States is high; for many patients, recent changes are necessary to confirm these findings. The associated factors significantly guide possible toxins that may be associated with the high prevalence of CKD of unknown cause in our state. 

PO2300
Incidence of Hypercalcemia with Calcitriol Compared with Paricalcitol in Pediatric Patients Receiving Hemodialysis
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Background: At our institution, both calcitriol and paricalcitol are available for use. Paricalcitol is generally used when adverse effects of calcitriol are observed or during times of calcitriol shortage. There are limited data on the efficacy and safety of vitamin D analogs in pediatric (ped) hemodialysis (HD) patients (pts) to support preference of either agent. This study evaluated the incidence of hypercalcemia in ped HD pts receiving calcitriol compared to paricalcitol.

Methods: Single-center, retrospective review of ped pts on HD treated between January 2012 – December 2018 who received in-center doses of calcitriol or paricalcitol. Pts were excluded if they had in-center doses of both paricalcitol and calcitriol in a 6-month time frame. The primary objective was to evaluate the incidence of hypercalcemia in those receiving calcitriol compared to paricalcitol.

Conclusions: The incidence of hypercalcemia in patients receiving paricalcitol compared to calcitriol was high but did not reach statistical significance. There is no clear advantage seen with the use of paricalcitol when compared to the calcitriol group in peds population.
CI=0.51, 3.42; p=15), adaptive skills (e.g., social skills, adaptability; β=1.03, CI=2.95, 0.89; p=20), or behavioral symptoms (e.g., hyperactivity, conduct problems; CI=0.51, 3.42; p=.15), adaptive skills (e.g., social skills, adaptability; CI=0.51, 3.42; p=.15) were independently associated with CKD progression in children.

Methods: In the prospective CKiD study, children aged 6 months to 16 years old with chronic kidney disease (CKD), but by increasing serum phosphate levels may also increase levels of fibroblast growth factor 23 (FGF23), which is associated with adverse outcomes in both adults and children with CKD. Our objective was to quantify changes in FGF23, α-klotho and vitamin D binding protein (VDBP) in children participating in a vitamin D supplementation trial.

Results: Thirty-four children were included in the analysis; 17 received the intervention dose of 4000 IU cholecalciferol, and 17 received the control dose of 400 IU. The mean (SD) age of the cohort was 10.9 (5.8) years, 26.5% female, 23.5% black, 58.8% white, and 17.7% other race. Mean (SD) GFR at baseline was 60 (17.6) ml/min/1.73m².

Conclusions: Low urine EGF and elevated urine αKIM1 and MCP1 concentrations are independently associated with CKD progression in children.

Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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B–baseline
W=4 week

PO2304

Improving Metabolic Acidosis in Patients with CKD

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Background: Pediatric chronic kidney disease (CKD) is characterized by multiple metabolic derangements including metabolic acidosis. Untreated acidosis is associated with bone disease, increased mortality, and CKD progression1. Current guidelines

PO2303

Effect of Cholecalciferol Supplementation on FGF-23 in Children with CKD

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Background: Cholecalciferol increases total vitamin D levels in children with chronic kidney disease (CKD), but by increasing serum phosphate levels may also increase levels of fibroblast growth factor 23 (FGF23), which is associated with adverse outcomes in both adults and children with CKD. Our objective was to quantify changes in FGF23, α-klotho and vitamin D binding protein (VDBP) in children participating in a vitamin D supplementation trial.

Methods: We utilized stored serum samples from a 4-week pilot randomized controlled trial of supplementation with 4000 (high dose) vs. 400 (DRI) IU per day of cholecalciferol in children with mild-to-moderate CKD. Intact and C-terminal FGF23, soluble α-klotho, and VDBP were measured using commercially-available ELISAs in the Johns Hopkins Institute for Clinical and Translational Research Core Laboratory. Statistical analyses conducted using Stata 14.

Results: Thirty-four children were included in the analysis; 17 received the intervention dose of 4000 IU cholecalciferol, and 17 received the control dose of 400 IU. The mean (SD) age of the cohort was 10.9 (5.8) years, 26.5% female, 23.5% black, 58.8% white, and 17.7% other race. Mean (SD) GFR at baseline was 60 (17.6) ml/min/1.73m². Median (IQR) baseline total vitamin D level was 29 (20, 34) ng/ml in the control arm and 32 (23, 39) in the intervention arm. Total vitamin D level did not change significantly after 4 weeks of supplementation in the control arm, but was increased to 38.5 (31, 50) in the intervention arm (p=0.001). The table compares baseline and 4-week FGF23, α-klotho, and VDBP levels in the control and intervention arms, and no significant differences were noted between the groups who received DRI vs. high dose cholecalciferol.

Conclusions: Cholecalciferol supplementation of 4000 IU/day in children with CKD was not associated with significant differences in FGF23, α-klotho, or VDBP levels compared to children who received only the DRI.

PO2302

Urine Biomarkers of CKD Progression in Children

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Background: Biomarkers of tubular injury, repair, and inflammation may improve the ability to identify children at high risk of rapid kidney function decline and help elucidate the pathophysiology of CKD progression. In this study, we investigated whether the urinary biomarkers EGF, KIM1, MCP1, YKL40, and alphal microglobulin are prognostic of CKD progression in children.

Methods: In the prospective CKiD study, children aged 6 months to 16 years old with an eGFR of 30-90 were enrolled and eGFR was assessed annually. We measured urine biomarkers collected 5 months after study enrollment. Urine biomarkers were indexed to urine creatinine. The primary outcome was CKD progression, defined as a composite of a 50% decline in eGFR or ESKD.

Results: Of the 375 children included, median age was 12 years [IQR, 8-15], 227 (60% were male, and baseline eGFR was 44 [IQR, 35-56]. Overall, 187 children (50%) reached the primary outcome over a median follow-up time of 6.2 years [IQR, 3.0–10.3]. All biomarker levels were higher in children with CKD progression, except for EGF which was lower in those with CKD progression (p for all <0.05). After adjustment for confounders, children with urine EGF concentrations in the highest quartile were at a significantly lower risk of CKD progression compared to those with EGF in the lowest quartile [EGF aHR; 0.20 (95% CI: 0.11-0.39] (Table). Children with urine KIM1 and MCP1 in the highest quartile were at a significantly higher risk of CKD progression compared to those with EGF in the lowest quartile [KIM1 aHR; 2.6 (95% CI: 1.6-4.1), MCP1 aHR; 2.8 (95% CI: 1.7-4.7)].

Conclusions: Low urine EGF and elevated urine KIM1 and MCP1 concentrations are independently associated with CKD progression in children.

Funding: NIDDK Support

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PO2306 Determining the Optimal Dose of Cholecalciferol Supplementation for Children with CKD (C, Trial): An Open-Label Multicentre Randomized Controlled Trial
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Background: The optimal treatment regimen for correcting 25-hydroxyvitamin D (25(OH)D) deficiency in children with CKD has not been established. We studied oral cholecalciferol treatment regimens that achieve and maintain 25OHD levels above 30ng/ml in children with CKD stages 2-4.

Methods: We performed an open label, multicentre randomized controlled trial in children with 25(OH)D <30ng/ml, randomized 1:1:1 to oral cholecalciferol as 3000IU daily, 25,000IU weekly or 100,000IU monthly for 3months intensive phase therapy. A maximum of 3 courses of intensive phase treatment were allowed if 25OHD was <30ng/ml. Patients achieving normal 25OHD entered maintenance phase with 1000IU cholecalciferol daily for 9 months. Primary outcome was achieving 25OHD levels ≥30 ng/ml at end of intensive phase therapy.

Results: Of the 150 children screened, 90 were 25OHD deficient and randomised to daily(n=30), weekly(n=29) or monthly(n=31) treatment arms. Age, gender, renal disease, eGFR and baseline 25OHD were comparable between treatment arms. At end of the intensive phase, 68.8% achieved 25OHD ≥30ng/ml with comparable levels between arms (median 44.3 39.4 and 39.3 ng/ml p=0.24) on daily, weekly, monthly regimens respectively. The time taken to achieve 25OHD ≥30 ng/ml was comparable between treatment arms (p=0.28) with 7.7% not achieving normal 25OHD after 3 courses. Irrespective of treatment arm, median 25OHD were lower in children with glomerular disease than non-glomerular disease [25.8 vs 41.8ng/ml; p=0.007]. There was no significant difference in 25OHD between treatment arms at end of intensive phase (p=0.24) or maintenance phase therapy (p=0.05).[Figure]. There was no hypercalcaemia or hypercalciuria.

Conclusions: Intensive phase therapy with oral cholecalciferol as daily, weekly or monthly regimens achieved similar 25OHD levels without toxicity. Children with glomerular disease require higher doses of cholecalciferol compared to non-glomerular disease.

PO2305 Factors Influencing Duration of Dialysis in Children with Shiga Toxin-Producing Escherichia coli-Associated Hemolytic Uremic Syndrome (STEC-HUS) at a Single Center
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Background: More than half the children with STEC-HUS require renal replacement therapy. Several factors influence the duration of dialysis.

Methods: We performed a retrospective cohort analysis using electronic medical records and chart review of 67 patients with STEC-HUS identified through billing data from July 1st 2008 to August 30th 2015. Cases of atypical hemolytic uremic syndrome (HUS), Streptococcus pneumoniae associated HUS were excluded.

Results: The mean age at presentation with STEC-HUS was 4.9yrs (range 0.99-17.16yrs). 44 (66%) were females compared to 23 (34%) males. Data on intravenous fluids (IVF) administration prior to diagnosis of HUS was available in 54 subjects of which 39 (72%) received IVF anytime during four days prior to presentation, and 15 (28%) did not. Of the patients receiving IVF, 22 (56%) required dialysis for an average duration of 11.4d whereas in subjects without IVF, 7 (47%) required dialysis for an average duration of 14.7d, 9 of 55 subjects received NSAIDS during the illness, and six of the nine required dialysis. For these 6 subjects, the average duration of dialysis was 17d compared to 10.3d in subjects without NSAID exposure. We also evaluated patients for antibiotic exposure before and after the diagnosis of HUS. In 30 (53%) subjects without any antibiotic exposure the average duration on dialysis was 9.8d. For 11 (19 %) subjects receiving antibiotics before the diagnosis of HUS average duration of dialysis was 13.6d. Dialysis duration in the 12 (21%) subjects receiving antibiotics after the diagnosis of HUS was 13.3d.

Conclusions: To our knowledge our study is first to evaluate the impact of NSAIDS on the severity of HUS, and demonstrates that the use of NSAIDS in STEC-HUS increases the duration of dialysis significantly. Confirming previous literature, the use of antibiotics results in prolongation of dialysis regardless of the timing of administration. We also note that IVF administration in the first 4 days prior to the diagnosis of HUS may result in a shorter time on dialysis.

PO2307 ESRD Risk in Type 1 vs. Type 2 Childhood-Onset Diabetes Mellitus
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Background: Diabetic kidney disease (DKD) is becoming increasingly common among children. We aimed to estimate the risk of end-stage renal disease (ESRD) and mortality among adolescents with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM) and normal renal function compared to non-diabetics. We hypothesized that childhood onset T1DM vs T2DM would be associated with a different risk profile for developing ESRD and its complications.

Methods: A nationwide, population-based, retrospective cohort study, including 1,500,522 adolescents examined for military service between 1967-1997, which were classified according to the presence and type of diabetes. Data were linked to the Israeli ESRD registry. Cox proportional-hazards models were used to estimate the hazard ratio (HR) for ESRD.

Results: At study enrolment, 1,183 adolescents had T1DM and 196 had T2DM. ESRD developed in 2,386 non-diabetic individuals (0.2%) compared to 72 individuals (6.1%) with T1DM, and 8 individuals (4.1%) with T2DM. Participants with T1DM were younger at ESRD onset than participants with T2DM (median age: 36.0 vs. 40.5 years, P<0.05). In a multivariate model adjusted for age, sex, paternal origin, enrollment year, BMI, and blood pressure, T1DM and T2DM were associated with HR of 36.4 (95% CI,
Prevalence of Renal Dysfunction in Youth with Epidermolysis Bullosa

PO2308

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Background: Little is known regarding the prevalence of renal disease in youth with epidermolysis bullosa (EB), which we describe here.

Methods: We conducted a retrospective review of electronic health records of 170 (48.8% female, 51.2% male) EB patients aged < 25 years followed by our institution within years 1980-2019. We report the age-based prevalence of hematuria (≥1 red blood cells per high power field) and proteinuria (≥30 mg/dL). We also describe the outcomes of those with persistently abnormal UA, defined as hematuria or nephrotic-range proteinuria on ≥2 consecutive tests. Finally, we compare mortality in EB youth with versus without acute kidney injury (AKI), defined per Kidney Disease Improving Global Outcomes.

Results: The overall prevalence of microscopic hematuria was 22.7%, with no significant difference between sex (p = 0.10). Age-based microscopic hematuria followed a bimodal distribution, with increased prevalence among younger (0-3 years) and older (>12 years) children (p = 0.003) [Fig. 1]. The overall prevalence of proteinuria was 16.9%, with no significant differences between sex (p = 0.35) or age (p = 0.73) [Fig. 1]. 10 patients (5.9%) had persistently abnormal UA, and were diagnosed with: C3 glomerulopathy (4), ureteral strictures (2), infection (2), IgA nephropathy (1), and acute tubular necrosis (1). AKI occurred in 19 patients (11.2%) and was significantly associated with mortality (47.4% in the AKI cohort versus 20.0% in the non-AKI cohort, p = 0.01). Identified causes of death in AKI patients were multiorgan failure including renal failure (3), respiratory failure (1) and severe malnutrition (1).

Conclusions: Many youth with EB have hematuria and/or proteinuria, suggesting glomerulonephritis and/or urologic abnormalities may be underdiagnosed in this population. AKI is significantly associated with mortality in EB youth, with renal failure as a potential common cause of death.

Cumulative ESRD incidence

PO2309

Clinical Relevance of Fluid Volume Status Assessment by Bioimpedance Spectroscopy in Children on Maintenance Dialysis

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Background: Bioimpedance spectroscopy (BIS) has been used as a noninvasive method to evaluate body fluid volume status in dialysis patients. However, reports in pediatric dialysis patients about the effectiveness of this method are rare. We asked if there is a correlation in the results of BIS and clinical characteristics, and if there is a subsequent change of cardiovascular characteristics in patients whose dialysis prescription was modified based on BIS.

Methods: Medical records of children on maintenance dialysis who were evaluated by multifrequency BIS between January 2016 and December 2019 were reviewed. Their first result of BIS was assessed and fluid overload status was correlated with hypertension, number of oral antihypertensive medications and echocardiography results. In patients with fluid overload, change of dialysis prescription and clinical characteristics over time were reviewed.

Results: Among the 47 patients (male:female 28:19, hemodialysis/peritoneal dialysis 17:30) with a median age of 13.5 years, 13 children were overhydrated with the proportional overhydration relative to extracellular water more than 15%. Majority of children (76.9%) with fluid overload were taking two or more oral antihypertensive medications, while less than half of those without fluid overload were. 11 out of 13 overhydrated children changed their dialysis prescription to reduce their target body weights. Subsequent BIS in overhydrated children revealed a significantly decreased amount of fluid overload (initial: median 22.9%, follow-up: median 13.4%). However, their mean blood pressure (initial: 89.8 mmHg; follow-up: 84 mmHg) and the number of antihypertensive medications (initial: median 2 [0-4]; follow-up: median 2 [0-3]) did not significantly change. Also, none of the children initially overhydrated had their left ventricle hypertrophy changed.

Conclusions: While BIS might be a useful and noninvasive method to assess fluid status, implementation of this tool did not lead to clinically meaningful improvement of cardiovascular characteristics in the children on maintenance dialysis. Long-term follow-up of a larger population and correlation with a more objective clinical indicator of fluid overload such as serum brain natriuretic peptide would be necessary to verify the clinical effectiveness of BIS in pediatric dialysis patients.

PO2310

Variants of SLC34A1, SLC34A3, and AGXT in an Infant with Nephrocalcinosis and Hypercalcemia

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Introduction: Idiopathic infantile hypercalciemia (IHH) is a rare genetic disorder that can lead to neonatal nephrocalcinosis. It is typically caused by loss of function mutations in CYP24A1 or less commonly in SLC34A1. SLC34A1 encodes the NaPi-IIa transporter which aids in phosphate reabsorption in the renal proximal tubules. Defects in AGXT are responsible for primary hyperoxaluria type 1 (PH1). Defects in either AGXT or SLC34A1 can lead to infantile nephrocalcinosis and subsequent renal damage.

Case Description: A term male infant had bilateral hydropneumothorax on prenatal ultrasound. Postnatal labs showed hypercalcemia, hypophosphatemia, high 1,25 dihydroxyvitamin D3 and acute kidney injury. The patient was treated with fluids, furosemide, and calcitonin without significant change in serum calcium. Pamidronate was given which decreased serum calcium and worsened hypophosphatemia. Phosphate supplementation was initiated. Whole exome sequencing revealed two variants in SLC34A1, one of which was pathogenic, and a variant in SLC34A3 of unknown significance. Incidentally, this patient was compound heterozygous for three variants in AGXT: one pathogenic and two benign. After these results, patient was found to have generalized aminoaciduria and mild hyperoxaluria for age. Serum calcium decreased with maintenance of adequate plasma phosphate levels.

Discussion: Compound heterozygous mutations of SLC34A1 can cause IHH type II, and the variant in SLC34A3 could be contributing to this patient’s clinical phenotype in a unique triallelic pattern. The pathologic AGXT gene variant could cause this patient to develop PH1. The combined effects of IHH and PH1 could significantly impact the clinical course of this patient. Mutations in both AGXT and SLC34A1 have not been previously described in the literature. During acute severe hypercalcemia, it might be necessary to use pamidronate to lower serum calcium to levels that are safe for the administration of phosphate supplements.
PO2311
Dent Disease Phenotype Caused by Immunodysregulation Polyendocrinopathy Enteropathy X-Linked (IPEX) Syndrome: Due to Anti-Tubular Basement Membrane Antibody Disease
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Introduction: Immunodysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is an X-linked recessive disorder characterized by autoimmune enteropathy, diabetes mellitus, and hypercholesterolemia, which is commonly associated with anti-TBMMA antibodies. It has been shown that CUL3 gene mutations can cause IPEX syndrome. Mutations in the CUL3 gene have been associated with IPEX syndrome, and it is believed that the pathogenicity of these genes is due to the production of unstable T cells. The purpose of this study was to report a novel case of IPEX syndrome associated with a CUL3 de novo heterozygous c.1376A>T (p.K459M) mutation in the Cullin 3 (CUL3) gene.

Case Description: A 5-year-old male presented at the end of the first month of life, with type 1 diabetes mellitus, hypothyroidism, and chronic diarrhea and diagnosed by IPEX syndrome by c.434C>T; p.Ala 145Val mutation in the FOXP3 gene. He underwent stem cell transplant at 6 months of age from a fully matched unrelated donor. Post stem cell transplant he had recurrent chimerism with low but relatively stable donor T cells. The patient remained relatively stable until 4 years of age when he presented with the clinical picture of Dent’s disease: nephrocalcinosis, tubular proteinuria, Fanconi syndrome (proximal RTA, phosphaturia, calciumuria, glycosuria and aminoaciduria) and renal insufficiency. No disease-causing mutations in CLCN5 gene or the OCRL1 gene were identified on genetic testing. Renal biopsy demonstrated non-sclerotic glomeruli with no capillary loop spike formation, no crescent formation, no endocapillary proliferation, or segmental necrosis. Immunofluorescence showed tubular basement membranes stain with IgG, C3, kappa and lambda. Glomerular basement membranes were negative. Tubular basement membranes show extensive small electron dense deposits without substructure.

Discussion: In this case report we presented child with confirmed IPEX syndrome with nephritic-range tubular proteinuria, proximal RTA, phosphaturia, calciumuria, medullary nephrocalcinosis, and renal insufficiency, in addition to the classical triad of enteropathy, dermatitis and polyendocrinopathy. Our report is the first to document the anti-tubular basement disease clinically manifesting as the Dent’s disease phenotype in association with IPEX syndrome.

PO2312
Severe Hyperkalemia in a 4-Month-Old Female due to Cullin-3 Mutation
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Introduction: Pseudohypoaldosteronism (PHA) type II, also known as familial hyperkalemic hypertension, is a rare autosomal-dominant disorder that causes renal tubular acidosis (RTA) type 4, characterized by late-onset hypertension, hyperkalemia, non-gap metabolic acidosis, and low or low-normal plasma renin and aldosterone levels. We present a case of a female infant with PHA type II who presented with asymptomatic severe hyperkalemia due to Cullin-3 Mutation. Treatment with thiazide diuretics resulted in rapid correction of her hyperkalemia.

Case Description: A 4-month-old infant with an unremarkable past medical history presented for management of right neck abscess. Family history was significant for an unspecified seizure and movement disorder in her older sister. She had appropriate growth for her age, with weight, length, and head circumference all measuring around the 20th percentile. Vital signs including blood pressure were normal. Admission laboratories revealed high potassium level of 8.4 mEq/L, low bicarbonate level of 10 mEq/L (normal for age is 19-24), high chloride level of 116 mEq/L (normal for age is 97–108). Anion gap was normal at 10 mEq/L. No electrocardiogram changes were noted. Additional studies revealed positive urine anion gap of 40 mEq/L, a normal serum aldosterone level of 22 ng/dl, and a low renin activity of 0.2 ng/ml/hr (normal for age is 2–27). She received intravenous calcium chloride, sodium acetate, and oral sodium polystyrene sulfonate for hyperkalemia management. Whole exome sequencing revealed a de novo heterozygous c.1376A>T (p.K459M) mutation in the Cullin 3 (CUL3) gene consistent with PHA type II. She was treated with thiazide diuretics, which quickly corrected her hyperkalemia.

Discussion: Our case of PHA type II with a CUL3 pathogenic variant is exceptionally rare, especially given the patient’s age at presentation and the negative family history. Her diagnosis could have been easily missed were she not hospitalized for her neck abscesses. Without genetic evaluation and prompt treatment, this child may have eventually suffered from failure to thrive and hypertension at a later point in life because of chronic hyperkalemia and metabolic acidosis. Primary care physicians and nephrologists should consider the possibility of PHA type II in any child who presents with hyperkalemia and metabolic acidosis with or without hypertension.

PO2313
A Rare Pediatric Case of Karyomegalic Tubulointerstitial Nephritis
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Introduction: Karyomegalic tubulointerstitial nephritis (KIN) is a rare type of interstitial nephritis that often progresses to chronic kidney disease. The pathogenesis is unclear but speculated to result from disruptions to tubular epithelial cell division by genetic predisposition or external insults. Only 6 pediatric cases have been reported and maybe this condition is underdiagnosed.

Case Description: A 2-year-old male with history of refractory AML received a matched unrelated donor stem-cell transplant following busulfan, fludarabine, and single fraction total body irradiation. His post-transplant course was complicated by engraftment syndrome, hyperacute graft versus host disease (GVHD), thrombotic microangiopathy, and acute kidney injury. He required ICU stay, treatment with eculizumab and two weeks of renal replacement therapy. His kidney function improved but serum creatinine stayed higher than baseline (picture). Four months post-transplant, he was treated with cefepime, acyclovir, ibuprofen for enterococcus bacteria and pericardial effusion. Seven months post-transplant, while off all immunosuppression, he developed eosinophilia, renal tubular dysfunction with increased serum creatinine. Eosinophilia resolved spontaneously. Bone marrow was negative for leukemia and infectious workup was negative. Eight months post-transplant, he developed GVHD, diagnosis was skin biopsy. He also had persistent high serum creatinine with normal urinalysis. Ultrasound showed echogenic kidneys. Kidney biopsy was performed because of unexplained high serum creatinine. Specimen tissue showed tubulointerstitial nephritis with widespread karyomegaly in medullary tubules. Glomeruli were unaffected. Some cortical tubules showed ultrastructural myelinosomes. His renal function improved with steroids.

Discussion: Our case highlights that KIN can develop in children after chemotherapy. Diagnosis requires high index of suspicion and thorough pathological examination of kidney biopsy specimen. A trial of corticosteroid therapy may be considered.

PO2314
Rescue Therapy with Eculizumab for Catastrophic Antiphospholipid Syndrome in Juvenile Systemic Lupus Erythematosus
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Introduction: Catastrophic antiphospholipid syndrome (CAPS) is a life-threatening condition, and is associated with acute multiorgan failure, small vessels thromboembolism, and elevated markers of antiphospholipid syndrome (APL). Early recognition and prompt treatment can improve the outcome. We present a case of juvenile systemic lupus erythematosus (SLE), who presented with CAPS, refractory to conventional treatment, but rescue with Eculizumab.

Case Description: The patient is a 10-year-old female, previously diagnosed with systemic lupus erythematosus (SLE) without renal involvement and treated with hydroxychloroquine and low dose steroid, who presented with acute kidney injury and hypertensive crisis. On exam, her weight was 31.3 Kg, height 133 cm. Her BP was 185/127 mmHg and pulse 118/ min. Initial investigation showed hemoglobin of 7.2 g/dl, platelet count of 182/xL, BUN 99 mg/dL, Cr 7.86 mg/dL, proteinuria < 10 mg/dL. Urine protein to creatinine ratio was 5 mg/mg. Serum complements were low and had positive serology for Anti-DSDNA, Lupus anticoagulant, Anti-beta 2 glycoprotein, and anticardiolipin. The presumptive diagnosis was CAPS associated with SLE and thrombotic microangiopathy (TMA) which was confirmed by kidney biopsy. She underwent Methylprednisone, therapeutic plasma exchange (TPE), renal replacement therapy and Nicardipine infusion. After 7 sessions of TPE, Methylprednisone, Rituximab, and Mycophenolate Mofetil, her renal function improved and was taken off hemodialysis. Blood pressure was still uncontrolled. She had evidence of on-going hemolysis with undetectable haptoglobin and elevated LDH. Repeat TPE did not control her BP or hemolysis, thus Eculizumab was administered as rescue therapy.
a rescue therapy for TMA associated with CAPS. After 2 weekly doses Eculizumab, her renal function, blood pressure and hemolytic markers were much improved. Currently, her serum creatinine was 1 mg/dL, without significant proteinuria. She remained on 3 antihypertensive medications with good BP control

Discussion: This is a rare but challenging case of juvenile SLE, complicated with CAPS and TMA, who responded partially to conventional treatment. Eculizumab served as a rescue therapy with good result. Our case supports the use of Eculizumab for refractory CAPS in SLE.

PO2315
Hypertensive Crisis in an Infant: The Mass Effect
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Introduction: It is unusual for congenital hydronephrosis to present with a hypertensive crisis. Recognition of this etiology and prompt urologic intervention to relieve the acute mass effect is critical to prevent further morbidity and mortality.

Case Description: A 3 month-old male with known, mild, right-sided hydronephrosis secondary to ureteropelvic junction obstruction (UPJO) presented to the ED with one week of poor feeding, emesis, and abdominal distension. His recent urine output had been normal. Right upper extremity blood pressure (BP) was recorded as 140/79 mmHg in the ED. Labs were unremarkable with a normal urinalysis and serum creatinine of 0.3 mg/dL. Abdominal ultrasound revealed massive pelvocalyceal system of the right kidney with the kidney parenchyma stretched and thinned over the massively dilated central collecting system. Findings were confirmed on abdominal CT which also revealed profound mass effect on abdominal organs and vessels, specifically compressing and displacing the aorta and inferior vena cava. He was admitted to the pediatric ICU for BP management, which was controlled with IV hydralazine. Pediatric urology placed a percutaneous nephrostomy tube and drained over one liter of urine from the right collecting system. At discharge, the patient was normotensive off medications. A right pyeloplasty was completed shortly following discharge.

Discussion: UPJO is the most common cause of antenatally detected hydronephrosis. The renal pelvis of infants exhibits increased compliance and can accommodate large urine volumes. Kidney function may be preserved or could undergo deterioration depending on UPJO severity. If missed prenatally, infants with UPJO may present with a palpable abdominal mass, urinary tract infection, hematuria, or failure to thrive. Kidney failure and hypertensive crises are rare presentations but are indications for prompt surgical intervention to prevent permanent damage and reduce blood pressure. Infants with preserved function can be monitored conservatively with serial imaging.

PO2316
Missed Diagnosis: A Case of Asymptomatic Isolated Orthostatic Proteinuria from Nutcracker Phenomenon
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Introduction: In children, proteinuria which exceeds 100 mg/m2 per day or 150 mg per day is considered abnormal. Isolated proteinuria is relatively common, but persistent proteinuria is abnormal and should be investigated. Persistent proteinuria can be further divided into orthostatic subtype if the recumbent Pr/Cr is <0.2 mg/mg but this rises to abnormal (>0.2 mg/mg) after standing. One cause of orthostatic proteinuria is entrapment of the left renal vein, which is known as the Nutcracker Syndrome. Orthostatic proteinuria, isolated hematuria and pelvic congestion pain are the most common manifestations, however Nutcracker Syndrome is highly heterogeneous and frequently missed.

Case Description: We present an 18 year-old female with intermittent proteinuria, hematuria and occasional flank pain for nine years. The patient had proteinuria on dipstick at age eight. At age 15, she again was noted to have proteinuria on serial urinalyses with up to 500mg/dL protein. ANA, anti-dsDNA, C3, and C4 were normal. Renal ultrasound was performed with unremarkable kidneys and urinary bladder. For several years, proteinuria was mild and intermittently negative and no further workup was done. Split urine collection demonstrated minimal protein on first morning void but over 1g/g Pr/Cr by afternoon. We ordered renal ultrasound with Doppler, which demonstrated Doppler ultrasoundography showed the left renal vein had significantly increased flow velocity and appeared to be compressed between the AO and SMA.

Discussion: Differential for etiology of orthostatic proteinuria should include Nutcracker Syndrome as this diagnosis requires a high degree of suspicion. Nutcracker Syndrome can involve proteinuria as well as hematuria but also pelvic pain, back pain, and pelvic congestion symptoms.

PO2317
Rare Presentation of Nephrotic Syndrome in 10-Year-Old Male
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Introduction: Review nephrotic syndrome 2/2 amyloidosis due to genetic mutation

Case Description: 10 year male w/ mild proteinuria, progressed to UPC of 4mg/mg over months, Cr 0.4, Alb 2.5. Got strep, treated w/ amoxicillin & motrin, after 3 days developed periorbital edema, poor PO, fatigue, admitted. Labs Cr 4.1, Alb 1.1, UPC 31 mg/mg, no blood. RUS b/l enlarged, echogenic kidneys. Biopsy w/ glomerular expanded by amorphous, acellular proteinaceous material in mesangium, walls of arteries and arterioles (Image 1), congophilic on Congo red stain (Image 2), apple green on light birefringence, & tubular injury, final read: amyloidosis and AIN. Completed 3 days of IV steroids for AIN, started colchicine for amyloidosis. Genetics w/ pathogenic Cys59Arg variant of TNFRS1A, c/w TNF Receptor-Associated Periodic Syndrome (TRAPS). Started canakinumab, human monoclonal anti-IL-1 Ab. After 3 months, Cr baseline, no edema, still nephrotic range proteinuria, low alb. MOC w/ ESRD as teen, required dialysis, transplant. Later both kidney and liver failure, died at 31. Diagnosed w/ Familial Mediterranean Fever, as was MGF.

Discussion: Autoinflammatory disease usually presents as intermittent fever, abdominal & joint pain. Second most common is renal involvement, which starts w/ proteinuria, progresses to nephrotic syndrome, renal dysfunction. Diagnosis of amyloidosis based on amyloid fibrils in biopsy of involved tissue, stain positive w/ congo red, apple green birefringence to polarized light. No clear relationship between extent of amyloid deposition & severity of clinical manifestations of renal disease. TRAPS treated w/ directed therapy (IL-1 inhibitor), but difficult to track response to therapy as serum amyloid A not available. Use inflammatory markers (i.e. CRP) given autoinflammatory syndrome.
Cyanotic Nephropathy (CN) in Pre-Fontan Congenital Cyanotic Heart Disease (CCHD) with Solitary Kidney

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Introduction: CN is a glomerulopathy seen in patients with CCHD. Chronic hypoxia leads to proteinuria and reduced GFR through tubular and glomerular injury.

Case Description: A 13-year-old male with single kidney and pre-Fontan CCHD presented with hematuria and proteinuria on cardiac transplant evaluation. He had 6 months of symptomatic hypoxia requiring increased supplemental O2, but no other recent illness. Exam was notable for 3/6 pansystolic murmur, tachypnea with clear lung fields, hepatoplenomegaly, cyanotic nailbeds with marked clubbing, but no peripheral edema. 24 hour urine protein measured 4.1g (normal < 0.2g), 38% was albumin. Serum albumin was 3.5 g/l (normal) and eGFR by Cystatin C was 72 ml/min/1.73m2. Hemoglobin was elevated at 20.1 (normal 12.5-16.1 g/dl), C3, C4, ANA, dsDNA, ANCA were normal. Ultrasound showed solitary left kidney with nephromegaly (12.5cm, 1008g/107g), and a solitary cystic mass. Renal biopsy consistent with minimal change syndrome. An initial 60mg/m2 course of glucocorticoids, which was successfully tapered without incident. Patient has since been stably maintained on his prior effective dose of MMF, and has had no relapses since.

Discussion: CN risk factors include duration of hypoxia, elevated hematocrit > 40%, and thrombocytopenia. All were present in our patient. Solitary kidney and elevated venous pressure may have contributed. After heart transplantation, renal function improved with most recent eGFR by Cystatin C 121 ml/min/1.73m2. Treatment and prevention of CN depend on correction of cyanosis. CN has become less common as most children with CCHD undergo Fontan in early childhood. There are limited data about medical management but proposed treatments include renin angiotensin system blockade, beta blocking drugs, diuretics, ivabradine, digoxin, and hydralazine/isosorbid dinitrate. Therapeutic phlebotomy has been reported. To our knowledge this is the first report of CN in a patient with solitary kidney. Low renal mass and baseline glomerular hyperfiltration may increase the risk of CN progression in this subset of patients.

Lupus Vasculopathy Successfully Treated with Eculizumab and Rituximab in an 8-Year-Old Male

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Introduction: Lupus vasculopathy of the kidney is a rare form of vascular disease in patients with systemic lupus erythematosus characterized by non-inflammatory, necrotizing vessel wall changes. The pathogenesis may be related to immune-mediated vascular injury from accumulation of immunoglobulins and complement in the vascular wall. Lupus vasculopathy carries a poor renal prognosis, and no standardized treatment has been established.

Case Description: An 8-year-old previously healthy male presented to the emergency department with fever, fatigue, headache, diarrhea, nosebleeds, decreased urine output and lower extremity swelling. He was found to have hypertension, fluid overload, active urine sediment and severe acute kidney injury necessitating renal replacement therapy. He had thrombocytopenia and hemolytic anemia without presence of antiphospholipid antibodies or abnormal ADAMTS13 activity. He met criteria for systemic lupus erythematosus including hypocomplementemia, positive ANA and dsDNA antibodies. Renal biopsy showed class III lupus nephritis and multifocal arterial and arteriolar large intimal complex deposits with endothelial cell necrosis, consistent with a diagnosis of lupus vasculopathy. He received 6 sessions of plasmapheresis without improvement. Based on renal biopsy, he was treated with cyclophosphamide per Euro Lupus protocol. Eculizumab was started for treatment of lupus vasculopathy. His anemia, thrombocytopenia, and proteinuria improved after initiation of eculizumab, but he remained dialysis dependent. Eculizumab was discontinued after 6 weeks of therapy, but he again developed thrombocytopenia, hemolytic anemia, worsening proteinuria and hypertension. These improved after restarting eculizumab. Due to ongoing evidence of lupus activity, rituximab was given after completion of cyclophosphamide. Hemodialysis was discontinued one month after his first rituximab dose with B-cell depletion. He remains on eculizumab therapy and has stable chronic kidney disease stage 2 despite B-cell repopulation.

Discussion: Prior case reports have documented effective treatment of lupus vasculopathy with rituximab. To our knowledge, no data exists on eculizumab for treatment of lupus vasculopathy. Given our patient’s clinical improvement with these therapies, we conclude that more research is needed to define their role in treatment of patients with lupus vasculopathy.
the transcription factor E3 (TFE3) gene. Patient did well post-operatively with no signs of cancer on recent imaging and did not require any chemotherapeutics.

Discussion: This case adds to the field of pediatric renal cell carcinoma and highlights a treatment approach that incorporates religious backgrounds into medical management.

PO2322
IgG4-Related Disease: Nephropathy and Bone Marrow Failure in a 2-Year-Old Child
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Introduction: IgG4 related disease (IgG4 RD) is a systemic immune-mediated disorder that can potentially affect every organ. It is characterized by fibro-inflammatory tissue damage, IgG4 positive plasma cells, and often by elevated serum IgG4. Renal involvement can include tubulointerstitial nephritis (TIN), membranous glomerulopathy (MGP), and retroperitoneal fibrosis. The disease is more frequent over 50 years of age and only a few cases of IgG4 RD are reported in children.

Case Description: A 2-year-old child was diagnosed with a trilineal bone marrow failure. Bone marrow biopsy showed poor and dyshomogeneous cellularity and lymphoplasmacytic infiltrate organized in follicular structures. Hematologic DNA analyses were negative. IgG subclass analysis showed elevated serum levels of IgG4 subclass (353 mg/dL). Kidney failure was also found (creatinine 1.3 mg/dL, proteinuria, and granular casts). A renal biopsy was performed. Light microscopy showed tubulointerstitial inflammatory infiltrate, thickening of the glomerular basement membranes, and subepithelial deposits Cd4 IF showed subepithelial glomerular IgG deposits with granular pattern and tubular wall deposits; C3 glomerular deposits and focal tubular deposits. A diagnosis of MGP associated with TIN was made. IHC staining for IgG4 demonstrated plasma cells with overlapping positivity for IgG and IgG4. After the diagnosis of IgG4 RKD, a therapy with steroids was started, without clinical response. Thereafter the patient underwent to bone marrow transplant.

Discussion: IgG4 RKD in adults with simultaneous TIN and MGP has been reported in a few cases. This is the first documented case of IgG4 RKD with simultaneous TIN and MGP in a pediatric patient. IgG4 RD is an emerging systemic disease and it should be taken into account in the differential diagnosis in systemic autoimmune diseases, also in pediatrics.

PO2323
Is a Single Static Cut Point Useful to Define Ambulatory Hypertension in Youth? The SHIP AHOY Study
Gilad Hamdani,1 Michael A. Ferguson,4 Marc Lande,2 Kevin E. Meyers,3 Mark Mitsnefes,2 Joshua A. Samuels,1 Joseph T. Flynn,4 Elaine M. Urbina,1 The SHIP AHOY Investigators; Schneider Children’s Medical Center of Israel, Petah Tikva, Israel; University of Rochester Medical Center, Rochester, NY; Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; Seattle Children’s Hospital, Seattle, WA; The Children’s Hospital of Philadelphia, Philadelphia, PA; Boston Children’s Hospital, Boston, MA; University of Texas Health Science Center at Houston, Houston, TX.

Background: Ambulatory blood pressure monitoring (ABPM) is increasingly utilized for the diagnosis of hypertension (HTN). While adult guidelines use absolute blood pressure (BP) cut points to define ambulatory HTN, current pediatric guidelines define ambulatory HTN based on a sex- and height-specific 95th percentile derived from limited pediatric normative data, in which many tall adolescents have a threshold for HTN higher than adult cut-points.

Methods: We compared absolute ABP values with sex- and height-specific ABP percentiles and predictors of left ventricular hypertrophy (LVH) in youth. We measured casual BP, ABPM, anthropometrics, and echo for LV mass index (LVMi) in 357 adolescents (mean age 15.5 ±1.7 years, 63% white, 59% male). ABPM was performed with Omtrax device (Spacelabs Inc., Snoqualmie, WA). ABP index was defined as mean ABP and sex- and height-specific 95th percentile. LVH was defined as LVMi ≥38.6 g/m².7 (pediatric cut-point). Logistic regression was used to assess different ABP measures as predictors of LVH. Sensitivity and specificity of different ABP cut points as predictors of LVH were calculated.

Results: Seventy participants (19.6%) had LVH. Systolic 24-hour, wake and sleep mean BPs and indexes were all significantly associated with LVH. The C-statistics for absolute 24-hour (AUC 0.642 vs. 0.612, p=0.042) and wake (AUC 0.628 vs. 0.590, p=0.03) SBP predicted LVH better than SBP indexes of the same time periods. Absolute SBP cut points also had better balanced sensitivities and specificities in predicting LVH (24-hour SBP 120%: 66% and 61%; wake SBP 125%: 63% and 59%; sleep 110%: 61% and 61%). There was no significant association between diastolic BP measures and LVH.

Conclusions: A single static cut-point using absolute ambulatory SBP is non-inferior to sex-and height-based SBP percentile in predicting LVH in youth. The cut-points for 24-hour and wake ABPM are lower than those for adults but may be used to define ambulatory HTN in this population.

Funding: Private Foundation Support

Table: AUC, sensitivities, and specificities of different ambulatory SBP measures in predicting LVH

PO2324
Proteinuria and Dipping on 24-Hour Ambulatory Blood Pressure Monitoring in Children
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Background: Absence of nocturnal blood pressure dipping is associated with adverse cardiovascular outcomes in adults. Risk factors for non-dipping in adults include obesity and proteinuria. In children, risk factors for non-dipping have not been well established.

Methods: We identified consecutive patients aged 5 to 19 years who underwent 24-hour ambulatory blood pressure monitoring (ABPM) at Rady Children’s Hospital from August 2018 to January 2019 and had a spot urine protein to creatinine ratio (PCR) measurement within one year of their ABPM. Dipping was defined as a 10% reduction in systolic and diastolic blood pressure from day to night. Multivariable logistic and linear regression models evaluated the association of proteinuria with dipping, employing backwards selection models to retain important confounders.

Results: Seventy-seven children had ABPM and urine PCR assessments during the study period, among whom 27 (35.1%) were non-dippers. Non-dippers had a higher left ventricular mass index as compared to dippers (mean difference 6.9 g/m², 95% CI 1.6 to 12.2). Doubling of urine PCR was associated with 38% higher odds of non-dipping in the multivariable model (Table). Doubling of urine PCR was also associated with a lower diastolic dipping percent by 1.33 (95% CI 0.31 to 2.34), after adjusting for age, body mass index, and estimated glomerular filtration rate.

Conclusions: Proteinuria is significantly associated with non-dipping in children. Pediatric patients with non-dipping should be evaluated with urine PCR, and conversely, those with proteinuria may benefit from a 24-hour ABPM.

Funding: NIDDK Support
PO2325
Association of Environmental Tobacco Exposure with Blood Pressure in US Children
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Background: Hypertension is a leading cause of cardiovascular and kidney disease in adults, and there is evidence that pathologic sequelae begin in childhood and young adulthood. Nicotine and other tobacco compounds have a variety of toxic effects, but to date their associations with chronic hypertension is unclear, especially in pediatric populations.

Methods: We examined the association between tobacco exposure and high blood pressure (HBP) in children who participated the National Health And Nutrition Examination Survey (NHANES) during 2008-2016. Children were classified as having tobacco exposure if they had blood cotinine levels >0.05ng/dL or reported living with a smoker or smoking themselves. High blood pressure was classified according to the 2017 AAP Clinical Practice Guidelines. Analysis was conducted by logistic regression with adjustment for baseline demographics, income and other possible confounders. Subgroup and sensitivity analyses were conducted.

Results: There was a positive association of high blood pressure with tobacco exposure in the study population. After adjustment for demographics, the odds of having high blood pressure was 1.39 (95% Confidence Interval (CI) 1.04, 1.87) for any tobacco exposure compared to no smoking exposure. The association was similar across participant subgroups. The association remained significant by sensitivity analysis using cotinine exposure as a continuous variable. Separately, the odds of having high blood pressure for passive smokers was 1.35 (CI 0.98, 1.85) while the odds for active smokers was 1.71 (CI 1.14, 2.54) compared to participants with no tobacco exposure.

Conclusions: Tobacco exposure is associated with high blood pressure in US children and adolescents.

Funding: Other NIH Support - 2T32DK007110-43

Association of Tobacco Exposure with High Blood Pressure

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PO2326
Hypertension and CKD at 7 Years After Surgical Repair of Congenital Heart Disease in Children
Jason H. Greenberg,1 Michael Zappitelli,2 Heather Thiessen Philbrook,3 Yaqi Jia, Prasad Devarajan,4 Chirag R. Parikh.1 TRIBE-AKI Consortium Yale University, New Haven, CT;2Hospital for Sick Children, Toronto, ON, Canada; 3Johns Hopkins University, Baltimore, MD; 4Cincinnati Children’s Hospital Medical Center Division of Child and Adolescent Psychiatry, Cincinnati, OH.

Background: We previously determined that children who require surgery for congenital heart disease are at an increased risk for hypertension and CKD 5 years after cardiac surgery. This study assessed the long-term risk of hypertension and CKD after cardiac surgery and if these outcomes are sustained.

Methods: We prospectively enrolled children from 1 month to 18 years old, undergoing cardiopulmonary bypass at three centers. Children who survived their surgical hospitalization had blood pressure, urine albumin to creatinine ratio, and serum creatinine measured at two-person follow-up visits (median 5.4 years and 7.4 years after surgery). Hypertension was defined using the American Academy of Pediatrics 2017 Hypertension guidelines. Estimated glomerular filtration rate (eGFR, mg/dL) was calculated using the CKD equation. CKD was defined as the presence of low eGFR (<90 ml/min/1.73m²) or microalbuminuria. We compared the risk of hypertension and CKD status at the 5 and 7-year visits using the McNemar test.

Results: Of 131 children with a follow-up visit 5 years after cardiac surgery, 88 (67%) children participated in the 7-year follow-up visit. The median age of the cohort at the 7-year follow-up visit was 10.7 [IQR: 7.8-13.0] years and 47% were female. 32 children had previously had a septal defect repair, 15 an inflow/outflow tract or valve procedure, 34 had a combined procedure, and 7 were not defined. Separate analysis of the 5-year and 7-year visit revealed hypertension and CKD were sustained in 86 (62%) and 4 (29%) patients, respectively.

Conclusions: The long-term risk of hypertension and CKD were common at the 7-year visit. Compared to the five-year visit, hypertension was sustained in the majority of children. Although CKD was not sustained, there was an increased incidence of new children with GFR<90 at the 7-year visit. The risk factors for sustained hypertension and kidney disease should be further studied in children with congenital heart disease.

Funding: NIDDK Support

PO2327
Evaluating the Role of the Kidneys in Posterior Reversible Encephalopathy Syndrome in Pediatric Patients
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Background: Kidney disease is a known risk factor for posterior reversible encephalopathy syndrome (PRES), but the specific markers of kidney function that are relevant to PRES are undetermined. The objective was to investigate the associations of various markers of kidney function with PRES.

Methods: In a case-control study of high-risk children, we recorded most-recent blood urea nitrogen (BUN), documentation of acute kidney injury (AKI), serum creatinine, serum albumin, and hemoglobin level and calculated the estimated glomerular filtration rate (eGFR). PRES cases were confirmed clinically and radiologically. We applied multivariable regression models to estimate the associations of the exposures with PRES. We utilized directed acyclic graphs to inform the following model adjustments: 1) history of kidney disease and nephrotoxic medication exposure for the kidney function models; 2) history of kidney disease, eGFR, and albumin treatment for the serum albumin model; and 3) age, sex, history of kidney disease, eGFR, fluid overload, and nephrotoxic medication exposure for the hemoglobin model.

Results: The mean age of the study population was 9.5 years (±4.9) and 51% were female. Of that population, 29% had a history of kidney disease, 67% had exposure to nephrotoxic medications, and 29% had AKI prior to the onset of PRES. BUN [adjusted OR (aOR) 1.03 per 1 mg/dl increase, 95% CI 0.99-1.07, p=0.09] and AKI (aOR 3.78, 0.68-21.13, p=0.013) were modestly associated with PRES. eGFR (aOR 1.0 per 1 ml/min increase, 0.98-1.02, p=0.17) was not associated with PRES. Hemoglobin (aOR 1.12 per 1 g/dl increase, 0.81-1.56, p=0.48) was not associated with PRES.

Conclusions: In a case-control study of children at high risk for PRES, we determined that among several markers of kidney function, BUN and AKI were modestly associated with PRES. Further prospective studies with larger sample sizes and higher power are necessary to fully evaluate the role of kidney function in the development of PRES.

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PO2328
Effect of Hypertension on Childhood-Onset Systemic Lupus Erythematosus in a Tertiary Medical Center in Korea
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Background: Hypertension (HTN) is prevalent in childhood-onset systemic lupus erythematosus (cSLE) and affected either by disease activity itself, cSLE medication or both. The purpose of this study is to evaluate the prevalence, clinical characteristics and long-term clinical effect of HTN in Korean cSLE patients treated in tertiary medical center in Korea.

Methods: The medical records of cSLE patients, diagnosed by 2019 SLE European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria, who visited Samsung Medical Center from January 2009 to May 2019 were reviewed retrospectively. The disease activity was evaluated by Modified Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and renal activity (renal SLEDAI) was measured by scores from SLDEA-2K. The long-term damage was evaluated by The Pediatric Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (Ped-SDI). The sex-, age- and height-blood pressure standards recommended by AAP 2017 guideline was used to define HTN. Left ventricular hypertrophy (LVH) was defined by sex, age specific left ventricular mass index (LVMi) at 95th percentile.

Results: Total 32 patients were enrolled in this study. The median follow-up duration was 7.3 year and female was predominant. Median age at SLE and HTN diagnosis were 14.2 and 14.3 year, respectively. Initial renal involvement was detected in 12.5%. The proportion of LN was detected in 84.4% (n=28) and 37.5% of them were class IV (n=12). The prevalence of HTN, including 2 transient HTN, was 34.4% (n=11) and stage 2 HTN was prevalent (n=9). The median dose of steroids, converted to prednisolone, at diagnosis of SLE and HTN were 1.0mg/kg/day and 0.5mg/kg/day. Among cSLE patients with HTN, 21 patients had 3 episodes of posterior reversible encephalopathy syndrome. LVH was detected in 2 patients with HTN. In the cSLE patients with persistent HTN (n=9), lower eGFR (OR=0.9, p=0.031) and higher BMI (OR 1.4, p=0.047) were shown at the time of SLE diagnosis. Every patient with HTN - including transient HTN - in cSLE (n=11) showed lower eGFR at the time of SLE diagnosis (OR 0.9, p=0.029) and higher Ped-SDI (OR 1.8, p=0.047) at last visit.

Conclusions: In conclusion, HTN in cSLE is associated with BMI and renal function at SLE diagnosis. Also, HTN affect long term damage accumulation in cSLE.
PO2329

Hemodiafiltration Maintains a Sustained Improvement in BP Compared with Conventional Hemodialysis in Children: The HDF, Heart and Height (3H) Study

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Background: Hypertension is prevalent in children on dialysis and associated with left ventricular hypertrophy, cardiovascular disease, and mortality. We studied the blood pressure (BP) trends as well as risk factors associated with the evolution of BP over 1 year in children on conventional hemodialysis (HD) vs hemodiafiltration (HDF).

Methods: This is a post-hoc analysis of the “3H - HDF-Hearts-Height” dataset, a multicenter, non-randomized, parallel-arm observational study. Mean arterial pressure (MAP) derived from 24-hour ambulatory BP monitoring was calculated and hypertension was defined as 24-hour MAP standard deviation score (SDS) <95th percentile.

Results: 78 children on HD and 55 on HDF who were followed-up for 1 year and had three ABPM measures were included. MAP-SDS was under-estimated by pre-dialysis systolic BP-SDS (mean difference: -0.6; 95% LoA -4.9 to 3.8). At baseline 82% on HD and 44% on HDF were hypertensive, with uncontrolled hypertension (BP >95th centile on medications) in 88% vs 25% respectively; p<0.001. At 12-months children on HDF had lower MAP-SDS compared to those on HD in all age groups (p<0.001). Over the one-year follow-up, the HD group had a mean MAP-SDS increase of +0.98 (95%CI 0.77 to 1.20; p<0.0001), whereas the HDF group had a non-significant increase of +0.15 (95% CI -0.10 to 0.40; p=0.23). Significant and independent predictors of MAP-SDS were dialysis modality (p<0.03 [95% CI 0.51 to 1.15] SDS for HD vs HDF, p<0.0001) and higher HDWG (p=0.13 [95% CI 0.06 to 0.19] p<0.0003).

Conclusions: Children on HD had a significant and sustained increase in BP over the 1-year study period compared to an attenuated and non-significant increase in HDF. Volume overload with higher HDWG, but not anti-hypertensive medications, was associated with a higher MAP-SDS in both groups.

PO2330

Novel Nephrin Protein/HLA Class II Complexes: A New Mechanism of Steroid-Sensitive Nephrotic Syndrome

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Background: We have recently identified the risk allele (HLA-DRB1*08:02) and the protective allele (HLA-DRB1*13:02) in the development of childhood steroid-sensitive nephrotic syndrome (SSNS) in a Japanese population (JASN 2018). HLA-DRB1*08:02, DQA1*02:01-DQB1*02:01 was also identified as a risk haplotype in other populations. In addition, we found that NPHS1, coding nephrin, which is a key component of podocytes, was associated with susceptibility to childhood SSNS (Kidney Int 2020). HLA class II genes are associated with susceptibility to many kinds of autoimmune diseases, with one of the mechanisms being misfolded protein/HLA class II complexes that are aberrantly transported to the cell surface inducing immune responses (Jim, Arase et al. PNAS 2014).

Therefore, we investigated the relationship between each HLA allele and nephrin, based on the hypothesis that nephrin protein/HLA class II complexes might be involved in the development of SSNS.

Methods: Nephrin lacking the transmembrane domain (Nephmis) was used as a model of misfolded protein that is not expressed on the cell surface. We co-transfected Nephrmis and HLA-DR to HEK293T cells and assessed the expression patterns by flow cytometry and immunoprecipitation.

Results: Nephrmis was detected on the cell surface in the presence of HLA-DR, which was more intense in the risk alleles than in the protective allele (DRB1*07:01-DRB1*08:02-DRB1*13:02). While Nephrmis communoprecipitated with HLA-DR, Nephrmis was not detected in the absence of HLA-DR. [Discussion] Podocytes are sometimes considered as immunecompetent professional antigen presenting cells because they present antigens on the cell surface via HLA class II and stimulate immune signaling. We showed that the risk HLA DR allele tended to present Nephrmis stronger than the protective allele, suggesting that an immune response could be more easily induced in the risk alleles than in the protective allele. Although there are a variety of possible mechanisms by which HLA polymorphisms could be associated with SSNS, the binding of specific molecules, such as nephrin or HLA mis, and their presentation may provide new insights into the pathogenesis of SSNS.

Conclusions: Our results suggest that nephrin protein/HLA class II complexes can be involved in the pathogenesis of childhood SSNS.

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PO2331

Efficacy and Safety of Ravulizumab in Pediatric Patients with Atypical Hemolytic Uremic Syndrome Previously Treated with Eculizumab: 26-Week and 1-Year Data

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Background: The complement C5 inhibitor eculizumab improves outcomes of atypical hemolytic uremic syndrome (aHUS) but must be administered every 2–3 weeks. Ravulizumab, engineered from eculizumab for a longer half-life, is efficacious and safe in adult aHUS with 8-week dosing intervals. This analysis was in eculizumab-treated children with aHUS.

Methods: ALXN1210-aHUS-312 (NCT03131219) is a phase 3, single–arm trial in complement inhibitor-naive children (Cohort 1; reported separately) and children who were receiving treatment with eculizumab without thrombotic microangiopathy (TMA; Cohort 2; reported here). This analysis assessed TMA activity, and the pharmacodynamic measure serum free C5 levels after patients switched from eculizumab to ravulizumab treatment. Patients received loading doses then maintenance treatment with ravulizumab every 4 or 8 weeks, dependent on weight, for 26 weeks. An extension phase is ongoing; here we report data on efficacy through 1 year and safety from all available follow up (median 50.2 weeks).

Results: Ten patients (mean [SD] age 11 [5.0] years) were enrolled into Cohort 2; all completed the 26-week initial evaluation period and entered the extension. Mean eGFR, hematologic outcomes (platelet, lactate dehydrogenase and hemoglobin normalization), and fatigue measures remained stable during both trial periods. At 1-year, the mean (SD) changes from baseline were: eGFR, -3.9 (8.3) mL/min/1.73m2; platelets, −17.8 (54.6) x10^10/L; LDH, −10.7 (19.2) U/L; hemoglobin, −4.5 (7.1) g/L. All patients were in the same eGFR category at 1 year as recorded at baseline (eGFR mL/min/1.73m2 ≥90, n=6; 60–89, n=1; 49–59, n=1). No patients required dialysis. Despite the increased dosing interval, serum free C5 levels were maintained below the threshold of 0.5 mg/mL. All patients experienced adverse events (AEs) but none discontinued the trial. No meningococcal infections occurred. One patient experienced serious AEs due to a respiratory tract infection.

Conclusions: Continued efficacy, no additional safety concerns and the benefit of reduced dosing frequency was demonstrated in pediatric patients with aHUS who were stable on eculizumab and switched to ravulizumab.

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PO2332

Typical Hemolytic Uremic Syndrome in Children: A Single-Center Experience

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Background: Typical hemolytic-uremic syndrome (HUS) associated with diarrhea can be a fatal disease in children. Diarrhea and blood-stained stools are early symptoms. Oliguria and renal failure can occur anywhere from 3-7 days after onset of diarrhea. Hemolytic-uremic syndrome (HUS) is a life-threatening disease presenting may decrease the need for dialysis. Oligo-amuria at admission and leukocytosis is associated with poor outcomes during hospitalization. After recovery, there is a risk of long-term renal complications such as hypertension, proteinuria, and chronic kidney disease (CKD).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Methods: We performed a retrospective analysis of 43 children admitted with diarrhea associated with HUS at our center in the last ten years. The ‘late presentation’ defined as serum creatinine >1 mg/dL, oliguria, or anuria at admission. The primary outcome was the presence of long-term renal sequelae. It included proteinuria, hypertension, or chronic kidney disease (CKD) (eGFR <75 ml/min/1.73m2) after one year of disease-onset. The Chi-square and correlation analysis performed on the SPSS platform.

Results: Overall, 32/43 presented late in the disease course, 30/43 required dialysis (median: 8 d), and 8/43 had a recent history of NSAID use. The administration of dextrose and saline containing iv fluids in the early presentation was associated with the decreased requirement of dialysis (p=0.023), but the effect was not significant with NSAID use (p=0.064). Peak white blood cell count (Wbc) had a strong correlation with days of hospitalization (p=0.001). 10/43 children were lost to follow up. 13/33 children showed renal sequelae (3 include with 3 CKD and 1 with ESRD who required kidney transplant) affecting 12/2000 children (p=0.0011) and duration of dialysis-14 days (at p=0.002) were associated significantly with the primary outcome. 6/43 children were un-immunized. There was no mortality.

Conclusions: High peak WBC count may be a useful prognostic marker to evaluate the risk of long-term renal complications. These children need monitoring periodically after disease recovery. Early diagnosis and iv fluids before the onset of renal failure may help to prevent dialysis-related morbidity at the time of admission. More awareness is needed to discourage the use of NSAIDs following initial symptoms of HUS.

PO2335

Hemoglobinuria for the Early Identification of Atypical Hemolytic Uremic Syndrome Relapse: Data from the ItalKid-HUS Network

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Background: Atypical hemolytic uremic syndrome (aHUS) is at risk of relapse any time, thus patients require lifelong monitoring. We suggested that patients could be monitored for relapses, with hemoglobinuria (twice weekly and during intercurrent diseases) based on the hypothesis that a thrombotic microangiopathy involving the glomeruli, cannot take place without hematuria. However this assumption has not been validated.

Methods: The aim of the study is to analyze our experience with the mentioned approach in patients with aHUS who have never been treated (group 1), on treatment (group 2) and who have discontinued C5 inhibition (group 3). The records of all aHUS patients managed or referred to our Center from January 2009 to March 2020 were included and the analysis for the presence of hemoglobinuria was restricted to the period following primary remission with the aim of validating this biomarker as a reliable one for the early identification of relapses. Patients with persistent hemoglobinuria, although in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were excluded. A positive test was defined as hemoglobin ≥0.5 g/L in documented TMA remission, were included.

Results: 84 patients with aHUS (50% females) were included with 1517 determinations of hemoglobinuria during a cumulative observation period of 261 patient-years (Figure). Hemoglobinuria for the early diagnosis of ongoing aHUS relapse shows a sensitivity of 100% and a specificity of 87.4% with a PPV of 10.5% and NPV of 100 %.

Conclusions: Hemoglobinuria is a very sensitive and acceptable specific marker of aHUS relapse. This finding and its validation may have an important positive impact both on patient’s quality of life and on the outcome of disease via an early diagnosis of relapses.

Funding: Private Foundation Support
PO2336

Extensive Complement Analysis in a C3 Glomerulopathy Cohort of Dutch Children with Benign Outcome

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Background: C3 glomerulopathy (C3G) is a rare renal disorder driven by dysregulation of the complement alternative pathway (AP) and characterized by predominant C3 depositions in the glomeruli. C3G can be subdivided in dense deposit disease (DDD) and C3 glomerulonephritis (C3GN). Patient cohort studies including clinical features offer important data in rare renal diseases. Moreover, biomarkers are increasingly used to select patients for clinical trials with novel complement-targeting therapies. This retrospective study describes complement biomarker profiles and outcome of 29 Dutch children.

Methods: Patients with a C3G diagnosis from 5 Dutch university medical centers (1992-2014) were included. Clinical, genetic, and laboratory findings were retrieved from patient files. Specialized biochemical assays were used to detect complement-directed autoantibodies and complement biomarkers. Results: A total of 29 patients with DDD (n=19) and C3GN (n=10) were included. Median (IQR) follow-up was 51 months (26-90). Patients presented with proteinuria and hematuria (>90%) and low serum C3 levels (84%). Ten patients (35%, 8 DDD, 3 C3GN) presented with an impaired glomerular filtration rate (GFR). DDD patients presented at younger age and with a lower GFR (P<0.05). C3 nephritic factors were found in 10 patients. 3 patients carried rare genetic variants in AP genes. Elevated levels of the complement activation markers C3d, C3bBbP, and C5b-9, combined with lowered C3 and C5 levels, indicated AP activation in the acute phase. Taking longitudinal data into account, a linear mixed model showed that C3G patients had higher C5b-9 and lower C3 levels than DDD patients (P<0.05). During follow-up, 13 (45%) patients experienced a relapse. No significant differences in clinical or laboratory features were observed between patients with and without a relapse and persistent renal sequelae. At last follow-up, only 4 patients (14%; all DDD) had a GFR below 60 ml/m²/1.73².

Conclusions: We present the extensive description of clinical, genetic, and biochemical complement features of a large pediatric C3G cohort. In most patients AP abnormalities were found. Overall, the outcome of the patients we described was relatively benign.

PO2337

Comparison of Clinicopathological Findings Between Childhood IgA Nephropathy and IgA Vasculitis Nephritis Using Oxford Classification

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Background: IgA nephropathy (IgAN) and IgA vasculitis nephritis (IgAVN) are nephritis with a common pathological feature of significant mesangial IgA deposition, but it remains controversial whether they are the same disease.

Methods: We compared clinical and pathological findings between 148 patients with IgAN and 100 patients with IgAVN who underwent renal biopsy from April 2000 to April 2019 to clarify the differences.

Results: Clinical findings showed significant differences in onset age (IgAVN vs IgAN, 10.7 vs 5.7 years, p<0.0001), duration of onset to renal biopsy (1.7 vs 6.6 months, p<0.0001), and amount of proteinuria (1.8 vs 0.5 g/gCr, p<0.0001). Pathological findings by Oxford classification showed significant differences in the frequency of M1 (90.8 vs 59.2%, p<0.0001), S1 (21.2 vs 9.2%, p=0.004), T present (28 vs 46.1%, p=0.004), G present (72 vs 58.1%, p=0.03) and P present (8 vs 19.1%, p=0.01), but no difference in that of E1 (52.8 vs 55.0%, p=0.75). Fluorescence findings showed significant difference in the frequency of fibrinogen deposition (93.3 vs 74.6%, p<0.0004) but not in that of glomerular peripheral capillary IgA deposition (86 vs 89.5%, p=0.35). Electron microscopic findings showed significant difference in the frequency of GBM lysis (35 vs 22.0%, p=0.0001). Degree of proteinuria is positively correlated with the frequency of M1 in IgAVN.

Conclusions: IgAVN has higher frequency of M1 lesion regardless of degree of proteinuria and frequency of chronic lesions such as S, T, and G, and higher frequency of acute lesions such as M and C compared with IgAN. Although IgAVN had some pathological similarities to that of IgAN, there seems to be differences which cannot be explained by the timing of renal biopsy.

PO2338

Race and Age at Onset of ESRD in Patients with Alport Syndrome

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Background: Angiotensin-converting enzyme (ACE) inhibitors have been shown to delay the onset of end-stage renal disease (ESRD) in both animal models and humans with Alport syndrome. In 2013, expert guidelines recommended the use of ACE inhibitors to slow the onset of ESRD. We examined temporal changes in the age at onset of end-stage renal disease (ESRD) and interaction between race and age at ESRD for patients with Alport syndrome.

Methods: We used the Scientific Registry of Transplant Recipients to identify all patients who received a kidney transplant in the United States for Alport syndrome between 1987 and 2017. We divided the study period into three equal eras (era 1, 1987-1997; era 2, 1998-2007; and era 3, 2008-2017) to assess changes in age at ESRD using a linear regression model adjusting for race and gender. Age at ESRD was defined as the earlier of the age at dialysis or the age at kidney transplantation.

Results: Between 1987 and 2017, 4105 Alport patients received a kidney transplant in the United States. Of these patients, 3115 (75.9%) were male and 3176 (77.4%) were white. Pre-emptive transplants were performed in 962 (23.4%) patients. Table 1 demonstrates temporal changes in median age at ESRD, demographic and clinical characteristics for patients with Alport syndrome. After adjusting for race and gender, the age at ESRD increased by a mean of 2.7 years (SE 0.51, p<0.01) for eras 2 and 4.4 years (SE 0.51, p<0.01) for era 3 compared with era 1. We also observed that age at ESRD was significantly lower for black (-9.3 years, p<0.01), Hispanic (-9.4 years, p<0.01), and Asian (-8.9 years, p<0.01) compared with the white race (Table 2).

Conclusions: The age at ESRD for patients with Alport syndrome has progressively increased over the last 30 years. White patients have delayed onset of ESRD compared with patients of other races.

Temporal changes in ESRD and transplant characteristics

PO2339

Risk of Rituximab-Associated Severe Adverse Events Increases with Young Age in Children with Nephrotic Syndrome

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Background: Rituximab prevents relapse in steroid-dependent frequently relapsing nephrotic syndrome (SDFRNS). We aimed to assess the safety of rituximab in children with steroid-resistant nephrotic syndrome (SRNS) or SDFRNS.

Methods: This single-center retrospective study included all children with SRNS/ SDFRNS treated with rituximab since 2007 at our institution. All information concerning adverse events (AE) were obtained from medical records. Severity of adverse events was graded according to the Common Terminology Criteria for Adverse Events. We performed a time-to-event analysis and log-rank tests or proportional hazards models to determine hazard ratios (HR) with 95% confidence intervals (CI) of risk factors associated with severe AE (SAE).

Results: Of the 38 children included in this study, most had a SDFRNS (n=36, 97%). Median age at diagnosis was 3.4 (interquartile range, 2.4-6.2) years and median age at rituximab initiation was 9.0 (6.8-11.6) years. Median [95% CI] time to relapse was 1.4 [1.16-2.27] years. Median follow-up time was 3.7 (2.2-4.9) years. No patient died during follow-up. Fourteen SAE occurred in 12 (32%) patients, including one case of Pneumocystis jiroveci pneumonia, 6 cases of severe neutropenia and 2 cases of inflammatory colitis. Rituximab initiation before 10 years of age was associated with a higher risk of SAE (HR [95%CI], 11.3 [1.44, 88.6], Figure 1) and all SAE occurred in children aged <10 years except for anaphylactic reactions. The occurrence of a SAE was not associated with an increased risk of relapse.

Conclusions: A young age at rituximab initiation for SRNS/SDFRNS is associated with an increased risk of SAE. Rituximab should be used with particular caution in children under 10 years old.

Funding: Government Support - Non-U.S.
Evaluating Nephrotic Syndrome Response to Rituximab in Children

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Background: Nephrotic syndrome (NS) is the most common cause of glomerular disease in the pediatric population. In children, 80% of cases are steroid sensitive (SSNS) & 20% are steroid resistant (SRNS). Rituximab (RTX) has been identified as a steroid-sparing therapy with minimal nephrotic side effects. The determinants of clinical response to rituximab is not completely known.

Methods: A retrospective review of patients aged 0-21 years with idiopathic NS who received at least 2 doses of RTX therapy over 6 years. Data collected included gender, race, ethnicity, age at diagnosis, steroid response, number of RTX doses, CD20 levels post therapy & outcomes. Outcome was defined as complete remission, CR (urine protein <30 mg/day), partial remission, PR (UPCR 0.3-1.9) & no response, NR (UPCR ≥2). Data were compared by Fisher’s exact & Wilcoxon Rank Sum tests.

Results: 48 patients met the inclusion criteria for the study comprising of 23(48%) with SSNS & 25(52%) with SRNS. There was no difference in race or age of onset between the patients with SSNS & SRNS. 18(37.5%) of patients who had CD20 lymphocyte levels measured following treatment achieved therapeutic end point of CD20 lymphocyte depletion. There was no difference in the proportion of patients who achieved this therapeutic end point between the patients with SSNS & SRNS (46% vs 72%). Overall, 72% of patients achieved partial or complete remission. The remission rate was significantly higher in the SSNS group compared with the SRNS group (87% vs 58%, p=0.001); however, there was no difference in remission rate between patients who achieved the therapeutic end point of CD20 lymphocyte depletion & those who did not in the entire cohort (56% vs 55%, p=1.0) as well as in subgroup of patients with SSNS & SRNS.

Conclusions: Children with both SSNS & SRNS achieved the desired therapeutic effect of CD20 lymphocyte depletion following treatment with RTX; however, disease remission rate was higher in children with SSNS. This data suggests that RTX can be administered at any phase of the disease (relapse or remission) without jeopardizing clinical response.
PO2343
Caregiver Perspectives of Pre-Transplant Evaluation for Children
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Background: Pre-transplant evaluation is mandated by Centers for Medicare and Medicaid Services, but there is institutional variation in implementation. The family experience of this process also is incompletely understood. Current literature largely focuses on adult transplant recipients. Our interview study aims to fill the knowledge gap about family experience of the evaluation for children.

Methods: Interviews took place 07/2019 - 02/2020 with caregivers of children referred for kidney transplant at our center 07/2017 - 12/2018. The interview guide included closed- and open-ended questions; responses were audio-recorded and then transcribed for coding of themes. Respondents also completed a brief electronic questionnaire.

Results: Our team interviewed 19 children; demographics in Fig. 1. Prominent themes included (1) the pre-transplant evaluation is overwhelming and emotional, (2) prior experiences and background knowledge are influential and (3) frustration with communication among teams was common. Fig. 2 highlights representative quotations from caregivers.

Conclusions: These findings are relevant to efforts by nephrologists to optimize delivery of information about transplant and other complex topics. The data highlight the importance of (1) acknowledging the scope of content and continually reevaluating accessibility of delivery (2) recognizing the influence of prior experiences and tailoring elements accordingly for increased family-centeredness and (3) making concerted efforts to define roles and set expectations, especially when multiple teams are involved in care.

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PO2344
Treatment-Related Anxiety in Children After Kidney Transplant
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Background: An increasing number of children experience anxiety and pediatric kidney transplant recipients are particularly susceptible to mental health conditions given the impact of their complex chronic medical histories on their quality of life. We performed a retrospective study to assess the impact of anxiety on health-related quality of life (HRQoL) in pediatric kidney transplant recipients in order to design targeted interventions to improve HRQoL after transplant.

Methods: We retrospectively analyzed scores from the disease-specific PedsQL 3.0 ESRD and Transplant Modules in pediatric ESRD and transplant patients ages 2-18 years between 2014 and 2019 at Rady Children’s Hospital. We used a linear mixed-effects model with a random intercept and ANOVA with Tukey post-hoc tests to analyze the effect of variables of interest on HRQoL in various groups.

Results: 180 modules were completed by pediatric patients who received dialysis and/or transplantation. Transplant recipients had significantly better total HRQoL scores compared to dialysis patients (p < 0.001). Treatment-related Anxiety was the lowest (worst) scoring domain among kidney transplant patients (p = 0.01), especially among patients ages 5-7 years old (p = 0.009). Patients 13-18 years old had the lowest scores in the Transplant domain, which measures social isolation related to a patient’s transplant (p = 0.008). Variables such as age at diagnosis, time on dialysis, diagnosis category, and time to transplant were not significant predictors of HRQoL.

Conclusions: These data suggest that children with kidney transplants have better HRQoL compared to children on dialysis. However, transplant recipients experience high rates of anxiety and social isolation. This may simply reflect the psychosocial stress surrounding medical care, but we may also be capturing more nuanced psychological issues in this population that requires further evaluation. Since transplant patients typically have frequent access to medical care, we have established a multi-disciplinary model in our clinic in part based on these data that utilizes psychologists to address acute and chronic psychological concerns simultaneous with their medical visits. This model may improve the HRQoL of transplant patients without increasing the overall burden of medical care and may have broader applicability to the general population of children with anxiety.

PO2345
Vaccination Status in Pediatric Kidney Transplant Recipients: An Integrated Pediatric Transplant Research Database Study
Jaya S. Parulekar,1 Eric J. McGrath,1 Amrish Jain,1 1Wayne State University School of Medicine, Detroit, MI; 2Division of Pediatric Nephrology, Children's Hospital of Michigan, Detroit, MI; 3Division of Pediatric Infectious Disease, Children’s Hospital of Michigan, Detroit, MI.

Background: The American Society of Transplant recommends candidates be immunized before transplantation. However, there is limited data on pre/post-transplant vaccination status for children with kidney transplants. Our study evaluates vaccination rates & an approach to increasing vaccination in our kidney transplant program.

Methods: Pediatric kidney transplant recipients at Children’s Hospital of Michigan from 2013-2019 were included. Official immunization records were obtained from the State of Michigan’s Michigan Care Improvement Registry. During the pre-transplant period, age-based catch-up or accelerated immunization was performed at primary care provider’s or at the in-house immunization center. Demographic, clinical & serology data were entered into an integrated database created through REDCap and analyzed with SPSS Version 26.

Results: Included were 58 children with mean age at transplant of 11.9±5.7 yrs, 66% Male, 52% African-American, 31% Caucasian, 76% deceased donor transplants & 10% re-transplants. Median duration of follow-up was 3 yrs. Pre-transplant vaccination rates of ≥95% were achieved for all vaccines, except PCV13 (69%), PCV23 (62%) & HPV4/9 (86%). Pre-transplant serology for HepA, HepB and Varicella showed immunogenicity of 95%, 93%, 88% respectively. Catch-up & accelerated immunization increased the vaccination rate to 100% from 53% (Varicella); 57% (HepA); 73% (MVC); 72% (MMR). Post transplant vaccination series was a 95% complete for all vaccines except PCV23 (43%); HPV4/9 (37%); MVC (30%).

Fig. 2

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

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PO2346
Decreased CD28 Expression in Memory CD4+ T Cells in Children Awaiting Kidney Transplant Is Associated with Increased Expression of Senescence Markers
Charlotte Duneton, Roshan P. George, Mandy L. Ford, Pamela D. Winterberg, Emory University, Atlanta, GA; Children’s Healthcare of Atlanta Egleston Hospital, Atlanta, GA.

Background: Despite improved patient and graft outcomes with CD28-CD80/86 costimulation blockade, increased early acute rejection has hindered the widespread use of CTLA-4Ig (belatacept) for kidney transplant. Our group has previously reported lower pre-transplant frequencies of CD28 effector helper T cells (CD4+TEM) in children awaiting kidney transplant. We aimed to determine if a similar T cell phenotype is detectable in children awaiting kidney transplant.

Methods: We analyzed existing flow cytometry data of unstimulated blood cells collected from children on dialysis (n=30) or healthy children (n=18) and examined expression of markers of costimulation (CD28), senescence (CD57, PD1), activation (CD45RA) and cytolytic effectors (Granzyme B, Perforin) on memory CD4+ T cells.

Results: None of the children had CD28+CD45RA-CD4-TEM frequencies as low as those we have previously observed in adults that were rejection-free on belatacept. However, 8 children on dialysis (27%) had CD28+CD45RA-CD4-TEM frequencies below the minimum value observed in healthy children (Fig1A-B). Patients with this “stable-like” T cell phenotype had higher frequency of CD4+TEM cells bearing senescence markers (CD57+Fig 1C) and cytolytic effectors (Granzyme B, Perforin, Fig 1D) but decreased activation markers (CD38+ Fig 1E).

Conclusions: Despite their young age and limited antigen experience, a subset of children on dialysis accumulate CD4+TEM cells that have lost CD28 expression and bear markers suggestive of impaired function, a phenotype reminiscent of adults with early rejection on belatacept. We aimed to determine if a similar T cell phenotype is detectable in children awaiting kidney transplant.

Funding: NIDDK Support, Clinical Revenue Support

PO2347
Predicting Allograft Survival in Young Pediatric Kidney Transplant Recipients
Florian Manca Barayre, Jerome Harambat, Amelia Le Page, Stephen D. Marks, Chanel Prestidge, Matthew P. Sypek, Stephen P. McDonald, Rachel E. Patzer, Julien Hogan, Emory University School of Medicine, Atlanta, GA; Robert-Debré Hospital, APHP, Paris, France; Bordeaux University Hospital, Bordeaux, France; Monash University Faculty of Medicine Nursing and Health Sciences, Clayton, VIC, Australia; Great Ormond Street Hospital For Children NHS Foundation Trust, London, United Kingdom; Starship Children’s Health, Newmarket, New Zealand; Australia and New Zealand Dialysis and Transplant Registry, Adelaide, SA, Australia.

Background: Kidney transplantation (kTx) presents specific challenges in younger recipients. There are no predictive model of renal allograft loss in young pediatric recipients to inform donor selection. We aimed to develop and validate a predictive model of graft loss in an international cohort of young kTx recipients.

Methods: We included first-time kTx recipients under 5 years of age in the USA, Australia, New Zealand, UK and France between 2005 and 2018. A multivariate Cox regression was used to develop a predictive model of graft loss or death on the US cohort. Model discrimination (C-statistics) and calibration were assessed internally and externally on the non-US cohort.

Results: 2543 kTx in children <5 years old were included. 10-year overall graft survival rate was 80.0% [95% CI = 77.7% – 82.2%]. Given the interaction between some predictors and recipient’s age, we developed two models stratified on recipient age (cut-off: 36 months) including donorrecipient body surface area ratio, ischemia time, donor weight and immunological matching. Immunological matching was a stronger predictor among older recipients, while morphological variables were stronger predictors in younger recipients. C-statistics on the training cohort were 0.63 (95% CI = 0.57 – 0.68) and 0.65 (95% CI = 0.59 – 0.71) and the models were well calibrated. Figure 1 presents the discrimination of the models at different time horizons and the calibration at 10 years on the validation cohort.

Conclusions: We confirm the overall good renal allograft survival in children transplanted under the age of 5. We developed and validated predictive models of graft loss or death based on pre-transplant factors in this population that may be used to inform donor selection.
PO2348
Safety and Efficacy of Low-Dose Rabbit Antithymocyte Globulin in Pediatric Renal Transplant Recipients
Vaka K. Sigurjonsdottir,1,2 Paul C. Grimm,1 Abanti Chaudhuri,1 1Landspitali, Reykjavik, Iceland; 2Stanford University, Stanford, CA.

Background: Currently there is no consensus among pediatric kidney transplant centers regarding the use and regimen for immunosuppressive induction therapy. The safety and effectiveness of reduced Rabbit Antithymocyte Globulin (rATG) ≤ 3.5 mg/kg cumulative dosing as induction therapy in low risk pediatric kidney transplant recipients is unknown.

Methods: Pediatric renal transplant recipients transplanted 1/1/2013-5/1/2018 were considered for inclusion. Recipients of deceased or living donor organs and with least 12-month follow-up were included. “High risk” was defined by a repeat transplant, preformed donor specific antibodies (DSAs), peak panel-reactive antibodies ≥20%, or African-American race. Maintenance immunosuppression protocol was tacrolimus and mycophenolate mofetil, steroid free unless high risk. Outcomes were de novo DSA (dnDSA) formation, graft survival, biopsy proven rejection (BFR) and EBV/CMV/BK viremia infection during the first 12 months. DSAs were routinely screened at 3.6 and 12 months. Protocol biopsies were done at 6 and 12 months and graded with Banff criteria. Subclinical/borderline findings were included with or without treatment. Additional DSA testing and/or biopsies were done if there was a clinical concern. Group 1: low risk patients, ATG dose of ≤ 3.5 mg/kg, Group 2: low risk patients receiving dose of >3.5 mg/kg and Group 3: high risk patients.

Results: A total of 181 patients met inclusion criteria. Age of patients was 11 years (11 mo-21 y), median (range), 21% received a living donor transplant and 49% were female. Graft survival and dnDSA formation did not differ significantly between the three treatment groups. Graft loss at 12 months was a rare event with 99.5% graft survival and patient survival was 100%. Patients outcomes based on groups is shown in the table.

Conclusions: Reduced ATG dosing (≤ 3.5 mg/kg) when compared with higher dosing (>3.5 mg/kg) is safe and effective. Reduced ATG dose was associated with lower rates of BK viremia and BK nephropathy without increasing risk of dnDSA or BFR.

PO2349
Pediatric-Specific Models Improve Prediction of Kidney Transplant Survival for Children Under 5 Years Old
Florian Manca Barayev,1 Larry A. Greenbaum,1 Rouba Garro,1 Pamela D. Winterberg,1 Rachel E. Patzer,1 Julien Hogan.1,2 Emory Transplant Center 1Emory University, Atlanta, GA; 2Robert-Debré Hospital, APHP, Paris, France.

Background: The kidney allocation system directs high-quality kidneys to pediatric recipients, but the kidney donor profile index (KDPI) used to quantify donor quality may not accurately predict graft survival in small pediatric recipients. We aimed to determine if a pediatric-specific KDPI could improve the prediction of graft longevity for young recipients.

Methods: We evaluated first-time kidney transplantations in pediatric recipients between 1/2005 and 8/2018 in the U.S. (SRTR) and used a Cox model to assess KDPI accuracy for combined primary outcome of death or graft loss in young recipients. We developed an adapted KDPI score for recipients ≤5 years old of deceased (SP-KDPI) or living (SP-LKDPI) adult donor transplants using multivariate cox regression and scaled these models to allow comparison between living and deceased donors. Models’ accuracies were validated internally by cross-validation.

Results: KDPI C-statistic was 0.52 (95% CI = 0.50 – 0.54) in recipients less than 5 years old. Ethnicity, age, body surface area, gender, cold ischemia time and number of HLA-A and -B mismatches, were significant predictors for deceased donors (SP-KDPI model) while race, age, HLA-B mismatch and donorrecipient body surface area ratio were used in the living donor model (SP-LKDPI). C-statistics were 0.64 (95% CI = 0.57 – 0.70) for SP-KDPI and 0.65 (95% CI = 0.58 – 0.73) for SP-LKDPI. Figure 1 shows allograft survival by donor type and SP-(L)KDPI stratum. The SP-LKDPI model identified 16.8% of living donors with predicted graft survival superior to any deceased donor (denoted as SP-LKDPI >0).

Conclusions: Our adaptation of the KDPI demonstrated a higher accuracy to predict graft loss in young recipients of deceased donors. Furthermore, our SP-LKDPI model may allow direct comparison of living versus deceased donors offered to the youngest recipients.

PO2350
Reduced 1-Year Allograft Function in Pediatric Renal Transplant Patients: Role of Subclinical Viral Replications
Raja Dandamudi, Stanley P. Hmiel, Vikas R. Dharmidhakara. Washington University in Saint Louis School of Medicine, Saint Louis, MO.

Background: BK virus (BKV) and Epstein-Barr virus (EBV) subclinical viral replications (SVR) are common after renal transplantation. The effects of SVR on the GF in pediatric kidney transplant (pKTx) recipients is not well defined and was the purpose of this study.

Methods: This retrospective study was done in our hospital from Jan 2012 to Dec 2018. 480 serum and urine samples from 39 pKTx were analyzed for viral load by quantitative PCR through the first post-transplantation year. Clinical characteristics, including graft survival and dDSA testing and/or biopsies were done if there was a clinical concern. Group 1: low risk patients, ATG dose of ≤ 3.5 mg/kg and Group 3: high risk patients

Results: A total of 181 patients met inclusion criteria. Age of patients was 11 years (11 mo-21 y), median (range), 21% received a living donor transplant and 49% were female. Graft survival and dnDSA formation did not differ significantly between the three treatment groups. Graft loss at 12 months was a rare event with 99.5% graft survival and patient survival was 100%. Patients outcomes based on groups is shown in the table.

Conclusions: Reduced ATG dosing (≤ 3.5 mg/kg) when compared with higher dosing (>3.5 mg/kg) is safe and effective. Reduced ATG dose was associated with lower rates of BK viremia and BK nephropathy without increasing risk of dnDSA or BFR.

Funding: Private Foundation Support

PO2350
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Raja Dandamudi, Stanley P. Hmiel, Vikas R. Dharmidhakara. Washington University in Saint Louis School of Medicine, Saint Louis, MO.

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Funding: Private Foundation Support
PO2352

Variability in Surveillance Monitoring and Management of Donor-Specific Antibodies Among Pediatric Transplant Programs Participating in the Improving Renal Outcomes Collaborative (IROC)

Lyndsay Harshman,1 Hiren P. Patel,2 Gina-Marie Barletta,3 David K. Hooper,4 Rouba Garro,5,6 The University of Iowa Stead Family Department of Pediatrics, Iowa City, IA; 4Nationwide Children’s Hospital, Columbus, OH; 2Phoenix Children’s Hospital, Phoenix, AZ; 3Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 5Emory University, Atlanta, GA; 6Children’s Healthcare of Atlanta Inc, Atlanta, GA.

Background: There have been few advancements in long-term outcome of pediatric kidney transplant (KT) recipients who develop rejection. Many centers perform surveillance monitoring for donor specific antibodies (DSA) to diagnose and treat subclinical rejection. Despite the existence of guidelines, there is variability in monitoring and management of DSA post-pediatric KT.

Methods: An IRB approved survey was distributed using REDCap among pediatric KT programs participating in IROC to evaluate practice patterns in monitoring and management of DSA post KT.

Results: Twenty-nine of 33 (88%) IROC centers completed the survey. Twenty-five of 29 (86%) centers perform surveillance DSA monitoring. Of those 25 centers, 20 (69%) check DSA twice or more in year one post KT. Nineteen (65%) check once in the second year and annually thereafter. Ten (35%) centers check DSA only by indication after year two post KT. Twenty-eight (97%) utilize MRI trend in interpreting DSA results and 10 (34%) centers use C1q complement fixation antibody assay to guide management. Management of patients with +DSA, stable creatinine and no evidence of antibody mediated rejection (AMR) on biopsy varies across centers from monitoring (34%) to intensive (19%) to base line immunosuppression (19%). Baseline immunosuppression is stopped in 19% (10/29, 66%). Very few centers reported giving IVIG alone (3/29, 10%) or IVIG and rituximab (3/29, 10%). Only 34% of centers (10/29) perform kidney biopsy if DSA develops with stable creatinine. When rituximab is used for treatment of DSA+ AMR, 11/29 (41%) centers use one dose and 15/29 (54%) use 2 doses with variable frequency. Of centers using IVIG, 14/29 (48%) use IVIG monotherapy for treatment of DSA+ AMR; 12/29 (41%) use 1 g/kg/dose and 6/29 (30%) use 2 g/kg/dose. The frequency of IVIG dosing is monthly in 16/20 (80%). The number of IVIG doses is variable ranging from 1 to 6.

Conclusions: There is significant variability in surveillance monitoring and management of DSA post-KT across pediatric centers. Large, multicenter studies should be considered to evaluate the ideal post-KT surveillance DSA monitoring strategy and to determine the effect of different treatment approaches on long-term outcomes in pediatric KT recipients.

PO2353

Assessment of Pediatric Nephrology Programs’ Readiness to Participate in Prospective Clinical Trials

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Background: Currently, there is a limited availability of effective, FDA-approved drugs for children with kidney disease in the United States; therefore, there is an increased need for clinical trials to evaluate drug effectiveness and safety for pediatric usage. Implementation and conduction of clinical trials is complex process, which requires a team approach, involves multiple inter-dependent steps, research infrastructure support, legal policies/procedures, equipment, and access to a regulatory oversight board. The conduct of clinical trials in small pediatric subspecialties (i.e. pediatric nephrology) may be hampered by provider clinical demands and small numbers of patients available for such studies. The goal of this survey was to assess the readiness to conduct clinical trials by pediatric nephrologists in institutions of different sizes. Assessment would provide a framework to help determine the size of the institution.

Methods: The survey was designed and tested by a small group of pediatric nephrology experts. Qualtrics Online Survey Platform and Statistical analysis were used. The survey was distributed to members of ASPN (60 sites in 30 U.S states and 2 Canadian Provinces). Respondents were asked to complete the survey on behalf of the institution/practice, not their individual preferences. There was a total of 17 survey questions, which assessed the respondent’s institution’s participation/interest in conduct of clinical research, availability of a clinical research coordinator/IRB, and access to equipment for trial execution (dry ice, centrifuges, freezers).

Results: Currently, we have recorded 68 survey responses. Two of the responding institutions had no interest in conducting clinical trials (2.9%). Notably, more respondents practiced at Academic Centers/Universities (91%) than in private practices (8.3%). We noted no major differences in access to clinical trial resources between large and small institutions.

Conclusions: Clinical trials remain vital to finding better treatments and cures for pediatric patients with renal diseases. Overall, pediatric nephrology programs have good infrastructure and readiness to conduct clinical trials independently of the size of the institution.
PO2354

Telemedicine During the COVID-19 Pandemic: Parents’ Experience in a Pediatric Nephrology Clinic at the University of Florida


Background: In the setting of the COVID-19 pandemic, pediatric nephrology clinics at the University of Florida were switched to telemedicine. This transition occurred quickly without much education to either providers or families. There are some attempts to study the experience of providers, but there is no data regarding to parents’ and patients’ experience with telemedicine.

Methods: We surveyed parents and patients (>18 years old) who had at least 1 telemedicine encounter via anonymous Qualtrics survey sent to their email. Results were analyzed via qualitative analysis.

Results: Out of the 80 parents, 47.5% (38) completed the survey. 95% of the patients participated via Zoom and 5% used the telephone. 10.5% experienced technical issues. 100% reported that telemedicine had a positive impact on their family life. In response to the quality of time spent with physicians, 84% reported that telemedicine was similar to the clinic, and 10.5% reported it was better. In terms of receiving virtual medical care, 50% reported that they were very comfortable, 50% reported that they were comfortable but preferred some interim clinic visits. 71% rated telemedicine experience 5, 25% rated 4, and 5% rated 3 out of 5.

Conclusions: We observed that parents perceived the effect of telemedicine clinics as positive in respect to ease in the incorporation, quality of time spent by the physician, receiving virtual medical care, and the impact on the families. Though telemedicine seems to be effective in the current setting, it can only be served as an alternative to in-person clinic visits in the future, since 90% of families preferred a mixture of clinic and telemedicine visits in our setting. Larger studies are needed to further evaluate the utility and efficacy of telemedicine in a pediatric setting.

PO2355

Prevalence and Determinants of Sickle Cell Nephropathy in Children Living in a Low-Resource Setting

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Background: Clinical and genetic factors have been reported to influence the development of sickle cell nephropathy (SCN). However, data on the association between these factors and SCN remain limited in the pediatric population, especially in sub-Saharan Africa. Our study aimed to: (i) determine the prevalence of the reported markers of SCN, including albuminuria, glomerular hypertrophy and reduced kidney function in a pediatric sickle cell anemia (SCA) population from the Democratic Republic of Congo (DRC); (ii) examine the association between these SCN markers and some clinical and genetic factors.

Methods: Clinical parameters were collected. All participants were genotyped for Apolipoprotein-L1 (APOL1) G1 (rs73885319, rs69010145) and G2 (rs71785313) variants, and for Heme oxygenase 1 (HMOX1) GT dinucleotide repeats (rs3074372). APOL1 high-risk genotype (HRG) was defined by the presence of 2 risk variants (G1/G1, G1/G2, and G1/G2) and low risk genotype (LRG) if 0 or 1 risk variants were present. HMOX1 GT dinucleotide repeats were categorized into two allele classes (≤ 25 repeats as short and > 25 repeats as long). As the main outcomes, albuminuria was defined as albumin-to-creatinine ratio (ACR) ≥ 30mg/g, reduced kidney function (eGFR < 60 ml/min per 1.73 m²) and glomerular hypertrophy (eGFR > 130 and 140 ml/min/1.73 m² for female and male, respectively).

Results: From 361 participants enrolled, 73 (20.2%) presented with albuminuria, 104 (28.3%) with hypertrophy and 19 (5.26%) had reduced kidney function. Logistic regression analysis revealed that blood transfusions (> 9 per year) were significantly associated with albuminuria (P = 0.0036); age (P = 0.015) and diastolic hypertension (P = 0.0099) were significantly associated with hypertrophy. APOL1 HRG emerged as the main genetic factor associated with both albuminuria (odds ratio [OR]: 3.70, 95% confidence interval [CI]: 0.037–1.25) and diastolic hypertension (OR: 1.84, 95% CI: 1.51–2.02, P < 0.001), while no association was found with HMOX1 GT repeats.

Conclusions: Kidney disease is highly prevalent in children with SCA in the DRC. APOL1 HRG is the main determinant associated with the risk of developing SCN.

Funding: Government Support - Non-U.S.
Clinical and Biopsy Characteristics in a Pediatric Cohort of C3 Glomerulonephritis (C3G) and Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN)

Bradley P. Dixon,1,2 Amy Goodwin Davies,3 Hanieh Razzaghi,3 Sherin Meloni,3 Melissa E. Thomas,3 Joseph T. Flynn,4 Donna J. Claes,5 Don Matsefana,6 Brian R. Slater,7 Vikas R. Dharmadhika,7 Caroline A. Gluck,7 Joshua Zaritsky,6 Michael J. Somers,7 Mahmoud Kallah,7 William E. Smoyer,7 Susan L. Furlt,6 Christopher B. Forrest,7 Benjamin L. Laskin,7 Michelle Denburg,7 Renal Section, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO; 2Children’s Hospital Colorado, Aurora, CO; 3The Children’s Hospital of Philadelphia, Philadelphia, PA; 4Seattle Children’s Hospital, Seattle, WA; 5Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 6Washington University in Saint Louis School of Medicine, Saint Louis, MO; 7Nationwide Children’s Hospital, Columbus, OH.

Background: C3G and IC-MPGN are rare diseases. The ability to identify and phenotype children with C3G and IC-MPGN using electronic health records (EHR) would aid description of natural history and prognosticative therapeutic response.

Methods: Using a computable phenotype algorithm, a pediatric cohort of children with glomerular disorders was identified in PEDSnet, a national network of pediatric health systems with aggregated EHR data, and refined using MPGN-specific SNOMED-CT codes to identify C3G and IC-MPGN patients at 6 centers. Discrete data elements were captured from electronic health records, and additional clinical data were extracted by standardized chart review. Biopsy diagnosis was classified as C3G or IC-MPGN by applying an automated algorithm to immunofluorescence data. Patients were then followed in an ongoing extension period. Here we report efficacy outcomes through 1 year of safety from all available follow-up (median 82.6 weeks).

Results: Of 285 identified patients, 173 were true cases of C3G or IC-MPGN (Tables 1 and 2). Median C3 level at diagnosis was lower in C3G compared to IC-MPGN (p = 0.006). There were no significant differences in light microscopic injury pattern or ultrastructure between C3G and IC-MPGN biopsies, but C3 intensity was higher in C3G (p = 0.005). The primary endpoint was complete TMA response (platelet count and lactate dehydrogenase normalization and ≥25% improvement in serum creatinine from baseline at 2 visits ≥28 days apart) through 26 weeks. Key secondary endpoints included eGFR and dialysis requirement. Patients were then followed in an ongoing extension period. Here we report efficacy outcomes through 1 year of safety from all available follow-up (median 82.6 weeks).

Results: Eighteen patients (mean [SD] age 6.4 [4.5] years; 55.6% female) were enrolled; 14 (77.8%) achieved complete TMA response by 26 weeks, and 3 more patients (94.4%) by 50 weeks. Patients were then followed in an ongoing extension period. Here we report efficacy outcomes through 1 year of safety from all available follow-up (median 82.6 weeks).

Results: Eighteen patients (mean [SD] age 6.4 [4.5] years; 55.6% female) were enrolled; 14 (77.8%) achieved complete TMA response by 26 weeks, and 3 more patients (94.4%) by 50 weeks. Further improvements in TMA parameters occurred with longer-term treatment (Table). Mean (SD) increase in eGFR from baseline was 85.4 (54.3) mL/min/1.73m² at 26 weeks, and 94.1 (50.7) at 50 weeks. Of 6 patients on dialysis at baseline, 3 (50%) discontinued eGFR and dialysis requirement. Patients were then followed in an ongoing extension period. Here we report efficacy outcomes through 1 year of safety from all available follow-up (median 82.6 weeks).

Results: Eighteen patients (mean [SD] age 6.4 [4.5] years; 55.6% female) were enrolled; 14 (77.8%) achieved complete TMA response by 26 weeks, and 3 more patients (94.4%) by 50 weeks. Further improvements in TMA parameters occurred with longer-term treatment (Table). Mean (SD) increase in eGFR from baseline was 85.4 (54.3) mL/min/1.73m² at 26 weeks, and 94.1 (50.7) at 50 weeks. Of 6 patients on dialysis at baseline, 3 (50%) discontinued eGFR and dialysis requirement. Patients were then followed in an ongoing extension period. Here we report efficacy outcomes through 1 year of safety from all available follow-up (median 82.6 weeks).
Conclusions: Ravalumab administration every 4–8 weeks improved hematologic and renal outcomes in 94% of patients, with no unexpected safety concerns. Renal function improved with longer-term treatment.

Funding: Commercial Support - Alexion Pharmaceuticals, Inc.

Complete TMA response components over time

<table>
<thead>
<tr>
<th>Variable</th>
<th>Initial cutout volume (mm^3)</th>
<th>Final volume</th>
<th>Positive</th>
<th>Negative</th>
<th>Discordant</th>
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<tbody>
<tr>
<td>MAE</td>
<td>14.77 ± 1.71</td>
<td>17 ± 4.64</td>
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<td>5.9%</td>
<td>0%</td>
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<tr>
<td>Positive</td>
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<td>19.0 ± 5.64</td>
<td>94.1%</td>
<td>5.9%</td>
<td>0%</td>
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<tr>
<td>Negative</td>
<td>15.0 ± 5.64</td>
<td>17.0 ± 4.64</td>
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<td>5.9%</td>
<td>0%</td>
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<tr>
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<td>16.0 ± 4.64</td>
<td>18.0 ± 4.64</td>
<td>94.1%</td>
<td>5.9%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Data shown as n (%). LDH, lactate dehydrogenase; TMA, thrombotic microangiopathy.

PO2359

A Pharmacologic “Stress Test” for Assessing Select Antioxidant Defenses in Patients with CKD

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Background: Oxidative stress is a hallmark and mediator of CKD. Diminished antioxidant defenses are thought to be partly responsible. However, there is currently no validated prospective determination of antioxidant defenses in humans. RBT-6 (N-[N-benzyl]-L-phenylalanine, SnPP) induces mild, transient oxidant stress in animal models, triggering increased expression of select antioxidant proteins (e.g., heme oxygenase 1 [HO-1], NAD(P)H dehydrogenase [quinone] 1 [NQO1], ferritin, p21). Hence, we tested the hypothesis that RBT-6 can also variably increase these proteins in humans and can thus serve as a pharmacologic “stress test” for gauging generative reserves and antioxidant reserves.

Methods: A total of 18 healthy volunteers and 24 participants with stage 3 CKD (n=12; eGFR 30–59 ml/min per 1.73m^2) or stage 4 CKD (n=12; iGFR 15–29 ml/min per 1.73m^2) received a single dose of RBT-6 at 9, 27, or 90 mg administered intravenously. Plasma and/or urinary antioxidant proteins were measured at baseline and for up to 4 days post-dosing. Kidney safety was assessed by serial measurements of BUN, creatinine, eGFR, albuminuria, and urinary AK1 biomarkers (kidney injury molecule 1, neutrophil gelatinase-associated lipocalin, cystatin C, and N-acetylglucosaminidase).

Results: Plasma HO-1, ferritin, p21, and urinary NQO1 were all elevated at baseline in CKD participants. Plasma HO-1 and urinary NQO1 levels each inversely correlated with eGFR (r=−0.85 to −0.95). All four proteins manifested statistically significant dose- and time-dependent elevations after RBT-6 infusion. However, marked inter-subject differences were observed. p21 responses to high-dose RBT-6 and HO-1 responses to low-dose RBT-6 were significantly suppressed in participants with CKD versus healthy volunteers. RBT-6 was well tolerated by all participants, and no evidence of nephrotoxicity was observed.

Conclusions: RBT-6 can be safely administered and, after its infusion, the resulting changes in plasma HO-1, NQO1, ferritin, and p21 concentrations can provide information as to antioxidant gene reserves/reserves in subjects with and without kidney disease. Additionally, baseline values of these markers may also be indicative of oxidative stress at baseline, especially in patients in CKD.

Funding: Commercial Support - Renibus Therapeutics

PO2360

Prediction of Kidney Drug Clearance: A Comparison of Tubular Secretory Clearance and GFR

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Background: Tubular secretion is the primary mechanism of kidney drug elimination. Few studies have empirically evaluated the role of tubular secretion on the kidney elimination of administered drugs.

Methods: We evaluated 54 participants with and without chronic kidney disease. We administered a single dose of iohexol, furosemide, and famciclovir at the start of the study visit. We used LC-MS/MS to measure furosemide, penciclovir (the active form of famciclovir) and transcutaneous measurements. GFR was estimated by renal clearance of the endogenous drug iohexol, and by transcutaneous measurements.

Results: Participants were characterized by a mean age of 55 years and a median iGFR of 73 ml/min/1.73m^2. Using iGFR as a single predictor, the MAE between model-predicted and measured furosemide and penciclovir clearance was 40.1 and 64.1 ml/min, respectively. The MAEs for models of individual secretory solute clearances were statistically similar to that of the iGFR model. The addition of kynurenic acid, pyridoxic acid, isovalerylglutamic acid and tiglylglycine clearances each individually improved the predictive accuracy of penciclovir clearance compared with the iGFR model.

Conclusions: The kidney clearance of secretory solutes and iGFR showed similar accuracy for predicting the clearances of furosemide and penciclovir, with some improvement from combining both measures. These findings provide cautious optimism that measurements of secretory clearances may improve kidney drug dosing.

Funding: NIDDK Support, Other NIH Support - National Institute of General Medical Sciences

Accuracy of GFR and secretory solute predictions for predicting kidney clearance of furosemide and penciclovir

**PO2361**

Reduction in Proximal Tubular Secretion Precedes Reduction in Glomerular Filtration Rate in the Adenine-Induced CKD Model


Background: Glomerular filtration rate (GFR) is frequently used to instruct dose levels of renally cleared drugs in patients with renal disease. This is based on the assumption that proximal tubule secretery clearance declines equally to GFR during disease progression. We tested this hypothesis in adenine-induced CKD mouse model.

Methods: C57BL/6 mice were fed either control or 0.2% adenine diet to induce progressive kidney damage. Body weight, urinary output, GFR and tubular secretion were monitored and histological analysis performed to assess disease progression at 1 and 3 weeks. Tubular secretion was estimated by measuring renal clearance of the endogenous secretory solutes indoxyl sulfate (IS), hippuric acid (HA) and cinnamoylglycine (CMG) using liquid chromatography couple to mass spectrometry. GFR was estimated by transcutaneous measurements.

Results: Mice on adenine diet developed kidney disease, indicated by progressive GFR decline. Histological assessment showed normal glomeruli throughout the study and a moderate tubular damage at 1 week which progressed to severe at 3 weeks. However, the maximum urinary albumin-creatinine ratio was reached already at 1 week of treatment, as was potassium tubular injury mark, suggesting extensive early tubular injury and functional damage preceding structural damage. Likewise, when tubular secretion was assessed directly, a profound decrease in renal clearance of IS was detected already after 1 week on adenine diet with only a small further decrease by the 3rd week. Similar trends were observed for HA and CMG. In direct comparison, the decline in GFR versus tubular secretion over time revealed that at 1 week GFR was decreased by 30% whereas tubular secretion was decreased by >65%, suggesting earlier impact on the latter. Immunohistological analysis revealed a reduction in Oat1 transporter expression, to an extent not fully accounting for the reduction in function. This suggests a component of Oat1 inhibition and/or involvement of other transporters.

Conclusions: Our results indicate that tubular secretory function can be dissociated from glomerular filtration. Thus, assessment of tubular function based on GFR alone can be misleading, which has implications for dosing of renally excreted drugs to patients with kidney disease.

Funding: Commercial Support - AstraZeneca
**PO2362**

**The Influence of Vitamin D Status and CKD on the CYP3A Metabolism Substrate Midazolam**

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**Background:** Patients with chronic kidney disease (CKD) have a high prevalence of vitamin D (25(OH)D) deficiency. Given its widespread use and knowledge of CYP gene induction, there is a paucity of data on how the pharmacokinetics (PK) of CYP3A substrates may be impacted by 25(OH)D in CKD. This study sought to investigate the role of 25(OH)D status (deficient vs. replete status) on CYP3A metabolism in CKD and healthy control (HC) subjects using midazolam (MDZ) as a prototypical probe substrate.

**Methods:** CKD (n=19) and HC (n=6) subjects with 25(OH)D deficiency (25(OH)D < 30 ng/mL) were enrolled in a 2 phase study. In phase 1, subjects were given one dose of oral midazolam (MDZ, 5000 IU) and oral MDZ (2 mg). In phase 2, subjects received D, 5000 IU daily for up to 14 weeks to repletion (25(OH)D >30 ng/mL) and were again given one dose of oral D, 5000 IU and MDZ 2 mg. Blood was serially collected for up to 48 h at each phase. MDZ plasma concentrations were measured by LC-MS/MS. Population PK analysis was performed using Phoenix NLME (v.8.2, Certara®).

**Results:** A 2-compartment model with delayed absorption and a mixed ratio residual error model was fit to the observed MDZ plasma concentration data. Glomerular filtration rate (GFR) and study phase were included as covariates in the model. MDZ population error model was fit to the observed MDZ plasma concentration data. Glomerular filtration analysis was performed using Phoenix NLME (v.8.2, Certara®).

**Conclusions:** MDZ PK status did not significantly influence the PK of MDZ in either HC or CKD subjects. There was a trend in CL/F being slower in CKD compared to HC regardless of phase, which may be due to decreased renal elimination or reduced ability for inductive CYP3A24 in CKD patients. Future analyses will explore whether additional covariates to further reduce the error on MDZ PK parameters in order to discern differences between subjects in this small study.

**Funding:** Other NIH Support - NIGMS

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**PO2364**

**CYP3A and Drug Transporter Activity Changes in Thai Elderly with CKD Assessed Using a Microdose Cocktail**

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**Background:** Chronic kidney disease (CKD) may influences cytochrome P450 (CYP) enzymes and drug transporters activity, resulting in the change of pharmacokinetics. This study investigated the effect of age and renal function on activity of CYP3A and various drug transporters in healthy Thai elderly and CKD patients using a validated microdose probe substrate cocktail.

**Methods:** Fifty three subjects were studied [healthy young subjects (Gr1, n=20), healthy elderly (Gr2, n=16) and elderly CKD patients (Gr3, n=17)]. Each subject was given a single dose of the microdose cocktail consisted of midazolam (M; for CYP3A), diphenhydramine (D; for CYP2D6 and 2C19), irinotecan (I; for CYP3A), dabigatran etexilate (D; for gut P-gp; pitavastatin (P; for OATP1B1), rosuvastatin (R; for OATP2B1), aminoglycoside (A; for ATP7C1/C), Pepstatin A (P) and probenecid (P) as MDR1 probe substrates. Plasma samples were collected at 0, 0.33, 0.67, 1.5, 1, 2, 3, 4, 6, 8, 10, 12, 24, 36 and 48 hours after dosing. All plasma drug concentrations were measured using a fully validated LC/MS/MS. Area under the concentration-time curve (AUC) were calculated using the trapezoidal rule.

**Results:** No side effect was observed. Multivariate analysis, adjusted for body mass index, co-morbidity and liver functions) showed negative effects of age and CKD on drug transporters activity, resulting in the change of pharmacokinetics. As compared to aged-matched healthy subjects, CKD subjects exhibited a doubling of AUC0-12 and 50% decrease in renal clearance of MNF after VitD repletion. No statistical significance was shown.

**Conclusions:** The FEX data suggest that nonrenal transporter function (likely intestinal P-gp and/or hepatic OATP) is decreased in VitD deficient CKD patients and may be improved by VitD repletion. Reasons for unchanged OLM PK likely relate to overlapping substrate specificity with other transporters that are minimally affected by CKD or VitD status. Conversely, MNM results may suggest that MATE1/2-K function is decreased by VitD.

**Funding:** Other NIH Support - NIGMS R01GM107122

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**PO2365**

**Tacrolimus and Mycophenolic Acid Pharmacokinetics in Young, Middle-Aged, and Elderly Stable Renal Transplant Recipients**

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**Background:** Tacrolimus (TAC) and mycophenolic acid (MPA) comprise a critical maintenance immunosuppressive regimen. Limited pharmacokinetic data are available comparing age-related differences of these immunosuppressive drugs which is an important factor considering the increase in renal transplants in older patients. This analysis compared TAC and MPA pharmacokinetics among young, middle age and elderly stable renal transplant recipients (RTR).

**Methods:** Twelve-hour TAC and MPA pharmacokinetic studies were conducted in 67 stable RTR at least 1-year post renal transplant. Tacrolimus dose regimes were adjusted to troughs (4 to 10 ng/ml) based upon time post-transplant. MPA regimes were adjusted using clinical responses only. Patients were categorized as: young: >21 & ≤40 years; middle age: >40 < 60 years and elderly>60 years. Non-compartmental pharmacokinetic analysis determined area under the concentration vs time (AUC). Curve 0-12hours (AUC0-12).

**Results:** TAC and MPA area under the concentration-time curve (AUC) were calculated using the trapezoidal rule.
AUC4-12/AUC0-12 (to define MPA enterohepatic recirculation), apparent clearance (CL) and renal clearance (CL/R). Univariate ANOVA was conducted.

Conclusions: The strict conservation of the contact residues within the conformational epitope of VP1 may explain the broad-spectrum antiviral activity of MAU868 and its high in vitro barrier-to-resistance, ideal characteristics for a potential first-in-class therapeutic agent for the treatment or prevention of BKV disease.

Funding: Commercial Support - Novartis Therapeutics, Inc.

PO2368
Pharmacokinetic Evaluation of Drug Interactions Between Vadadustat and HMG-CoA Reductase Inhibitors (Statins)
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Background: Cardiovascular disease is the most common cause of mortality in patients with chronic kidney disease (CKD). Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) in late-stage development for the treatment of anemia due to CKD. The prevalence of dyslipidemia in CKD is very high, and nearly 50% of patients have been prescribed statins to decrease cholesterol levels. The disposition of most statins is dependent on metabolic enzymes and transporters. This study evaluated the drug interaction potential for statins when co-administered with vadadustat.

Methods: In this 3-part study (NCT03801733), 108 healthy adults were enrolled for vadadustat-statin pharmacokinetic (PK) evaluation. Vadadustat (600 mg daily) was administered concomitantly with either rosuvastatin (20 mg; n=34), pravastatin (40 mg; n=23), or atorvastatin (40 mg; n=30) for 7 days. Steady-state plasma concentrations for statin and vadadustat were measured following single and multiple oral doses of each drug. The PK parameters were compared in the presence and absence of each statin.

Conclusions: There were no clinically significant interactions with rosuvastatin or atorvastatin, suggesting that vadadustat has a low likelihood for OATP1B1-mediated drug interactions. Increases in exposures to rosuvastatin and simvastatin are possibly due to BCRP inhibition. In summary, these results provide information to aid in the management of concomitant administration of vadadustat with statins. Funded by: Akemia Therapeutics, Inc.

Funding: Commercial Support - Akemia Therapeutics

PO2367
Preclinical Characterization of MAU868, a Novel Neutralizing Antibody Targeting BK Virus
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Background: Reactivation of BK virus (BKV) can cause significant kidney and bladder disease in immunocompromised patients. There are currently no effective BKV-specific therapies. MAU868 is a novel human monoclonal IgG1 that binds to the BKV major capsid protein VP1. Its binding affinity, antiviral activity, and resistance profile were investigated in vitro.

Methods: Binding affinity was determined using a solution equilibrium titration assay. Neutralization of BKV infection in primary renal proximal tubule epithelial (RPTE) cells was evaluated by quantitating Tag-expressing cells using an immunofluorescence-based assay. Reduction of BKV-infected cell yields (IC50) with reduced susceptibility to MAU868 was investigated in two long-term selection studies with BKV genotypes 1 and 4 RT and HEK-293 cells. Crystallographic studies were conducted using the MAU868 single-chain variable fragment bound to VP1 peptide.

Results: MAU868 had pM binding affinity and sub-nM neutralizing activity against the 4 major BKV genotypes, with EC50 and EC50 values ranging from 0.009 to 0.093 μM (0.0062 to 0.645 nM) and 0.102 to 4.160 μM (0.708 to 28.865 μM). No cytotoxicity effects were observed. IC50 concentration for each BKV genotype tested (50 μg/ml) was 0.102 to 4.160 μM (0.708 to 28.865 μM). No cytotoxicity effects were observed.

Conclusions: MAU868 is a novel human monoclonal IgG1 that binds to the BKV major capsid protein VP1. Its binding affinity, antiviral activity, and resistance profile were investigated in vitro.

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Underline represents presenting author.

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KBP-5074 may present an extended therapeutic window as compared to the steroidal 24.24 for KBP-5074 vs 0.62 for eplerenone. Thus, the TI against hyperkalemia of KBP-reduction was 538 nM and 22.0 nM respectively for KBP-5074, and 666 nM and 1071 nM AUCinf and t1/2 renal clearance of roxadustat and its metabolites decreased with lower baseline RF. Mean the amount of unchanged roxadustat excreted in urine was <1%; urinary excretion and

Centre de Recherche des Cordeliers, Paris, France

Frederic

Hyperkalemia in an Animal Model of CKD

Reduces Urine Albumin-to-Creatinine Ratio and the Risk of KBP-5074, a Nonsteroidal Mineralocorticoid Receptor Antagonist,

PO2370

A Genotype-Guided Antihypertensive Therapy and CKD Care Precision Health Initiative

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Background: A precision health initiative was implemented, wherein pharmacogenomic predictors of antihypertensive response and genomic predictors of chronic kidney disease (CKD) were provided to clinicians caring for nephropathy patients.

Methods: This is a prospective cohort study of 580 individuals who presented to outpatient nephrology clinics. Subjects were genotyped for 60 antihypertensive response variants and 10 chronic kidney disease (CKD) predictors. Predictors included variants of CYP2D6 for metoprolol dosing and CYP2C9 for angiotensin receptor blocker dosing. Variants in APO1, UMOD, and SHROOM3 were markers of CKD risk prediction. Subjects were followed to ascertain utilization of the genetic information by nephrologists.

Results: The cohort was 66% female and 43% African American. Actionable variants were found in 85% of subjects. These variants are known to affect metabolism of a drug, or contribute to CKD progression. The prevalence of actionable genotypes was 66% for CYP2D6, and 36% for CYP2C9. In African American subjects, 23% of CKD patients had two or more CKD risk variants. Clinicians adapted treatment for 43% of individuals with actionable genotypes. The primary nephrologist was surveyed for each subject. In the 143 subjects who completed follow-up, nephrologists reported a change in diagnosis in 44% of their patients and a change in management in 28.0% based on genomics. Clinicians discussed the genetic testing results with their patients in 83.9% of cases.

Conclusions: Nephrologists utilized a genetic testing panel of up to 60 variants in the routine care of their CKD patients. Pharmacogenomics predicts of disease response may prove to be very valuable the care of patients with chronic kidney disease.

Funding: NIDDK Support

PO2371

KBP-5074, a Nonsteroidal Mineralocorticoid Receptor Antagonist, Reduces Urine Albumin-to-Creatinine Ratio and the Risk of Hyperkalemia in a Model of Chronic Kidney Disease

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Background: KBP-5074 is a novel non-steroidal mineralocorticoid receptor antagonist (MRA) being developed for uncontrolled hypertension and advanced chronic kidney disease. The primary objective of this study was to evaluate KBP-5074 and eplerenone for renal protection against aldosterone-mediated renal disease in a nephroprecipitated Sprague-Dawley (SD) rat model.

Methods: Uninephrectomized rats were maintained on a 6% high salt diet, and received aldosterone infusion for 27 days. Urinary albumin to creatinine ratio (UACR), urinary sodium and potassium, and serum potassium were measured in the SD rat model. Three groups of SD rats were treated with KBP-5074 or eplerenone and the control group was treated with vehicle. Blood samples were collected on days 1 and 27 to determine the PK profiles. PK/PD analyses were performed on urinary Na/K ratio, UACR, and serum K.

Results: KBP-5074 (1, 3, and 10 mg/kg/day) significantly reduced UACR by 77%, 90%, and 99% respectively on day 14 and 59%, 86% and 108% respectively on day 26 in a dose dependent manner, while eplerenone (100 and 900 mg/kg/day) reduced UACR by 40% and 99% respectively on day 26. PK/PD analysis of Urinary Na/K ratio indicated that KBP-5074 was approximately 18-fold more efficacious than eplerenone. Analysis of UACR and serum K indicated that the EC50 for serum K+ increase and UACR reduction was 538 nM and 22.0 nM respectively for KBP-5074, and 666 nM and 1071 nM respectively for eplerenone. In a therapeutic index (TI) against hyperkalemia of KBP-5074 was approximately 24.24 for KBP-5074 vs 0.62 for eplerenone. Thus, the TI against hyperkalemia of KBP-5074 was 39-fold superior to eplerenone. One group of SD rats received KBP-5074 for 14 days, followed by saline. KBP-5074 may present an extended therapeutic window as compared to the steroidal MRA eplerenone.

Conclusions: KBP-5074 demonstrated a significant effect on UACR reduction with less risk for hyperkalemia compared to eplerenone in a rat model of nephropathy.

Funding: Commercial Support - KBP Biosciences Inc

PO2372

Pharmacological Inhibition of Vanin 1 Is Not Protective in Models of Acute and Chronic Kidney Disease


Background: Dysregulated oxidative stress handling is a hallmark of acute and chronic kidney diseases. The pantheinein Van-1 is highly expressed in tubular cells and renal HT29 cells and produces protection against oxidative stress by inhibiting the replenishment of cellular anti-oxidative glutathione stores. The aim of this study was to elucidate whether pharmacological inhibition of Van-1 protects mice from acute or chronic kidney injury.

Methods: C57Bl6 mice undergoing ischemia reperfusion injury and Col4A3/- (Alport syndrome) mice were treated orally for 1 and 3wk, respectively, with a potent and selective Van-1 inhibitor or placebo. In vitro oxidative stress insult was mimicked in human renal proximal tubular epithelial cells either chemically or by hypoxia/ reoxygenation. Kidney function was determined by serum and urinary creatinine as well as serum urea and urinary albumin. Furthermore, mRNA and protein expression, Van-1 activity, oxidative stress level and tubular apoptosis were monitored.

Results: Oxidative stress levels were elevated in all models. Treatment with the Van-1 inhibitor resulted in ameliorated systemic compound exposure and full inhibition of Van-1 activity in kidney tissue in vivo. However, this did not translate to a relevant reduction of oxidative stress level. Moreover, kidney function (serum Crea, blood urea, albuminuria), fibrosis marker gene expression and tubular cell apoptosis were not improved with Van-1 inhibition.

Conclusions: Pharmacological inhibition of Van-1 is insufficient to protect kidneys from oxidative stress insults contributing to acute and chronic kidney injury. The biological relevance of pharmacological Van-1 inhibition for the treatment of kidney diseases remains to be proven.

Funding: Commercial Support - Bayer AG

PO2373

Evaluation of Veverimer Drug Interaction Potential in Human DDI studies

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Background: Veverimer is orally administered, non-absorbed polymer that selectively binds and removes hydrochloric acid (HCl) from the gastrointestinal tract, providing an increase and UACR decrease in chronic kidney disease patients. Vanin-1 is a pantetheinase highly expressed in the kidney and involved in the handling of oxidative stress insults contributing to acute and chronic kidney injury. The action of Veverimer on gastrointestinal acid binding is not affected by Vanin-1 inhibition.

Methods: We observed: 1) no effect of veverimer on the bioavailability of drugs with pH-dependent solubility (warfarin, dabigatran) were chosen for human DDI studies. In vitro studies showed the most important determinant for binding to veverimer in vitro. Three DDI studies were performed on gastric pH and the pH of the intravenous and the oral drug. Based on these results, 2 drugs with a direct binding or 2 increased in gastric pH resulting from HCl binding.

Results: In vitro studies showed the most important determinant for binding to veverimer is negative charge, with small size as a secondary determinant. Veverimer did not bind any positively charged, neutral or weakly ionized drugs. Negatively charged drugs (warfarin, dabigatran) were chosen for human DDI studies. Veverimer increased gastric pH by ~3.0 (fasted) and 1.5 (fed) pH units. The gastric pH increase was transient, peaking by 1 h after dosing and returning to baseline after 1.5 (fasting) and 3 (fed) hours. Based on these results, 2 drugs with PD-dependent solubility (warfarin, dabigatran) were chosen for human DDI studies. In human DDI studies, no clinically meaningful changes in bioavailability were observed for warfarin, aspirin, dabigatran, or warfarin when coadministered with veverimer.

Conclusions: We observed: 1) no effect of veverimer on the bioavailability of drugs most susceptible to binding to the polymer; 2) modest, transient effects of veverimer on gastric pH; 3) no effect on bioavailability of drugs with pH-sensitive solubility. We conclude that there is a negligible risk of clinically significant veverimer DDIs.

Funding: Commercial Support - Tricida, Inc.

PO2374

Action of Veverimer on Gastrointestinal Acid Binding Is Not Affected by Omeprazole

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Background: Veverimer, an orally administered, non-absorbed polymer that selectively binds and removes hydrochloric acid (HCl) from the gastrointestinal tract, has been shown to correct metabolic acidosis in patients with CKD. Unlike proton pump inhibitors (PPIs), which do not affect systemic acid-base status, the removal of HCl

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from the gastrointestinal tract by veverimer leads to a net increase in blood bicarbonate. Veverimer was designed to bind HCl across a wide range of intraluminal pH, but the effect of veverimer on acid binding in the presence of PPIs has not been previously described.

Methods: To evaluate the effect of veverimer on gastric pH, we conducted a Phase 1, open-label, 2-stage study in which subjects (N=46) were randomized 1:1:1:1 to receive 1 of 4 study drug treatments (water fasted; water fed; veverimer fasted; veverimer fed) in the presence and absence of a steady-state level of omeprazole. Gastric pH was measured continuously for 22 hours (hrs) using a microelectrode pH probe positioned in the gastric fundus.

Results: Ingestion of veverimer caused a modest, transient increase in gastric pH that peaked within 1 hr post-dose. In the absence and presence of food, the median (distribution-free 95% CI) times to peak pH after veverimer administration was 0.25 (0.17, 1.00) and 0.71 (0.25, 1.17) hrs, respectively. Peak pH after veverimer administration was ~3 and ~1.5 pH units greater than that observed after water control in the fasted and fed states, respectively. The magnitudes of these increases were in the same range in the presence of omeprazole. Gastric pH returned to baseline after ~1.5 hrs under fasting conditions and after ~3 hrs under fed conditions. In the presence of omeprazole, the veverimer-induced gastric pH increase dissipated by 4 hrs post-dose or shortly after initiation of the subsequent meal.

Conclusions: The effect of veverimer on gastric pH is transient and similar in the presence or absence of omeprazole. The magnitude of the individual effects of food, veverimer, and omeprazole on gastric pH were similar (increase of 2–4 pH units). These findings are consistent with prior studies in patients with CKD in which the magnitude of efficacy of veverimer was unaffected by use of H2-receptor antagonists and PPIs (Wesson et al. Lancet, 2019).

Funding: Commercial Support - Tricida, Inc.

PO2376
Circulating Heparin and Its Relevance to Thrombin Generation Profile in ESRD Patients Undergoing Maintenance Hemodialysis
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Background: End stage renal disease (ESRD) is a complex pathophysiologic syndrome which results in vascular disorders and hemostatic disturbance. Despite the use of heparin during maintenance hemodialysis some of these patients exhibit hypercoagulable state. The purpose of this study was to characterize the thrombin generation (TG) profile in ESRD patients in relation to circulating heparin levels.

Methods: Citrated blood samples from 95 patients with ESRD undergoing maintenance hemodialysis were collected. NHP was prepared for referencing purposes. Individual samples were supplemented with heparin. TG parameters such as peak thrombin, lag time and area under the curve (AUC) were compiled. Circulating heparin levels were determined using activated partial thromboplastin time (aPTT) and chromogenic anti-Xa and IIa assays. The ESRD cohort was stratified into heparinized and heparin naïve groups.

Results: ESRD group showed decrease in peak thrombin (107.1 vs 168.3 nM) and AUC (589.8 vs 815.7 nM*min) with increase in lag time (2.9 vs 2.2 min) compared to NHP. Heparin supplementation increased the lag time (3.4 min, p value 0.0001), while decrease the peak thrombin (100.0 nM, p value 0.0245) and AUC (503.4 nM*min, p value <0.0001). Such parameters as aPTT (43.2 vs 31.1 sec), anti Xa (0.21 vs 0.14 U/mL) and anti-IIa (0.27 vs 0.15 U/mL) decreased with heparinization treatment. Heparin naïve group showed decreased peak thrombin and AUC values whereas the lag time was increased. Simultaneously aPTT, anti-Xa and anti-IIa levels were decreased in this group. Heparinized patients did not show any difference in peak thrombin, decrease in AUC values and an increase in lag time. However, the aPTT, anti-Xa and anti-IIa were decreased in this group.

Conclusions: These studies showed that heparinization treatment of plasma samples from ESRD patients resulted in the decrease in aPTT, anti-Xa and IIa levels suggesting the digestion of heparin. However, contrary to these results, TG parameters such as peak thrombin and AUC were decreased whereas lag time was increased suggesting that the depolymerized heparin fragments provoked thrombin generation inhibitory properties.

PO2377
Clinically Apparent AKI Secondary to Suspected Vancomycin Toxicity: A Cellular Kinetic Analysis
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Background: The use of antimicrobial therapies for treatment of hospitalized patients is abundant. While the usage rate of antibiotics has remained stable over the last decade, however, with the emergence of methillin-resistant staphylococcus aureus, vancomycin usage has increased during that same time period. Although vancomycin induced AKI or vancomycin associated nephrotoxicity (VAN) has been a topic of debate since its generalized use approximately 50 years ago, the proposed mechanism of VAN is an on-going focus of research. The current study aims to answer whether proximal tubular creatinine secretion, which can account for upwards of 20% of creatinine clearance, is impacted by vancomycin dosing, and whether vancomycin trough levels seen in clinical practice alter this relationship.

Methods: For the cellular kinetic analysis, we took immortalized human proximal tubule epithelial cells, and after allowing them to epithelialize on a semi-permeable membrane, evaluated creatinine secretion in the presence of varying concentrations of both vancomycin and vancomycin, while measuring eliminated levels for up to 24 hours. For the patient analysis, IRB approval was obtained to evaluate the cases of possible VAN on the renal consult service.

Results: Creatinine secretion through the cellular epithelium was not affected by vancomycin at levels up to 4X therapeutic, the upper limit of those seen on a cohort of patients in the renal consult service at the university of Colorado. This is consistent with other pharmacokinetic data, indicating that vancomycin is able to inhibit transporters of creatinine, but at levels not seen in clinical practice. The patient cohort analysis identified thirteen patients who were deemed to have “possible VAN,” and in all of these the rise in Cr did happen temporally related to vancomycin, and there were many other factors potentially confounding their AKI.

Conclusions: Proximal tubule dysfunction from vancomycin inhibition of cellular transporters does not cause significant creatinine elevation in concentrations used clinically. The cases of clinically apparent vancomycin associated nephrotoxicity are multifactorial. Therefore the nephrotoxicity associated with vancomycin administration does not seem to be the sole cause of creatinine elevation in patients with AKI.

PO2378
Systemic Absorption of Vancomycin from Sternal Slurry Contributing to Vancomycin Nephrotoxicity
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Introduction: Vancomycin has come a long way since its start as “Mississippi mud”. It has been a valuable and safe agent in general. Adverse reactions include flushing and anaphylaxis injury. Clinicians are developing strategies to circumvent these problems. One strategy is the use of antibiotic powder paste applied to infusorium tissue. This has
traditionally not been associated with systemic vancomycin toxicity. We report here an incidence of vancomycin nephrotoxicity secondary to a sternal vancomycin slurry that required dialysis.

Case Description: A 62-year-old 91 kg man with Marfan’s Syndrome and total aortic arch replacement presented with mediastinal abscess and recurrent sternal osteomyelitis. An antibiotic susceptibility test of sternal slurry revealed a circumferential fluid collection around the aortic graft. He underwent a “redo” sternotomy, exploration and drainage. Plasma creatinine concentration (P_cr) on admission was 0.76 mg/dL, his known baseline. He received one dose of 1250 mg IV vancomycin prior to the operation. Intra-operatively 4 grams of vancomycin paste was applied to his sternum. That evening he received cefepime 2g IV and vancomycin 1250 mg IV (see figure), both scheduled to be repeated every 12 hours. P_cr and vancomycin troughs are detailed in the figure. On POD2 serum vancomycin trough was 42 mg/L. Intravenous vancomycin was undetectable and P was discharged on POD14 on daptomycin and ceftriaxone. On POD21 at follow-up, serum vancomycin was 48 mg/L and P

Discussion: There can be substantial unaccounted systemic absorption from vancomycin paste. The POD 4 AM serum level was 48 mg/dL and he was dialyzed 14 hours later under operating conditions such that the level should be reduced by at least one-third. The post dialysis level was 47 mg/dL, so by conservative estimation his predialysis level was about 70 mg/L, suggesting that there was a substantial contribution of vancomycin to the serum level in that 17-hour interval from sternal slurry.

PO2379

Efficacy of the Recommended Ceftazidime/Avibactam Dose in Treating Carbapenem-Resistant Enterobacteriaceae in Critically Ill Patients Using Renal Replacement Therapies

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Background: Ceftazidime/avibactam (CEF/AVI) is a novel antibiotic used to treat multi-drug resistant (MDR) and gram-negative bacteria, including Carbapenem-Resistant Enterobacteriaceae (CRE). Data on CEF/AVI dosing and outcomes in patients with acute kidney Injury (AKI) are lacking. The aim of this study was to assess the efficacy of the recommended dose of CEF/AVI in patients utilizing renal replacement therapy.

Methods: A retrospective cohort study was conducted at our quaternary care institution between May 2015 and December 2019. All hospitalized adults with CRE were included. Clinical data such as CEF/AVI dose, C/FS, AKI duration, infection type, and clinical cure during the follow up periods up to 3 months, recurrence/relapse occurred in 9 of the 24 patients. Eight patients deceased within 30 days of follow up and 4 more within 90 days. Only one patient did not have relapse or recurrence within the 90 days of follow up.

Conclusions: The CEF/AVI recommended dose could achieve uncertain clinical outcomes. Pharmacokinetics and pharmacodynamics studies are urgently needed to determine the adequacy of CEF/AVI dosing in this population.

PO2380

Extracorporeal Removal of Valproic Acid in Overdose: A Case Report

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Background: Valproic acid (VPA) is considered not dialyzable at therapeutic concentration and dialyzable at supratherapeutic concentration because of saturable protein binding which increases its free fraction (from 10% to 90%).

Case Description: We report a case of a 53-year old 50kg woman admitted for suicidal polydrug intoxication. She had ingested 15g of VPA, 300mg of atorvastatin, 3g of quetiapine, and 750mg of naltrexone 3 hours prior to admission. Her vital signs were stable on admission and she was somnolent but arousible. Toxicology assays for ethanol, acetaminophen, and salicylates were negative. Biochemistry, blood gases, and complete blood count were unremarkable. She was initially treated with intravenous saline, naloxone, and intravenous caffeine. Despite these, she became progressively oliguric for 24 hours during which the serum VPA concentration rose from 60 to 422 mg/L (therapeutic concentration 50-125mg/L) and ammonia concentration rose from 17 to 56 mmol/L. Hemodialysis (HD) was initiated for 6h (GFS-210, Qb=400mL/min, Qd=750mL/min) via a right temporary femoral catheter because of concerns for further volume and sodium-induced hyperammonemia and reduced access to VPA measurements. Her level of consciousness normalized during HD. No complications occurred during HD. VPA concentration and ammonia concentrations at the end of HD were 78 mg/L and 15 mmol/L, respectively, and did not re-increase thereafter (Figure 1). She was given three 50g doses of activated charcoal after HD and she eventually made a full recovery. VPA half-life was 3.0h during HD, 18.9h during multidose charcoal, and 4.9h without treatment. VPA was 48% unbound at the onset of HD. Instantaneous VPA clearance (calculated using simultaneous plasma and effluent VPA concentrations) decreased from 4.5 L/min during HD as protein binding increased.

Discussion: HD removed 1.4g of VPA which would have been higher had HD been performed sooner after admission. This case illustrates that the dialyzability of VPA depends on its protein binding which itself depends on its serum concentration.

PO2381

Gabapentin Toxicity in Existing and Developing Renal Failure


Introduction: Gabapentin is a medication used to treat partial onset seizures, neuropathic pain caused by diabetic neuropathy, postherpetic neuralgia, & central neuropathic pain. This medication is nearly completely excreted by the kidneys. It is recommended as one of a number of first-line medications for the treatment of pain.

Case Description: Here we report two cases of potential gabapentin toxicity across the spectrum of renal insufficiency. The first case was a 46-year-old female with a history of ESRD (HD X 3 times/week), HCV, DM, HTN and spinal abscess presented with new onset seizure, body stiffening with head and eye deviation, confusion, fall and hypertensive emergency while awaiting for dialysis. She had a second seizure while in the ED and was started on anti-seizure medication Leviteracetam. Home medications included Gabapentin (800 mg TID). Head CT was unremarkable. The second case was a 69-year-old female patient with a history of DM, peripheral vascular disease, coronary artery disease & atrial fibrillation who presented with new onset seizure, body stiffening with head and eye deviation, confusion, fall and hypertensive emergency while awaiting for dialysis. She had a second seizure while in the ED and was started on anti-seizure medication Levetiracetam. Home medications included Gabapentin (300 mg 3 times daily). The patient developed contrast-induced AKI due to a CT angiogram procedure on admission. Following the development of AKI, the patient became confused without evidence of significant azotemia (BUN 33). Both the cases were found to be arousable and GCS of 12/15, intact strength & sensation of both extremities, no ataxia, dysarthria, hemineglect or signs of pronator drift. In both cases, Gabapentin toxicity was suspected and the dosage of Gabapentin was reduced to 100 mg orally at night. There was a drastic improvement of confusion and other symptoms within 2 to 3 days post dosage adjustment in both patients.

Discussion: Renal insufficiency predisposes patients to increased risk of gabapentin induced toxicity due to reduced clearance. Advanced age and other comorbidities may further accelerate the risk. The range of Gabapentin toxicity across the spectrum of renal insufficiency is underestimated. In this case report, the patient with AKI only was confused and the patient with ESRD had myoclonus and seizure in addition to confusion. There seems to be a graded increase in toxicity with the corresponding deterioration of renal function. Heightened awareness about medication toxicity developing in renal failure is important to prevent significant adverse effects.
Case Description: An 85-year-old male with a past medical history of stage 4 chronic kidney disease secondary to diabetic nephropathy (baseline serum creatinine 2.2 mg/dL; Type 2 Diabetes Mellitus, diabetic neuropathy, and hypertension, presented to clinic for worsening of serum creatinine. Pertinent home medications included bumetanide 3 mg BID, metolazone 2.5 mg daily and gabapentin 600 mg TID. Bumetanide and metolazone were up titrated for worsening bilateral lower extremity edema over last 3 months with 20-pound weight gain. Exam was notable for 2+ LE edema. His serum creatinine progressively increased from 2.4 to 4 mg/dL in the setting of aggressive diuresis. A recent TTE showed only grade 1 diastolic dysfunction. The presumed diagnosis was heart failure with preserved ejection fraction. Urine sediment was bland. After identification of gabapentin as potential culprit agent for his edema, both gabapentin as well as his diuretics were discontinued with a resultant significant drop in his weight and serum creatinine to 218lbs and 2.7mg/dL respectively over next one month and complete resolution of his edema.

Discussion: Incidence of gabapentin induced edema varies from 2% to 8% and has been correlated to dosage. Exact mechanism is unknown but possibly related to loss of venoarteriolar reflex leading to increased capillary hydrostatic pressure and hence increased net capillary fluid filtration into the interstitium. Gabapentin induced edema, just like calcium channel blockers induced edema, is not associated with salt and water retention and hence diuretics are ineffective. Physicians, especially nephrologists, should be mindful of uncommon side effect of this commonly prescribed medication as distinguishing this early can prevent a lot of unnecessary work up and potentially prevent harm to the patient.

PO2384
Glimmering Changes in Transplant Glimmerulopathy
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Background: Transplant glomerulopathy (TG) affects 20% of transplanted kidneys 5 years post transplantation. It carries an important significance due to its correlation with decreased graft survival. Repeated endothelial cell injury by chronic active antibody mediated rejection (cAMR) leads to glomerular basement membrane (GBM) reduplication and thickening, the hallmark finding of TG. Based on our previous molecular mapping of the GBM, we aim to define the composition of the thickened GBM in TG using super-resolution microscopy.

Methods: Two super-resolution microscopy techniques, STORM (Stochastic optical reconstruction microscopy) and Airyscan, were used to image confirmed TG and control biopsies. For STORM, fresh frozen, 200 nm sections were imaged. While for Airyscan, 1-3 microns, formalin fixed paraffin embedded (FFPE) sections were used. Samples were labeled with antibodies for Laminin a5, Integrin a8, Myosin IIA, Vimentin, Synaptopodin, Integrin b1, Fibronectin, and several Collagen IV chains.

Results: STORM TG samples showed increased distance between Integrin b1 labeled GBM, indicating thickening of the GBM. Collagen a3a5a(V) did not change, while Collagen a1a2a(V) was increased at the GBM's endothelial aspect. There was an increase in Fibronectin, suggesting a role for the TGFβ pathway. Airyscan TG images showed Vimentin- and Integrin a5-positive areas inside the GBM, indicating cellular protrusions extending into the GBM. Since these markers stain mesangial as well as endothelial cells, this suggests differentiation of endothelial cells and transition to mesenchymal cells. We detected alternating Myosin IIA and Synaptopodin labeling in the form of “Sarcomere-like structures”.

Conclusions: Our data revealed increased Collagen a1a2a(V) secreted from the endothelial side, while Collagen a3a5a(V) was unchanged. The increase in Fibronectin, cellular protrusions positive for mesenchymal markers, and sarcomere-like structures inside the diseased GBM suggest an endothelial to mesenchymal transition as culprit for increased Collagen IV rather than injury signals from podocytes.

PO2385
Calcineurin Inhibitor Cyclosporine A but Not Tacrolimus Induces Proapoptotic Endoplasmic Reticulum Stress in Kidney Epithelial Cells
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Background: Current immunosuppressive strategies in solid organ transplantation rely on the calcineurin inhibitors (CNI), cyclosporine A (CsA) or tacrolimus (Tac). Their nephrotoxicity is a major limitation for long-term usage. We hypothesized that CsA compared to Tac exerts more pronounced toxic side effects at the cellular level, with endoplasmic reticulum (ER)-stress and maladaptive unfolded protein response (UPR) as the most prominent markers.

Methods: To test this hypothesis we treated human embryonic kidney (HEK293) cells with CsA (10 μM) or Tac (10 μM) for 6h. The established ER stress-inducing agent, thapsigargin, served as positive control. To study the molecular mechanisms of CNI-induced cell toxicity we studied genetically-modified HEK293 cells lacking the crucial UPR elements, PERK or ATF6. Abundances of the ER-stress sensor IRE1α, adaptive transcription factor XBP1, and proapoptotic transcription factor CHOP were evaluated as endpoints.

Results: Treatment of native HEK293 cells with CsA or Tac equally increased phosphorylation of the known calcineurin substrate, NFAT, verifying the treatment protocols. CsA increased levels of activating IRE1α phosphorylation (pIRE1α) and stimulated both CHOP and spliced XBP1 (sXBP1) products. In contrast, Tac enhanced pIRE1α abundance only. CsA but not Tac significantly increased the number of cleaved caspase 3-positive cells suggesting enhanced apoptosis rate. Treatment with the chemical chaperone, TUDCA, partially abolished the CsA-induced increases of CHOP but did not affect sXBP1, suggesting alleviation of ER-stress. Knockdown of CsA binding partners, cyclophilin A and B, by siRNA reduced their expression approximately by half and increased CHOP expression suggesting that suppression of cyclophilins may contribute to CsA-induced cellular toxicity. PERK- or ATF6-deficiency blunted the increases of CHOP and sXBP1 in response to CsA, suggesting an implication of these pathways in CsA-induced ER-stress and UPR.

Conclusions: In summary, CsA but not Tac induces pronounced ER-stress and proapoptotic UPR. Pharmacological modulation of UPR bears the potential to alleviate CNI nephrotoxicity.

Funding: Government Support - Non-U.S.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
fibrosis (P<0.001). The relative binding of FoxO1 is predictive of a fibrogenic response in transplanted kidneys. A high 1-month TF ratio was abnormal in a diverse range of fibrotic transplant diseases. A high 1-month TF ratio was associated with pathological and clinical outcomes was evaluated.

Conclusions: In conclusion, differential binding of β-catenin to TFCT1 rather than FoxO1 is predictive of fibrogenic response in transplanted kidneys.

Funding: Government Support - Non-U.S.
PO2391

B-Cell Maturation Phenotypes and Time Post-Transplant

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Background: Over the past decade, B cell participation in allograft response has been progressively elucidated. Beside the occurrence of DSA (donor-specific alloantibodies), different patterns of B cell phenotypes are also being related to graft outcome. Loss of naive B cells and appearance of memory B cells have been linked to chronic rejection and ultimately to graft loss. Here we show the impact of time post-transplant on phenotypic B cell changes, particularly regarding different distributions of naive B cells.

Methods: Single-center, observational cohort of 82 kidney transplant recipients (KTr), adults and clinically stable. Blood samples were collected between January 2015 and November 2018. Peripheral blood mononuclear cells (PBMCs) were isolated and analyzed on flow cytometry. B cells (CD19+) were stained for CD38 and IgD and classified according to BM classification (IgD vs CD38).

Results: The median time post-transplant was 2.9 [0.9-9.89] years and the mean age was 54±13 years. 63% of the patients were males and mean eGFR was 49±17 mL/min. B cells absolute counts were lower in later phases post-transplant (R=-0.04, p<0.01). Among all B cell subtypes, Bm2 compartment (comprised mainly by naive B cells) had the most significant reduction in both absolute counts (R=-0.62, p<0.01) and relative percentage (R=-0.58, p<0.01) over time. On the opposite, mature B cells (both Bm5 and early Bm5 compartments) absolute counts did not differ over time (R=-0.04 and 0.11 respectively, p<0.05) whereas the percentages of them were positively correlated with time post-transplant (R=0.40 and 0.36 respectively, p<0.01). Linear regression model showed that the absolute reduction in Bm2 cell compartment (i.e naive B cells) was independent of age, sex, graft function and immunosuppression scheme.

Conclusions: Patients with longer time post-transplant have fewer circulating peripheral B cells. Phenotypic analysis of B cells reveals that this reduction is due to an absolute decrease in naive B cells counts. Maturing B cell absolute numbers, on the other hand, did not change significantly. Either exhaustion due to long-term immunosuppression or immunologic accommodation due to chronic allograft exposure could explain these observations.

PO2392

Donor Derived Cell-Free DNA in Renal Transplants, AlloSure vs. Prospera

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Background: The risk for allograft loss remains high due to rejection. Measuring donor cell free DNA has recently become an important noninvasive test for renal allograft injury and rejection. Two of the commercially available tests to measure dd-cfDNA, are AlloSure(AS) and Prospera.

Methods: We measured dd-cfDNA in 44 post kidney transplants simultaneously using both tests. Patients were 3 to 50 months post kidney transplant and all samples were drawn for cause. Eleven of the 44 patients had allograft biopsies, see table. All patients had routine labs including trough CNI levels and in some cases DSA and/or BK PCR.

PO2393

Donor-Derived Cell-Free DNA Kinetics After Kidney Transplant Biopsy

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Background: Donor-derived cell-free DNA (dd-cfDNA) has generated interest as a potential biomarker for kidney transplant (KT) rejection. It is possible that the KT biopsy procedure itself can cause the release of dd-cfDNA in the blood stream, therefore affecting the reliability of this assay in the post biopsy period. In this study we evaluated the effect of KT biopsy on the level dd-cfDNA and assessed the magnitude and duration of this effect.

Methods: We conducted a single arm prospective study. Samples were collected from 16 adult KT recipients undergoing renal allograft biopsy. All participants had samples drawn within eight hours prior to the biopsy (pre-biopsy), within 20 minutes (hour 0), 2 hours after (hour 2), and 24-48 hours (hour 24-48) after the biopsy.

Results: Mean age at the time of biopsy was 50.6±7.02 years. Most participants were men and Caucasian. Mean serum creatinine at the time of biopsy was 2.24±0.42 mg/dL. The most common reason for obtaining biopsy was rise in serum creatinine, while 4 patients had the biopsy due to elevation in dd-cfDNA. The pre-biopsy time point was compared against all remaining time points. At hour 0 and hour 2, there was a significantly larger log dd-cfDNA mean scores compared to pre-biopsy time point (0.37 vs -0.44, p<0.05). By 24-28 hours post biopsy there was no significant difference in log dd-cfDNA mean score compared to the pre-biopsy score.

Conclusions: KT biopsy leads to an increase in dd-cfDNA percentage after the procedure, however, this rise is transient and resolves by 24-48 hour after the biopsy. Providers can obtain dd-cfDNA level as soon as 48 hours post biopsy with high confidence that the levels have not been affected by the biopsy.

Funding: Commercial Support - This study was an investigator initiated study supported by CareDx, Inc., Brisbane, CA.
**PO2394**

**Development and Clinical Experience with a Cell-Free DNA Monitoring Algorithm for Kidney Re-Transplants**

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**Natera, Inc, San Carlos, CA.**

**Background:** The presence of donor-derived cell-free DNA (dd-cfDNA) in blood samples from kidney transplant recipients can be utilized as a biomarker for transplant rejection. 1 Failure of the original allograft due to rejection, infection, or recurrent disease leads to retransplants, observed in up to 10% of all kidney transplant patients. 2, 3 In these cases, the original transplanted kidney is generally left in situ. A rapid, accurate, and noninvasive diagnostic test assessing dd-cfDNA using single nucleotide polymorphism (SNP) based massively multiplexed PCR (mmPCR) test (Prospera10) may be utilized to detect allograft rejection. 4 Among retransplant patients, this test can detect both donor fractions in the plasma, when both the new and previously transplanted kidneys are releasing cfDNA. 5

**Objective:** To present the clinical performance of the SNP-based mmPCR test analysis algorithm on samples from patients with kidney retransplants in which alloplasms are present from two genetically distinct donors.

**Methods:** Plasma samples from a cohort of second transplant patients were collected and processed as described previously. 1-5 The SNP-based mmPCR test algorithm is designed to detect all donor fractions in the plasma, when both the newly transplanted kidney as well as previously transplanted kidney(s) may be releasing cfDNA into the plasma. This algorithm estimates the total fraction of DNA due to all donor fractions combined.

**Results:** We present the clinical performance of patients with a second kidney transplant by this retransplant algorithm. In our dataset to date, no significant difference in dd-cfDNA levels compared to single allograft recipients was observed, suggesting limited cfDNA shedding from the initial kidney transplanted. Our results confirm the ability of this assay to analyze and quantify dd-cfDNA levels in kidney retransplant patients.

**Conclusions:** Our results indicate that performance of this SNP-based mmPCR test is preserved in repeat transplant recipients. Non-invasive assessment of dd-cfDNA in retransplant patients may be used to detect the presence of injury or rejection of the transplanted organ at an early stage, facilitating physician management around change of anti-rejection therapy.

**Funding:** Commercial Support - Natera, Inc.

**PO2395**

**Correlation of Donor-Derived Cell-Free DNA with Histology and Molecular Diagnoses of Kidney Transplant Biopsies**

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**Background:** Circulating donor-derived cell-free DNA (dd-cfDNA; CareDX, Brisbane, USA), a non-invasive test that could detect rejection in kidney transplants, was validated using histologic diagnoses. The interpretation of these findings could be difficult due to variable inter- and intra-observer agreement with regards to histologic diagnoses and evolving classifications overtime. The centralized Molecular Microscope (MMDx; Edmonton, AB) tissue gene expression platform may provide increased precision to traditional histology.

**Methods:** In this single-center prospective study of 208 biopsies, we present novel data on quantification of cfDNA using simultaneous assessments of all ‘for-cause’ and surveillance biopsies with histology(Hx) and MMDx. AUC curves were calculated using the previously published dd-cfDNA cut-offs of < 0.21% to rule-out rejection and > 1% to rule-in rejection

**Results:** Of 208 biopsies done at a median of 5.8 months post-transplant, 108(52%) were done for allograft dysfunction; 74(36%) for surveillance (up to DSA) and 26(12%) for post-rejection treatment surveillance. There were significant discrepancies between Hx and MMDx; with MMDx(92; 44%) identifying a higher number of rejection cases vs Hx(79; 38%). While MMDx identified a higher number of antibody-mediated rejection cases(65; 31%) than Hx(43; 21%); the opposite was true for T-cell mediated rejection(TCMR; Hx:27(13%) vs MMDx: 13 (6%)). AUC Curves for cfDNA concentration and prediction of rejection were more robustly correlated with MMDx(AUC=0.830; p<0.001) than with Hx(AUC=0.75; p<0.001). The median cfDNA level was raised significantly to rejection treatment(median 0.94 to 0.29; p<0.015) vs non-responders(0.76 to 0.82; p=0.25)

**Conclusions:** In this single-center study, for the first time we describe the calibration of dd-cfDNA with simultaneous assessment of kidney transplant biopsy with traditional histology and MMDx. We confirmed and expanded on the data from the DART study where a cut-off of 1% was highly sensitive and specific for ruling-in rejection. We report the correlation of cfDNA with response to rejection therapy. We propose that the combination of tissue gene expression using the molecular microscope and blood-based dd-cfDNA may add precision to traditional histology and could change future practice and treatment paradigms.

**PO2396**

**Elevated Donor-Derived Cell-Free DNA (dd-cfDNA) in Renal Transplant Patients with Donor-Specific Antibodies**

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**Introduction:** Complications of renal transplants include graft rejection and failure. Noninvasive dd-cfDNA values greater than 1% detect renal allograft injury and rejection, prior to changes in creatinine. Although antibody mediated rejection (AMR) typically involves donor specific antibodies (DSA) to human leukocyte antigens (HLA), non-HLA antibodies may also impact allograft outcomes. This series of re-transplantation patients with graft injury from AT1R-Ab (>10 U/mL) shows improvement in dd-cfDNA levels with initiation of anARB, Losartan.

**Case Description:** Case #1: 23 year-old man with history of CKD IV due to hypoplastic kidneys. First transplant living unrelated donor failed due to renal vein thrombosis. Received a 2nd deceased donor transplant (DDRT) with thymoglobulin induction. Complement 3 (C3) was reduced and dd-cfDNA 3.3%. Post-transplant allograft function was excellent with nadir creat of 1.0mg/dL. Non-invasive allograft surveillance was initiated with initial dd-cfDNA (ALLOSURE, CareDx, Brisbane, CA) elevated at 1.8%. Antibody assessment was negative for DSA but positive for AT1R-Ab at 28 U/mL. Losartan was initiated with a sustained decrease in dd-cfDNA to <0.3% and stable creatinine levels. Case #2: 63 year-old woman with ESRD from hypertension. Prior living donor transplant failed due to chronic allograft nephropathy. Received 2nd DDRT with thymoglobulin induction given cPRA of 98%, with no DSA. Post-transplant allograft function was excellent with nadir creatinine of 0.8 mg/dL. Non-invasive allograft injury surveillance showed an acute rise in dd-cfDNA to 3.9% on post-operative week 5. Despite stable creatinine, a renal biopsy showed C4D-negative, mild antibody mediated rejection with peritubular capillaritis (ptc 2) and glomerulitis (g1). Antibody assessment showed no DSA but positive AT1R at 16 U/mL. Following Losartan initiation, dd-cfDNA decreased to <1%, with continued excellent graft function.

**Discussion:** AT1R-Ab may be more prevalent in the re-transplant population and is a causative factor for accelerated allograft injury, chronic fibrosis, and graft loss. Quantification of kidney injury via dd-cfDNA, prompt assessment of AT1R-Ab, and initiation of ARB therapy may lead to preserved allograft function, particularly in high immunologic risk patients.

**PO2397**

**Class II Donor-Specific Anti-HLA Antibody Level Is the Major Determinant of Elevated Donor-Derived Cell-Free DNA in Renal Allograft Recipients**

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**Background:** dd-cfDNA is a biomarker of allograft injury used for rejection risk monitoring. We sought to analyze the relationship between dd-cfDNA and DSA.

**Methods:** We included all kidney transplant recipients (n=171) who underwent DSA and dd-cfDNA testing as part of their clinical care between 9/17-12/19 at our center. We aimed to identify independent predictors of high dd-cfDNA (at a cut-off of 1%).

**Results:** Table 1 outlines clinical characteristics. There was a strong association between absolute dd-cfDNA level and DSA MFI category (Figure 1). In multivariate logistic regression analysis, DSA MFI was an independent predictor of high dd-cfDNA (Figure 2).

**Conclusions:** dd-cfDNA is strongly associated with class II DSAs and MFI level. Variably observed identifies dd-cfDNA as a potential biomarker for monitoring allograft injury status in patients with DSA.

**Funding:** Commercial Support - CareDx Inc, Clinical Revenue Support
Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age (for each 1 y)</td>
<td>0.98 (0.96-1.01)</td>
<td>0.22</td>
</tr>
<tr>
<td>Gender (female vs. male)</td>
<td>1.9 (0.87-4.14)</td>
<td>0.1</td>
</tr>
<tr>
<td>Ethnicity (other vs. Caucasian)</td>
<td>1.07 (0.67-1.72)</td>
<td>0.95</td>
</tr>
<tr>
<td>Type of transplant (cadaveric vs. living)</td>
<td>0.66 (0.29-1.51)</td>
<td>0.33</td>
</tr>
<tr>
<td>Time from Tx to dd-cfDNA measurement (for each 1 y)</td>
<td>1.01 (0.97-1.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>Serum creatinine (for each 1 mg/dl)</td>
<td>0.57 (0.25-1.29)</td>
<td>0.18</td>
</tr>
<tr>
<td>Urine protein/creatinine ratio (for each 1 g/l)</td>
<td>1.0 (0-9.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Calculated Panel Reactive Antibody (1+0 units, &lt;20%)</td>
<td>0.84 (0.26-2.67)</td>
<td>0.77</td>
</tr>
<tr>
<td>DSA category (vs. negative DSAs)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DSA MFI &lt;500</td>
<td>1.81 (0.56-5.23)</td>
<td>0.47</td>
</tr>
<tr>
<td>DSA MFI &gt;5000 10000</td>
<td>8.16 (1.35-5.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Induction II (ATG vs. Basilime)</td>
<td>1.05 (0.45-2.82)</td>
<td>0.56</td>
</tr>
<tr>
<td>FK level (for each 1 mg/l)</td>
<td>0.99 (0.71-1.31)</td>
<td>0.87</td>
</tr>
<tr>
<td>Micronucleated dose (for each 1 mg/l)</td>
<td>1.00 (0.019-1.019)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

PO2398

Case Series: Systemic Infection Alters Background Cell-Free DNA and Influences Donor-Derived Cell-Free DNA Transplant Rejection Assays

Suphamai Bunnapradist,1 Philippe M. Gauthier,2 Hossein Tabriziani,2 Ryan Swenerton,2 Ebad Ahmed,2 Trudy McKenna,2 Paul R. Billings.2
1University of California Los Angeles, Los Angeles, CA; 2Natera, Inc, San Carlos, CA.

Introduction: Donor-derived cell-free DNA (dd-cfDNA), a biomarker for kidney transplant rejection, (1,2) is reported as a percentage of background cfDNA. Various factors affect total cfDNA levels (3,4). We present 3 cases with elevated background cfDNA where dd-cfDNA was assayed for rejection assessment.

Case Description: 1 A 78 year old man with end-stage renal disease (ESRD) underwent a kidney transplant. A biopsy at +6 months (m, all time points relative to transplant date) due to an elevated creatinine level indicated an acute T cell-mediated rejection (TCMR). At +7m, the patient tested positive for BK viremia, and was treated. He was admitted for nephrectomy of his native kidney at +14m and tested positive for herpes and cytomegalovirus (CMV) exophagitis and treated. A cfDNA analysis was negative for rejection with background cfDNA = 10,326 Arbitrary units (AU)/mL (~21X median cfDNA).) Banff chronic active cellular rejection was confirmed from a subsequent biopsy.

2 A 62 year old woman with ESRD who underwent a kidney transplant had a cfDNA assay +3 years, that was reported as a negative result. However, the background was elevated at 3,466 AU/mL (~7X median). She had a biopsy that showed BK virus-associated nephropathy and TCMR. 3 A 53 year old woman with ESRD had a kidney transplant from an ABO incompatible donor. A month later, she was diagnosed with dengue fever followed by acute allograft dysfunction. A biopsy at +6m showed active antibody-mediated rejection (ABMR). On a cfDNA assay at +7m indicated a negative result; however with an elevated background (6344 AU/mL, ~13X median). A biopsy showed resolution of ABMR and borderline acute cellular rejection.


PO2399

Donor-Derived Cell-Free DNA Identifies Patients with Antibody-Mediated Rejection and Strongly Correlates Histologically with Microvascular Inflammation

Bogdan Obrisa,2 Maria Butiu,1 Ramsamy Bakhavatsalum,1 Kelly D. Smith,1 Iris C. De Castro,1 Christopher D. Blosser,1 Lena Sibulesky,1 Catherine Kling,1 Genner Ismail,2 Bogdan M. Sorohan,1 Nicolae Leca,1 University of Washington, Seattle, WA; 2Fundeni Clinical Institute, Bucharest, Romania.

Background: Accurate and timely detection of rejection is central to improving long-term kidney transplant outcomes. We sought to characterize the association of dd-cfDNA level with rejection status and histological lesions.

Methods: We included all patients (n=54) that underwent a kidney transplant biopsy for suspicion of rejection at our center between 9/17-12/19. Concurrent dd-cfDNA and DSA testing was obtained. Rejection type (Banff 2017) and histological lesions were tested for association with dd-cfDNA level.

Results: 18 patients had ABMR (6 mixed ABMR/TCMR), while 12 patients had TCMR alone. Of those with ABMR, 94.4% had a dd-cfDNA level >1%, compared to 16.6% of those with TCMR alone (p<0.001). Of those with a high dd-cfDNA (>1%), 76.2% had both DSA and ABMR. In multivariate logistic regression analysis, a high dd-cfDNA was a more important predictor of ABMR than a DSA MFI level over 2500 (Fig1).

A high dd-cfDNA accurately discriminates ABMR (AUC=0.96; 95%CI, 0.92 to 1.00; p<0.001), with a positive and negative predictive value of 80.9% and 96.9%, respectively. A high dd-cfDNA level showed a strong correlation with microvascular inflammation (Fig2), but not with tubulitis or interstitial inflammation.

Conclusions: Our study confirms the high diagnostic accuracy of dd-cfDNA for ABMR, while the strong association with elementary lesions of microvascular inflammation supports the specificity of this test for antibody-mediated allograft injury.

Funding: Commercial Support - CareDx, Clinical Revenue Support

The absolute level of dd-cfDNA and its correlation with rejection type and individual pathological lesions

Binary logistic regression analysis regarding variables associated with antibody-mediated rejection

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2400
Impact of Body Mass Index on Baseline Donor-Derived Cell-Free DNA in Kidney Transplant Recipients

Background: Donor derived cell free DNA (dd-cfDNA) is useful in predicting acute rejection in renal allografts. The technology uses next generation sequencing and does not require donor genotyping. dd-cfDNA is expressed as a percentage of the total (including self and non-self) circulating DNA fragments. Since self-portion of cell free DNA can vary according to body size, we aimed to test the hypothesis that expressed percent of baseline dd-cfDNA can vary by the recipient’s body mass index (BMI).

Methods: Our center has been doing for cause as well as surveillance (for high immunologic risk) dd-cfDNA in kidney transplant recipients (KTRs) using AlloSure (CareDx, Brisbane, CA). We identified patients who underwent kidney transplantation between September 2017 and June 2019 and had serial dd-cfDNA levels. A dd-cfDNA value ≥1% prompted allograft biopsy. KTR with biopsy evidence for rejection or other injuries were excluded from the analysis. Study subjects were divided into BMI (kg/m²) groups as follow: <25, 25-29.9, ≥30. Baseline dd-cfDNA values were compared between BMI groups.

Results: There were 88 (81 first-time and 7 repeat) KTRs during the study period who had dd-cfDNA measurements and available BMI. We excluded 16 first-time and 3 repeat KTRs from the analysis due to biopsy evidence of rejection. The remaining 69 patients had 227 dd-cfDNA levels available for analysis. Patients were divided based on BMI categories with stratification of baseline dd-cfDNA values as shown in table 1. There were no significant differences in baseline dd-cfDNA values for BMI groups <25 vs. 25-29.9 (0.63 ± 0.63% vs. 0.41±0.27% p=0.16) and BMI groups 25-29.9 vs. ≥30 (0.41±0.27% vs. 0.33±0.16%, p = 0.22). However, there was a trend towards significantly higher baseline dd-cfDNA values in BMI group <25 vs. ≥30 (0.63±0.63% vs. 0.33±0.16%, p=0.06).

Conclusions: Our study showed a trend towards significant differences in dd-cfDNA values between extremes of BMI groups. These differences could become significant with larger study subjects. Our findings point towards the need for normalization of dd-cfDNA values with respect to body size for reporting purposes.

Table 1. BMI and dd-cfDNA

<table>
<thead>
<tr>
<th>BMI category</th>
<th>Number of patients</th>
<th>dd-cfDNA % (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>19</td>
<td>0.03±0.0</td>
</tr>
<tr>
<td>25-29.9</td>
<td>75</td>
<td>0.63±0.63</td>
</tr>
<tr>
<td>≥30</td>
<td>15</td>
<td>0.33±0.16</td>
</tr>
</tbody>
</table>

PO2401
Protocol-Based Donor-Derived Cell-Free DNA Surveillance in Kidney Transplant Recipients: A Single-Center Experience
Pichanach Tirirawongsakorn, Het Patel, Martha Pavlakis, Amtul Aala, Nikhil Agrawal. Beth Israel Deaconess Medical Center, Boston, MA.

Background: Kidney biopsy is invasive and has limited utility when used as a surveillance test post-transplant. Donor-derived cell-free DNA (dd-cfDNA) surveillance testing has never been studied in comparison with other routinely performed surveillance tests.

Methods: Our transplant center implemented the dd-cfDNA (AlloSure) surveillance program (1,2,3,4,6 months and then quarterly post-op) in kidney transplant recipients starting July 2018, in addition to our existing protocol measurements of serum Cr, proteinuria and DSA. We retrospectively reviewed all kidney alone transplant recipients starting July 2018 through June 2019 at our center. Donors were classified using AKN criteria for AKI based on increase of terminal serum creatinine (Scr) over initial Scr. Death-censored graft survival and eGFR (MDRD) were compared.

Results: 911 recipients received kidneys from donors with no AKI (Stage 0). 208 (18.6%) received kidneys from donors with AKI. AKI 45 (4.02%) had Stage 1 AKI, 59 (5.27%) had Stage 2 AKI, and 104 (9.29%) had Stage 3 AKI. There were no significant differences between the AKI and non-AKI groups in recipient age, gender, ethnicity, or Estimated Post-Transplant Survival score. Using a Cox Proportional Hazards Model, death-censored graft survival at 1 year was not distinguishable between recipients whose donor had any stage of AKI versus donors without AKI (HR 0.94, p=0.854) nor among AKI stages (Figure 1). Mean eGFR by MDRD formula for recipients alive and with followup at 1 year was 60.0 (SD 23.2) in recipients with non-AKI donors and 61.9 (SD 26.1) in recipients with AKI donors, which was of no statistical significance (p=0.4384).

The rate of delayed graft function was significantly higher in recipients from AKI donors (62.0%) versus non-AKI donors (31.5%), p<0.0001.

Conclusions: Recipients of AKI donors did not yield inferior outcomes to those of non-AKI donors at 1 year. Increased DGF can be anticipated, but does not appear to have any lasting impact on graft survival or renal function. As such, transplant centers should consider expanding the use of these kidneys for any waitlisted candidate.

Funding: Clinical Revenue Support

PO2402
Successful Transplantation Outcomes Using Deceased Donors with AKI

Background: Kidneys from deceased donors with acute kidney injury (AKI) are discarded at a higher rate than those without AKI, exacerbating the organ shortage. This paper reviews outcomes of kidneys from deceased donors with AKI over a four-year period at a single transplant center.

Methods: We analyzed 1119 consecutive deceased donor kidney adult recipients transplanted from 2016 through 2019 at our center. Donors were classified using AKN criteria for AKI based on increase of terminal serum creatinine (Scr) over initial Scr. Death-censored graft survival and eGFR (MDRD) were compared.

Results: 911 recipients received kidneys from donors with no AKI (Stage 0). 208 (18.6%) received kidneys from donors with AKI. AKI 45 (4.02%) had Stage 1 AKI, 59 (5.27%) had Stage 2 AKI, and 104 (9.29%) had Stage 3 AKI. There were no significant differences between the AKI and non-AKI groups in recipient age, gender, ethnicity, or Estimated Post-Transplant Survival score. Using a Cox Proportional Hazards Model, death-censored graft survival at 1 year was not distinguishable between recipients whose donor had any stage of AKI versus donors without AKI (HR 0.94, p=0.854) nor among AKI stages (Figure 1). Mean eGFR by MDRD formula for recipients alive and with followup at 1 year was 60.0 (SD 23.2) in recipients with non-AKI donors and 61.9 (SD 26.1) in recipients with AKI donors, which was of no statistical significance (p=0.4384).

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Conclusions: Recipients of AKI donors did not yield inferior outcomes to those of non-AKI donors at 1 year. Increased DGF can be anticipated, but does not appear to have any lasting impact on graft survival or renal function. As such, transplant centers should consider expanding the use of these kidneys for any waitlisted candidate.

Funding: Clinical Revenue Support

PO2403
Combined Impact of Presensitization and Delayed Graft Function on Allograft Outcome in Deceased Donor Kidney Transplantation: Nationwide Cohort Study
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Background: Pre-sensitization to HLA has detrimental effect on allograft rejection, worse allograft function and survival. Delayed graft function (DGF) is associated with poor allograft outcome by ischemia-perfusion injury. We undertook analysis to determine combined association of presensitization to HLA and DGF on allograft outcome in deceased donor kidney transplantation (DDKT) and whether there is a synergistic effect.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Clinical and Immunologic Predictors of Post-Transplant Outcomes

PO2404

The Clinical Significance of Preformed C1q-Binding Donor-Specific HLA Antibodies in Kidney Transplantation

Sun Lee, Byung Ha Chung, Chul Woo Yang. Seoul National University Hospital, Jongno-gu, Seoul, Republic of Korea; Catholic University of Korea, Seoul, Republic of Korea.

Background: The anti-human leukocyte antigen (HLA) antibodies are well known for risk factor of rejection or allograft loss in kidney transplantation (KT). De novo complement component 1q-binding donor-specific anti-HLA antibodies (C1q-binding DSAs) are already reported to be associated with an increased risk of acute allograft rejection in KT. This study investigated the clinical significance of identification of preformed C1q-binding DSAs for predicting graft outcomes in KT.

Methods: From December 2016 to December 2018, 323 recipients underwent KT at Seoul St. Mary’s Hospital. If the results of panel reactive antibodies (PRA) were positive in the pre-transplant examination, DSAs and C1q-binding DSAs were performed using Luminex Single Antigen Bead Assay (SAB) at the same time. Graft outcomes in term as Chronic Kidney Disease-Epidemiology Collaboration estimated Glomerular Filtration Rate, biopsy proven acute rejection and graft survival were compared between recipients with preformed C1q-binding DSAs and recipients without preformed C1q-binding DSAs.

Results: Eighty-two of 323 recipients (25.4%) were evaluated DSAs and C1q-binding DSAs before transplantation. Among them, 40 recipients (48.8%) had preformed DSAs and 8 recipients (9.9%) had preformed C1q-binding DSAs. The higher MFI values of DSAs had higher prevalence of C1q-binding DSAs (9263.9 ± 3670.3 vs. 5955.3 ± 5245.5; p < 0.050). There was a strong correlation between the presence of DSAs against Class II and C1q-binding DSAs (p = 0.007; CI 95%, OR 3.403). Five of 21 patients (23.8%) with positive at least one of complement-dependent cytotoxicity (CDC) or flow cytometry crossmatch (FCXM) had preformed C1q-binding DSAs. There was a strong correlation between positivity of crossmatch and preformed C1q-binding DSAs (p = 0.024; CI 95%, OR 6.042). Four of 8 recipients (50%) in C1q-binding DSAs(+) group were confirmed acute antibody mediated rejection. C1q-binding DSAs(+) group had higher incidence of acute antibody mediated rejection than C1q-binding DSAs(-) group (p=0.048; CI 95%, OR 4.286).

Conclusions: The identification of preformed C1q-binding DSAs may be important in predicting acute antibody mediated rejection. Therefore, the surveillance such as protocol allograft biopsy is required for early detection of acute antibody mediated rejection after transplantation in patients with preformed C1q-binding DSAs.

PO2405

Potential Combined Use of Kidney Donor Profile Index (KDPI) and Estimated Post-Transplant Survival (EPTS) Scales to Predict eGFR Decline in Deceased Donor Kidneys

Pablo Magrini, Sergio Hernández-Estrada, Odette Del Carmen Díaz Avendaño, Christian P. Flores, Benjamin Gomez-Navarro, María Guadalupe R. Ramírez, Jose H. Cano, Maria Concepcion Osegueda-Vizcaíno, Daniel F. Ovando-Morga, Mayra M. Matias Carmona. Renal Transplant Unit, National Medical Center “20 de Noviembre”, Mexico City, Mexico; Renal Transplant Unit, Hospital Civil de Guadalajara Fray Antonio Alatorre, Guadalajara, Jalisco, Mexico; Centro Medico Nacional de Occidente, Guadalajara, Jalisco, Mexico.

Background: Utility of the sum of EPTS and KDPI scales to predict the decline of eGFR in patients who received a cadaveric donor kidney transplant. Assess the reproducibility of the Organ Assignment System of the USA in our country.

Methods: In our prospective cohort study, between May 2014 and June 2019, 139 deceased donor kidney transplant patients were assigned into 2 groups; pre-sensitized and non-pre-sensitized. Each group was divided into 2 subgroups according to DGF. Pre-sensitization was defined as the presence of donor specific antibodies (DSA) or the presence of panel-reactive antibody (PRA), combination with crossmatch positive. DGF was defined as the need for dialysis before discharge. We compared the clinical outcomes including allograft rejection, the change of allograft function, infectious and cardiovascular complication and allograft survival.

Results: Pre-sensitization group was 137 (10.0%) patients and others (n=233, 90.0%) belonged to non-sensitized group. Pre-sensitization-DGF subgroup was 21 (15.3%) and pre-sensitization-non-DGF group was 116 (84.7%). Non-pre-sensitization-DGF subgroup was 133 (9.7%) and non-pre-sensitization-non-DGF group was 1100 (80.3%). In both pre-sensitization and non-pre-sensitization groups, allograft function using eGFR by CKD-EPI equation (mL/min/1.73m²) was lower in DGF subgroup than non-DGF subgroup. In contrast, allograft rejection rate showed no significant difference between DGF and non-DGF subgroup within non-pre-sensitization group (15.0% vs 12.9%, p=0.493). There was no significant difference between DGF and non-DGF subgroups in both groups in regard to allograft survival and patient survival.

Conclusions: DGF combined with pre-sensitization had much worse effect on allograft outcome in terms of allograft rejection. Therefore, we suggest more careful monitoring or surveillance for allograft rejection when DGF occurred in DDKT with pre-sensitization.

PO2406

Vasopressin Use After Deceased Donor Kidney Transplant (DDKT): Patient Characteristics, Graft Function, and Clinical Outcomes

Muhammad Y. Jan, William Goggins, Muhammad S. Yaqub, Tim E. Taber, Dennis P. Mishler, Sharon M. Moe, Ranjani N. Moothi, Michael T. Eadon, Jeanne Chen, Asif A. Shafriuddin. Indiana University School of Medicine, Indianapolis, IN.

Background: Vasopressin (AVP) is used for maintenance of volume status and hemodynamics due to its vasopressor activity with less arrhythmogenic and ischemic potential. It has catecholamine sparing effect. AVP has been shown to improve rates of deceased organ donation. We studied AVP use post DDKT for improving hemodynamics with resultant effect on graft function and clinical course.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

730
PO2407
Differences in Urinary Inflammatory Profiles in Donor-Recipient Pairs
Elizabeth Spiwak, Corina Nailescu, Andrew L. Schwaderer. Riley Hospital for Children at Indiana University Health, Indianapolis, IN

Background: Renal transplant is the most common type of transplant performed in the US. Immunosuppressants are used in transplant recipients to prevent rejection. Kidney transplant recipients are at a higher risk for infection in the pre- and post-transplant state. Urine inflammatory profiles may lend insight to this balance between infection and rejection. Since donor and recipient urine is generated by genetically identical kidneys, it represents an ideal bio-sample for paired analysis.

Methods: Urine samples were obtained from stable children > 2 months post-transplant along with their donors (n=6) and another 8 recipient-donor-recipient pairs (adult and children) that were collected for longitudinal samples; of which a pretransplant sample has been obtained. Using the V_PLEX Human Cytokine Panel (Mesoscale Discovery, Rockville MD) urine inflammatory mediators were quantified. The paired sample has been obtained. Using the V_PLEX Human Cytokine Panel (Mesoscale Discovery, Rockville MD) urine inflammatory mediators were quantified. The paired sample has been obtained. The V_PLEX Human Cytokine Panel (Mesoscale Discovery, Rockville MD) urine inflammatory mediators were quantified. The paired sample has been obtained.

Results: Interleukin (IL)7, IL15, Monocyte chemotactic protein-1 (MCP-1) and Granulocyte-macrophage colony-stimulating factor (GM-CSF) were higher in the pediatric post-transplant recipients compared to their donors P values of 0.017, 0.037, 0.046 and 0.031 respectively. IL-9 was higher in recipient urine in pre-transplant patients (p=0.004) compared to donors.

Conclusions: Transplant patients have an elevated urine inflammatory mediator profile. Pretransplant patients have elevated IL-9 compared to their donors. Reasons for this altered inflammatory profile include immunologic, hemodynamic or physiologic changes intrinsic to the transplant procedure versus medications used to manage transplant patients.

Funding: NIDDK Support

PO2408
LIMS1 Gene Mismatching and Risk of Rejection in Kidney Transplant Recipients
Yasar Caliskan,1 Safak Mirioglu,2 Halil Yazici,2 Ahmet B. Dirim,2 Erol Demir,2 Ozgur A. Oto,2 John C. Edwards,1 Rosemary Ousoph,1 Aydin Turkmen,2 Krista L. Lentine,1 'Saint Louis University, Saint Louis, MO; 'Istanbul University, Istanbul, Turkey.

Background: Recent advances in precipitation medicine have provided new insights into the pathogenesis of kidney transplant (KxT) rejection such as the potential role of genetic risk variants in LIM Zinc Finger Domain Containing 1 (LIMS1). We aimed to evaluate the relationship between donor and recipient LIMS1 genotype matching status and allograft rejection and survival.

Methods: We genotyped 41 prevalent living KxT recipient [24 (59%) males; mean age 34 ± 13 years] and donor [15 (37%) males; mean age 47 ± 13 years] pairs for LIMS1 rs893403 variant by Sanger sequencing in order to assess their impact on rejection and survival. The recipients homozygous for LIMS1 rs893403 GG genotype which tags a common 1.5-kb deletion (CNVR915.1) received a transplant from a nonhomozygous donor were defined as risk mismatched. CNVR915.1 deletion is confirmed by PCR in recipients with rs893403-AG and GG genotypes. Rejections were defined as T-cell mediated (TCMR) or antibody mediated rejection (ABMR) defined by Banff 2013 criteria. Outcomes were abstracted by review of medical records.

Results: There were no differences between recipients with risk LIMS1 mismatching (n=5) and recipients without risk LIMS1 mismatching (n=36) regarding demographic factors, duration of dialysis, pretransplant PRA, HLA mismatching, immunosuppressive protocols and follow up time. After a median post-KTx follow up of 10.5 (IQR 8.7-12.6) years recipients with risk LIMS1 mismatching had significantly higher risk of allograft rejection (60%; median 1 month) compared to recipients without risk LIMS1 mismatching (13.9%; median 72 months) (HR=4.32, 95CI% 1.46-12.76, p=0.015). TCMR was higher in recipients with risk LIMS1 mismatching (40%) compared to recipients without risk LIMS1 mismatching (11.1%) (p=0.087). There were no significant differences found between patients with and without risk LIMS1 mismatching regarding risk of post-KTx DSA, ABMR and allograft failure. The mean eGFR levels at last follow up were also similar among recipients with and without risk LIMS1 mismatching.

Conclusions: Genomic mismatching at LIMS1 gene appears to impact risk of TCMR. LIMS1 may be a potential minor histocompatibility antigen and pre-transplant genetic testing may have clinical implications for the prediction and clinical management of KxT rejection.

Funding: Private Foundation Support
PO2409

Monitoring of Gene Expression in Tacrolimus-Treated De Novo Renal Allograft Recipients Facilitates Individualized Immunosuppression: Results of the IMAGEN Study

Claudia Sommerer,1 Merce Brunet,2 Klemens Budde,3 Olga Millan,2 Lluís Guirado,4 Petra Glander,5 Stefan Meuer,6 Martin G. Zeiër,7 Thomas Giese.8 1Nephrology, University Hospital Heidelberg, Heidelberg, Germany; 2Pharmacology and Toxicology Laboratory, Barcelona, Spain; 3Nephrology, University Hospital Charité, Berlin, Germany; 4Renal Transplant Unit, Nephrology Department, Fundació Puigvert Barcelona, Barcelona, Spain; 5Immunology, University Hospital Heidelberg, Heidelberg, Germany.

Background: The expression of nuclear factor of activated T-cells (NFAT)-regulated genes in the peripheral blood has been suggested as a potentially useful immune monitoring tool to individualize tacrolimus (Tac) therapy. The aim of the present study was to characterize the possibility and clinical utility of monitoring of residual NFAT-regulated gene expression in renal allograft recipients in a multicenter approach.

Methods: The IMAGEN study enrolled 64 de novo renal transplant recipients from three European centers. All patients were treated with Tac, mycophenolic acid, and corticosteroids. NFAT-regulated gene expression (NFAT-RGE; IL-2, IFN-g, GM-CSF) was evaluated by quantitative real-time PCR in whole blood samples at day 7, month 1, 2, 3, and 6 after transplantation.

Results: Altogether, 60 patients could be evaluated. Tac concentrations (0 and C1.5 [pg/ml]) correlated inversely with gene expression (p<0.001). NFAT-RGE showed a high interindividual variability (1 to 61%). RGE increased in the first two months from 164±9 to 34±21%. Patients (n=20) with high residual gene expression (NFAT-RGE>30%) were at the increased risk of acute rejection in the following months (35% vs 5%, p=0.002), whereas patients (n=40) with low residual gene expression (NFAT-RGE<30%) showed a higher incidence of viral complications, especially cytomegalovirus and BK virus replication (52.5% vs 10%, p=0.001).

Conclusions: NFAT-RGE was confirmed as a potential non-invasive early predictive pharmacodynamic marker in the immediate post-transplant period for the risk of acute rejection and infections complications in Tac-treated renal allograft recipients. Monitoring of NFAT-RGE may provide additional useful information for physicians to achieve individualized treatment adjustments based on the immunomodulatory effect of Tac, thus preventing serious clinical events. The method of NFAT-RGE measurements can be applied in trials with multicenter approach.

PO2410

The Role and Inducers of Nonclassical HLA-G in Renal Transplanted Allografts

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Background: Non-classical class I molecule HLA-G has a high potential to modulate immune response. However, the mechanism of HLA-G induction was still unknown. In this background, expression of HLA-G on proximal tubular epithelial cells (pTECs) and the inducer of HLA-G were investigated.

Methods: Our subjects comprised 40 adult Japanese subjects whose allograft had survived for at least 1 year (35 patients from a living donor, 5 patients from a deceased donor). They were evaluated for HLA-G1/5 expression using an immunofluorescence method. We investigated inducer of HLA-G using primary cultured human pTECs treated with cytokines and immunosuppressants.

Results: In renal biopsy tissues, 2 to 4 weeks or 1 year following the transplantation, HLA-G expression was noted in the peritubular region or on the basement membrane side of pTECs in 12 of 40 cases (30 %). Further, for median 8.8 years, the time taken for a 30 % reduction in eGFR was longer in the HLA-G-positive group than in the HLA-G-negative group (p=0.016, Figure). HLA-G1/5 expression on pTECs was also found to be an independent predictor of the improvement in renal allograft function by Cox’s proportional hazard model (p=0.030). In vitro study, interferon-beta (INF-β) was the strongest inducer of HLA-G expression, while immunosuppressants (everolimus, tacrolimus, cyclosporin, and dexamethasone) did not induce expression.

Conclusions: The study showed that HLA-G1/5 expression on pTECs was an independent improving predictor of renal allograft. Furthermore, the strongest HLA-G1/5 inducer was INF-β, but not the immunosuppressive agents. These results suggested the possibility that acquired expression of HLA-G exhibits a long-term renal preservation effect, different from the effect of immunosuppressants.

PO2411

The Clinical Impact of Preformed HLA-DQ Donor-Specific Antibodies on Graft Outcomes in Kidney Transplantation

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Background: De-novo HLA-DQ donor-specific antibody (DSA) has been identified as a risk factor for graft rejection and loss in kidney transplantation (KT). Recently, the impact of preformed HLA-DQA DSA has been discussed. This study aimed to investigate the clinical impact of preformed HLA-DQA DSA on graft outcomes.

Methods: We evaluated 990 recipients who underwent kidney transplantation at Seoul St. Mary’s Hospital from January 2010 to July 2019. According to the result of DSA using luminex single antigen bead assay, recipients were classified as no DSA, only DQ, non-DQ, and DQ + non-DQ. Primary outcomes were the incidence of biopsy-proven acute rejection and the rate of death-censored graft loss.

Results: In total cohort, 611 recipients (61.7%) and 379 recipients (38.3%) underwent living-donor KT and deceased-donor KT, respectively. Recipients were classified as no DSA (909 recipients, 91.8%), only DQ (18 recipients, 1.8 %), non-DQ (57 recipients, 6.3%), and DQ + non-DQ (6 recipients, 0.7%). The overall incidence of acute rejection and acute antibody-mediated rejection (AMR) were 20.3% and 7.5%. Only DQ, non-DQ, and DQ + non-DQ group had significantly higher the incidence of acute AMR compared to no DSA group (p < 0.05, respectively). There was no significant difference in the incidence of acute AMR between sensitized groups. There was no difference in the rate of death-censored graft loss between groups. In univariate Cox regression analysis, all of 3 groups with DSA were associated with high risk of acute AMR (Only DQ; HR 5.051; CI 95%, p = 0.002, non-DQ; HR 6.005; CI 95%, p < 0.001, DQ + non-DQ; HR 7.748; CI 95%, p = 0.005, respectively). HLA-DQA DSA and other DSAs (HLA-A, HLA-B, HLA-C) had a tendency to interact with acute AMR, although no statistical significance (p = 0.05).

Conclusions: Preformed HLA-DQA DSA is associated with the development of acute rejection, especially acute AMR. Therefore, the identification of preformed HLA-DQA DSA may be necessary to improve graft outcomes.

PO2412

Outcomes of High Kidney Donor Profile Index Kidneys at a Large Center


Background: Kidneys from donors with high Kidney Donor Profile Index (KDPI) are often discarded due to concerns about outcomes. Despite decreased survival, the survival benefit of receiving a transplant and avoiding time on dialysis is beneficial, especially for selected patients.

Methods: We increased use of high KDPI (KDPI>85) deceased donor kidneys (DDK) over several years. We performed a single-center analysis of 1119 consecutive adult DDKT from 2016-2019. Our endpoints were Kaplan-Meier death-censored survival.

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PO2414

Gluomeral Blood Flow in Living Donor Kidney Transplant Recipients
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Background: Renal graft hemodynamics may be a valuable predictor of graft survival and long-term outcomes. Although several studies have reported that renal blood flow was correlated with graft function and decreased remarkably during acute rejection episode, the glomerular hemodynamic changes during kidney transplantation are lacking because there is no method of measuring neaphron number in vivo. In this study, we calculate glomerular blood flow (GBF) by estimating the nephron number and investigate changes in GBF after kidney transplantation and their clinicopathological relationship.

Methods: We performed a retrospective analysis of 42 patients who underwent living donor kidney transplantation. The number of glomeruli (Ngлом) was calculated as the cortical volume of both kidneys as assessed on computed tomography times the 1-hour posttransplant renal biopsy-determined glomerular density. Effective renal plasma flow (ERPF) was assessed as 99mTc-MAG3 clearance. GBF was calculated as follows: GBF (nl/min) = ERPF/Nглом/(1-hematocrit/100) x10 317.4 nl/min.

Results: Prior to transplantation, the GBF in donors was 559.7±257.3 nl/min, whereas the GBF in recipients on day 2 post-transplantation was decreased to 502.6±317.4 nl/min. After successful transplantation, the GBF one-month post-transplantation has settled down to 491.9±291.1 nl/min, while the eGFR progressively rose (48.7±18.4 ml/min/1.73m²) together with the hematocrit (31.1±3.9 %). The GBF at one month was positively associated with eGFR at one month (p<0.05). Of note, the GBF ratio was correlated with the eGFR and urinary protein excretion at one month and urinary protein excretion at one year but was not correlated with eGFR at 1 yr.

Conclusions: We first reported the GBF in kidney transplant recipients before and after kidney transplantation. Our findings suggest that abnormal change in GBF may be considered predictive indices for short-term allograft outcomes.

PO2415

Characteristics of Anonymous Living Donors and Their Recipients and Outcomes: Appropriate Use of a Rare and Valuable Gift
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Background: Anonymous Living Donors are a special select set of donors. We review the trends and the characteristics and utilization of such donors nationally.

Methods: All Living Donors (code=10 “Anonymous”) and their recipients who were recorded in the UNOS database from Oct 1997 through Sep 2017 were reviewed for demographics and recipient outcomes.

Results: There were a total of 2286 such donors during the study period. There was an increasing trend of the donors over the time period. Demographics and Outcomes are shown in the Table. DCGS was significantly superior when donor was 20 years or more younger than the Recipient (p<0.019) and significantly inferior when the 20 years older than the recipient (p=0.065). There was no difference in cumulative graft survival between adult and pediatric graft survival (p=0.055), although DCGS was superior in the adults (p=0.021).

Conclusions: To our knowledge, this is the first comprehensive report on the characteristics of Anonymous Living Kidney Donors and their Recipients and outcomes. Better characteristics matching in a minority of such transplants may improve further longevity from such donors.

Donor, Recipient and Transplant Characteristics

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2416
Outcomes of Delayed Graft Function: A Systematic Review and Meta-Analysis
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Background: Delayed Graft Function (DGF) is a frequent complication of kidney transplantation, but its impact on long and short-term outcomes remain uncertain.
Methods: We conducted a literature search for studies investigating the association of DGF on subsequent outcomes from 2007-2020. Outcomes were abstracted and used to create cumulative forest plots with pooled odds ratios, stratifying our analysis between center-studies and registry-studies and follow-up time where possible. The outcomes analyzed were graft failure (GF), acute rejection (AR), patient survival, and renal function.
Results: Of the 1464 articles reviewed, 27 were included. In single center-studies, DGF patients experienced higher GF at 1 year (OR 2.45, 95% CI 1.79-4.29, p<0.001), 3 years (OR 1.70, 95% CI 1.01-2.86, p=0.001), increased AR 1-year post-transplant (OR 1.48, 95% CI 1.79-4.28, p=0.001), and decreased 1-year patient survival (OR 0.46, 95% CI 0.28-0.73, p<0.001). Registry-studies showed a similar significant association with GF at 1 year (OR 2.76, 95% CI 1.79-4.28, p<0.001) and 3 years (OR 1.70, 95% CI 1.01-2.86, p=0.046), with AR within 1 year (OR 1.48, 95% CI 1.45-8.67, p<0.005) and 3-years (OR 0.54, 95% CI 0.41-0.72, p<0.001), and 1-year survival (OR 0.45, 95% CI 0.26, 0.77, p<0.001). Qualitative analysis showed that DGF had significant effect on eGFR and creatinine levels, though studies conflict on timeframe. Few studies investigated outcomes stratifying DGF severity or KDPI.
Conclusions: DGF was associated with increased risk of GF, AR, and mortality, although effects were largest within 1 year post-transplant. Our analysis indicated a need for a standardized method to measure DGF severity and further studies on DGF outcomes on varying KDPI. These results should inform the selection process, treatment, and monitoring of transplanted kidneys at high risk for DGF.

PO2417
Duration of Delayed Graft Function Predicts Kidney Allograft Function and Survival
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Background: The current study evaluated the duration of DGF as a measure of severity of ischemic injury to kidney transplant outcome.
Methods: This single center study evaluated DD kidney transplant recipients with DGF between Jan 2014 and Dec 2019. DGF was defined as the need for dialysis within 7 days post-transplant & were divided into three groups according to post transplant dialysis duration. Group I: dialysis ≤7 days, Group II: dialysis 8-14 days and Group III: dialysis >14 days. All primary & repeat adult kidney recipients of DD transplants were included. We excluded multiorgan recipients and pediatric en-bloc kidneys. We calculated eGFR over time using CKD EPI formula. Statistical analysis was performed to identify differences in variables, Linear Mixed Model for eGFR over time. Log-rank test was used to evaluate differences in graft & patient survival & composite end point (graft loss, patient loss & GFR, 20ml/min) for all 3 subgroups.
Results: A total of 132 DD KT recipients with DGF were identified: Group I: n=84 (64%), Group II: n=24 (18%) & Group III: n=24 (18%). The recipient/donor demographics and Donor (KDPI) & Transplant variables were similar across groups. Figure 1(left) shows significantly lower eGFR values over time using linear mixed model among patients who needed dialysis for >14 days (Gr III vs I&II, P=0.006). Table 1 shows the incidence of Isolated Graft Loss, Patient death and combination of graft loss & patient death among 3 groups. Figure 1(right) shows significantly lower composite end point (combination of patient loss, graft loss and impending graft loss) for among patients who needed dialysis for >14 days (P=0.0002).
Conclusions: In conclusion, we found a strong association between prolonged DGF>14 days with lower GFR values and survival outcomes. No differences in eGFR or survival rates were noted among patients with DGF patients <7 days vs 7-14 days.
Funding: Clinical Revenue Support

PO2418
Design of the Graft Improvement Following Transplant (GIFT) Trial, a Phase 3 Study of ANG-3777 in Kidney Transplantation Patients with Delayed Graft Function
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Background: Patients after kidney transplantation can experience acute kidney injury (AKI) resulting in delayed graft function (DGF). The Food and Drug Administration has prioritized the development of new treatments for DGF. A Phase 2 trial demonstrated that treatment with ANG-3777, a hepatocyte growth factor (HGF) mimic, improved renal function up to 12-months in patients with signs of DGF.
Methods: Objective: To describe the GIFT trial (Study 001-15), designed to evaluate the efficacy and safety of ANG-3777 in renal transplantation patients with signs of DGF.
Results: GIFT is a Phase 3, multicenter, prospective, randomized, placebo-controlled, study enrolling patients who have undergone a kidney transplantation with a deceased donor kidney who exhibit signs of DGF (producing a mean of <50cc urine per hour over 8 hours in the first 24-hours post-transplantation). Patients are randomized 1:1 to ANG-3777 (2 mg/kg) or placebo administered intravenously once daily for 3 consecutive days starting within 30 hours after transplantation. The primary endpoint is estimated glomerular filtration rate (eGFR) at 12 months. Secondary endpoints include proportion of subjects with eGFR > 30 mL/min/1.73m2 at days 30, 90, 180 and 360; proportion of subjects whose graft function is slow, delayed or primary non-function; length of hospitalization; duration of dialysis through day 30. A study schematic is shown in Figure 1. Adverse events are being assessed throughout the study.
Conclusions: No pharmacologic intervention has been demonstrated in a rigorous trial to be effective preventing or improving the outcome of DGF. The GIFT study will generate data that are critical to advancing the treatment of DGF.

PO2419

Clinical Outcomes of Kidney Transplant Recipients Living Away from Their Home Country


Background: Many people leave their home country looking for better job opportunities and among those are kidney transplant recipients. However, taking care of such recipients might be challenging especially when information regarding induction immunosuppression, donor HLA typing, donor-specific antibodies, crossmatch and/or infections are not available. The aim of this study was to compare clinical outcomes of kidney recipients transplanted in their home country with kidney recipients transplanted locally.

Methods: In this retrospective cohort, we included all adult recipients transplanted between 2005 and 2016 and followed at our transplant clinics within their first year of transplant. Patients were categorized into two groups; local group including recipients transplanted at our center and abroad group including recipients transplanted in their home country.

Results: There were 111 patients in local group and 110 patients in abroad group. The mean age at transplant in local and abroad groups were 48 and 42 year-old, respectively. 63% of recipients in local group were from the Middle East, while 53% of patients transplanted abroad were from South Asia. Deceased donation was higher in local group (41% vs. 3%; p<0.001). There was no difference in recipient sex, native kidney disease, presence or absence of neoplasms, or neoplastic transplants. Most patients were on CNIs and steroid immunosuppression (n=209; 95%). The mean follow up post transplantation was 6.3 years. The risk of acute cellular rejection was statistically significant in abroad group (13% vs 3%; p=0.005). However, the risk of ABMR or borderline rejections were similar. The incidence of post-transplant diabetes and malignancies were similar in both groups. There was no difference in 1-, 3- and 5-year creatinine and proteinuria between both groups. Patient and graft survival rates were excellent in both groups and 5-year patient and death-censored graft survival rates in local and abroad groups were 100% vs 93% and 95.2% vs. 96.6%, respectively.

Conclusions: Transition of care between countries carries its risks as it may be related to drug disruption or incomplete medical record. Kidney recipients transplanted abroad are at increased risk of acute cellular rejection; however, patient and graft survival rates remain excellent.

PO2420

Factors Associated with the Use of Hypothermic Machine Perfusion in Kidney Transplant Recipients

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Background: Delayed graft function (DGF) is associated with an increased risk of graft loss. The use of cold hypothermic machine perfusion (HMP) has been shown to reduce the incidence of DGF in kidney transplant recipients (KTRs), especially when extended-criteria donors (ECDs) are used. However, there is a paucity of data on the determinants of HMP use in real-life setting.

Methods: We aimed to determine the factors associated with the use of HMP in a cohort of donors and KTRs. We collected data on consecutive brain-dead donors admitted to our organ procurement organization and their KTRs between June 2013 and December 2018 in 5 adult transplant centers in Canada. There is no standardized protocol for the use of HMP in the province of Quebec. The use of HMP is left at the discretion of the surgeon recovering organs. However, a HMP device was available for organ recovered at the organ procurement organization. Generalized estimating equations were used to predict the use of HMP.

Results: The cohort included 159 deceased donors and their 281 KTRs. Thirty-three percent of donors were ECDs, and 59% of KTRs received organs placed on HMP. The mean cold ischemia time (CIT) was 12.4 (IQR 7.9-22) hours. There was no difference in use of HMP over time. In univariate analysis, none of the donors’ characteristics were associated with the use of HMP. The use of HMP was similar in ECD and standard criteria donors (33% vs 34%, p=0.82). For KTRs, in univariate analysis, race (non-Caucasian), cold ischemia time, use of basiliximab/alemtuzumab, and KTR center were associated with the use of HMP. In multivariate analysis, CIT (odds ratio [OR] 1.09, 95% confidence interval [CI] 1.03-1.16) and KTR center were significantly associated with use of HMP.

Conclusions: We found that use of HMP was strongly associated with the transplant center in which the surgeon practiced, suggesting that practice preference/training plays an important role in determining the use of HMP. The presence of ECD did not influence the use of HMP. The reasons underlying the differences in practice between centers should be explored in further studies.

Funding: Government Support - Non-U.S.

PO2421

Microvascular Inflammation Is the Main Determinant of Elevated Donor-Derived Cell-Free DNA in Kidney Transplantation

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Background: Microvascular inflammation (Mi) is the main histological lesion for ABMR. Mi may occur separate from other ABMR criteria, early in the injury process, and may not be captured by the current Banff criteria. Donor-derived cell-free DNA (dd-cfDNA) has the potential to identify early allograft injury and supplement the current diagnostic criteria for rejection.

Methods: We included all patients (n=54) who underwent a kidney transplant biopsy for suspicion of rejection at our center from 9/17-12/19. Determinants of a biopsy were renal dysfunction, elevated dd-cfDNA, or presence of DSAs.

Results: Dd-cfDNA correlated strongly with the presence of ABMR, Class II DSA≤2500, and histological lesions of ABMR. The strongest association was with Mi lesions (OR 192.95%CI: 18.6, 1984, p<0.001). Of the 18 patients with Mi, 2 did not meet the criteria for ABMR and had a dd-cfDNA level of 0.32% and 1.9%. All patients with Mi that met the criteria for ABMR had a dd-cfDNA over 1%. There was no association with renal function or histological lesions of tubulitis or interstitial inflammation (Fig 2).

Conclusions: Dd-cfDNA has the potential to identify early allograft injury and allow for early and less aggressive interventions that can benefit allorecipients before long-term outcomes of kidney transplant recipients.

Funding: Commercial Support - CareDx, Clinical Revenue Support

The absolute level of dd-cfDNA and its correlation with rejection type and microvascular inflammation

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Underline represents presenting author.

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PO2422

Point-of-Care Creatinine Self-Testing in Renal Transplant Patients: An Assessment of Accuracy, Precision, and Patient Experience
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Background: During the Covid-19 pandemic it has become increasingly important to provide virtual care for patients with CKD. Point-of-Care testing of capillary creatinine (POC-Cr) is now available and has demonstrated validity, ease of use, improved efficiency and cost-efficiency. We aimed to determine patients’ desire to self-monitoring of POC-Cr and their characteristics.

Methods: Renal transplant patients were shown how to perform self-POC-Cr testing with a NovaBio StatSensor®Xpress device, then undertook a test independently and answered survey questions about their attitude to self-testing of POC-Cr.

Results: All patients (N=189; Median age 52 years (IQR 40,64); 44 (23%) English as a second language; 128 (66%) male; Median eGFR 49 mls/min/1.73m2 (IQR 34,64) successfully performed a POC-Cr test and 110/120 (91%) of patients who completed the survey reported they would like to self-monitor POC-Cr. Most patients wished to reduce their clinic attendance and the majority were willing to have telephone consultations. Characteristics of the cohort are described in Table 1.

Conclusions: All transplant patients successfully performed a POC-Cr test with written instructions and a demonstration. Most patients would like to self-monitor POC-Cr and reduce clinic attendance. Limitations include the single-centre design, number of participants and language barrier. Virtual care including patient self-monitoring using POC-Cr should be explored.

Characteristics of patients who would and would not like to self-monitor POC-Cr at home:

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<th>Would not like to self-monitor POC-Cr</th>
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<td>52 (IQR 40,64)</td>
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PO2424

Defining a Minimal Clinically Meaningful Difference (MCMD) in Estimated Glomerular Filtration Rate (eGFR) for Kidney Transplantation
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Background: eGFR is an established measure of renal function & predicts clinical outcomes. A MCMD for eGFR has never been clearly defined.

Methods: Data source: United Network for Organ Sharing (OPTN) database Study population: Adults ≥18 years of age; received deceased donor kidney 01/01/2013 to 12/31/2018; multi-organ & non-incident transplants were excluded. Analysis: Cox proportional hazards regression Primary outcome: Death-censored graft survival starting 12-months post-transplantation. Predictors: Recipient (gender, age, race, diabetes, body mass index, panel reactive antibodies); Donor (age, diabetes, hypertension, proteinuria); Transplantation (cold ischemia time, pump, DR locus mismatch, delayed graft function); 12-month eGFR (CKD-EPI). Analysis, eGFR was stratified by bands of 5, 7 or 10 mL/ min/1.73m2. Regressions compared each band to the next sequential band. A weighted mean hazard ratio was calculated using OPTN population eGFR distribution.

Results: The relationship between 12-month eGFR & graft failure is non-linear: HR=3 to 4 at eGFR <15 mL/min/1.73m2; HR=1.1 at eGFRs ≥ 55. Mean HR=1.47 for 10 mL/min/1.73m2 bands; 1.30 at 7 mL; 1.19 at 5 mL.

Conclusions: Controlling for multiple factors, 12-month eGFR is a strong predictor of death-censored graft survival. Mean HR (1.19) is consistent with an effect size considered significant, clinically meaningful, & supporting of regulatory approval (eg, angiotensin receptor blockers; statins). This supports 5 mL/min/1.73m2 as the eGFR MCMD in kidney transplantation. DISCLAIMER: The interpretation & reporting of these data are the responsibility of the authors & in no way should be seen as an official policy or interpretation by the OPTN or the US Government.

PO2423

Short-Term Variability in Graft Function Is Associated with Long-Term Mortality but Not Allograft Survival in Kidney Transplant Recipients
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Background: It is critical to identify kidney transplant recipients (KTR) at highest risk of graft failure and death to focus on monitoring and interventions to improve long-term outcomes. Variability in native kidney function is associated with the risk of mortality and hospitalization in chronic kidney disease, but it remains uncertain whether such associations exist in KTR. We examined the hypothesis that short-term graft function variability is associated with long-term outcomes in KTRs.

Methods: Using the Wisconsin Allograft Recipient Database (WisARD), we identified 2919 KTR who had a functioning allograft at least 2 years after transplantation and at least 3 outpatient estimated glomerular filtration rate (eGFR) measurements from 1 to 2 years post-transplant. Graft function variability was defined for each patient as the coefficient of variation based on a linear regression of eGFR from 1 to 2 years. Associations between eGFR variability and total graft loss, death and graft failure were estimated in competing risk models.

Results: Patients with greater variability were more likely to be female, have more comorbidities, and have more prior hospitalization events and have. Compared to the lowest quartile, the highest quartile of eGFR variability was associated with a higher risk of total graft loss (adjusted HR 1.51, 95% CI: 1.11-2.06) and a higher risk of death (adjusted HR 1.85, 95% CI: 1.23-2.76), but not with a higher risk of graft failure (subHR 1.08, 95% CI 0.64-1.83 in competing risk analysis), independent of eGFR and slope of eGFR. The associations remained consistent across strata of acute rejection, diabetes, peripheral arterial disease, baseline eGFR, history of cardiovascular disease, baseline hospitalization, and with all variability indicators and modeling approaches.

Conclusions: Short-term eGFR variability is associated with long-term death but not graft failure. Variability in eGFR provides independent prognostic information on transplantation outcomes and may be an indicator to differentiate the risk of death and graft failure.
PO2425
Composite Events Associated with Increased Expected Post-Transplant Survival Scores
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Background: Kidney transplant candidates on the waiting list are assigned an expected post-transplant survival score (EPS) score. This score is used to determine allocation of kidneys in the kidney allocation system (KAS). The outcomes of candidates with an EPS >95% at the time of listing is limited.

Methods: UCLA kidney Transplant Program data of waiting list with EPS > 80% from January 2015 – December 2018 were included. Median follow up time of waiting list was 885 days. The outcomes included kidney transplant rate, 3 year death censored graft survival and patient survival in candidates with EPS > 95%.

Results: A total of 124 patients were identified with an EPS score > 95% at the time of listing during the study period. Of these 23 patients received a kidney transplant during the specified time frame (transplant rate of 16.9%). Recipients of kidney transplant had a longer dialysis vintage (2368.6 days vs. 9881 days, P=0.001) and were more sensitized at the time of listing (34.8% vs. 11.8%, P=0.018). Compared to a group with an EPS between 80-94% at time of listing (n=170) there were no differences in mortality (4.3% vs. 4.5%, P=0.969), graft failure (14.3% vs. 6.4%, P=0.254), or 3 year death censored graft survival (70.0% vs. 84.5%, P=0.517). The EPS > 95% group was older, had a longer dialysis vintage, had a higher proportion of candidates with diabetes as a cause of ESRD, and was less likely to undergo transplantation. Candidates with an EPS >95% who did not receive a transplant had a mortality rate of 7.9% and waitlist removal rate 16.9%

Conclusions: Kidney transplantation in candidates with an EPS > 95% provides comparable outcomes to candidates with an EPS between 80-94%, which was superior to remaining on dialysis. Despite this benefit, the transplantation rate of this group was low and a quarter of those not transplanted either died or were removed from the waitlist. Strategies are needed to improve transplantation rates in this population.

PO2426
Transition of Renal Transplant Care from Pediatrics to Adolescence and Young Adulthood: Retrospective Study Comparing Serum Creatinine-Based GFR Estimating Equations
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Background: The evaluation of graft function is vital in the management of pediatric kidney transplant (pKTx) recipients. Measured GFR (mGFR) using exogenous markers is very accurate, but not suitable for daily use. Estimated glomerular filtration rate (eGFR) using Serum creatinine (Scr) is the easiest way and equations are categorized as either pediatric or adult specific. None of the equations were formally compared in adolescents and young adults with renal transplants. The aim of study was to assess the performance of creatinine-based formulas in a cohort of pKTx in pediatric, adolescents and young adult age groups.

Methods: This retrospective study was conducted at our hospital from January 2000 to March 2019 from 125 pKTx recipients. We compared 415 mGFR values to 5 different Scr-based eGFR formulae (original Schwartz(OS), BS, Pottel, Modification of Diet in Renal Disease (MDRD), CKD-EPI, and average of BS and CKD EPI. Basing on the age and maturity of the child, BS and Pottel formulae were calculated with and without body surface area adjustment.

Results: Pottel and BS performed well across pediatric and adolescent age groups with 90% accuracy in children <12 years old and 96% in >12 years old. BS and CKD EPI outperformed all other equations with minimal bias (0.006 ml/min/1.732 m²) and 90% accuracy in young adults.

Conclusions: Height independent Pottel and height dependent BS formulae had low bias and high accuracy in children and adolescents. Average of BS and CKD EPI outperformed other equations in young adults and provides an overall unbiased estimate of GFR.

PO2427
A Comparison of the Associations of Urine Markers with the Rate of Decline in Kidney Allograft Function
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Background: Various urine markers are proposed to predict renal outcomes. However, there are few head-to-head comparison studies comparing their clinical relevance among kidney transplant recipients (KTRs).

Methods: In a prospective clinical trial, we enrolled 153 KTRs with anemia and >1 year history of transplantation across 23 facilities and followed them for 2 years. The annual change in eGFR was estimated based on mixed effects model. We then selected 102 patients who had baseline urine data on total protein, beta-2-microglobulin ([β2MG], N-acetyl-beta-D-glucosaminidase (NAG), and L-type fatty acid binding protein ([L-FABP] total protein, NAG, and L-FABP were standardized according to urine creatinine concentration. We then compared the associations of the quintiles of each urine marker with annual decline in eGFR using univariate and multivariable linear regression models.

Results: Patients were 51 ± 12 years-old and 54% were male. The median (IQR) of transplant vintage was 8 (5, 12) years, and the baseline eGFR levels were 31 ± 11 mL/min per 1.73 m². The annual eGFR change was -1.6 ± 2.0 mL/min per 1.73 m²/year. The median urine levels of total protein, β2MG, NAG, and L-FABP at baseline were 0.5 (0.2-1.1) g/g Cr, 1535 (238-4780) µg/L, 0.06 (0.04-0.12) IU/L, and 16.7 (4.2-42.1) µg/g Cr, respectively. The higher levels of L-FABP and total protein were significantly associated with more rapid annual eGFR decline (P for trend <0.001 for both; Figure) while there was no significant association for β2MG or NAG. R² was 0.10 (P=0.03) and 0.18 (P=0.001) for L-FABP and total protein, respectively. After adjustment for age, gender, mean arterial blood pressure, and baseline eGFR, the association remained significant for total protein but not for L-FABP (Figure).

Conclusions: Among urine markers of total protein, L-FABP, NAG, and β2MG, total protein appears to have greatest predictive value for eGFR decline among KTRs.

Funding: Commercial Support - Chugai, Kissei, Roche Diagnostic K.K.

PO2428
Chronic Graft vs. Host Disease in Pancreas After Kidney Transplant Recipient: An Unrecognized Entity
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Introduction: Graft-versus-host disease (GVHD), a common complication after allogenic bone marrow transplantation is rarely seen after solid organ transplants (SOT). Reports of acute GVHD (maculopapular rash, diarrhea and cholestatic liver disease described after SOT invariably happened in the early post-transplant period (days to months). In contrast, reports of SOT recipients with clinical features more consistent with chronic GVHD (cGVHD) (resembling autoimmune disease with chronic inflammation/ fibrosis) are lacking. We present a case of cGVHD in pancreas after kidney transplant (PKT) recipient diagnosed at 42 months post transplant.

Case Description: A 43 year old man received a HLA 5/6 mismatch, CMV mismatch (donor positive, recipient negative) deceased donor pancreas transplant two years after receiving a HLA 5/6 mismatch living unrelated kidney transplant. Anti-thymocyte

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Underline represents presenting author.
globulin induction was given along with a maintenance immunosuppression - tacrolimus, mycophenolate mofetil and prednisone. Post-transplant course was complicated by multiple opportunistic infections (Figure 1) leading to immunosuppression reduction. At 42 months post transplant, he developed dry eyes, arthralgia, anorexia, elevated alkaline phosphatase, dyspnea on exertion, lichen simplex chronicus dermatitis, and severe pancytopenia. GVHD was suspected which lead to peripheral blood chimerism testing revealing 90% pancreas donor-derived DNA in CD3-positive fraction of T cells. Patient passed away.

Discussion: The infections may have represented the immune dysfunction associated with GVHD. Do-escalation of immunosuppression could have led to an unopposed activation of donor cytotoxic T-lymphocytes resulting in worsening GVHD. Donor-derived T lymphocytes received during pancreas transplant may have targeted the bone marrow, causing severe pancytopenia, hence compounding the dysregulated immune state. Transplant professionals should be aware of the possibility of the rare but challenging diagnosis of GVHD in PAK recipients and hence identify it appropriately.

PO2429
Graft vs. Host Disease Following Simultaneous Liver-Kidney Transplant
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Introduction: Solid organ transplant associated GVHD is uncommon with an incidence of 0.5 to 2%. Risk factors include donor HLA homozygosity, younger donor, recipient age >50 years and sex mismatch. We present a case of GVHD following a simultaneous liver kidney transplant (SLK).

Case Description: A 64-year-old female with NASH cirrhosis and CKD due to diabetic nephropathy underwent SLK from a 38-year-old male deceased donor. The pair had 3 HLA AB mismatches and 1 DR mismatch. A total of 3.5mg/kg of thymoglobulin (ATG) was used for induction. Renal and liver parameters were stable at discharge on a maintenance tacrolimus, mycophenolate and prednisone. She was readmitted after 1-month with diarrhea and fever. Infectious work up was unrevealing. She developed a maculopapular rash, mucositis and pancytopenia. Skin biopsy showed grade 2 acute GVHD. Donor lymphocyte chimerism in peripheral blood confirmed diagnosis of GVHD with 65% donor T cells, 10% donor CD8 cells and 42% donor natural killer (NK) cells. Treatment with high dose steroids and ATG was ineffective with worsening in CD8 and NK cell donor chimerism to 91% and 53% respectively. Weekly infliximab (INX) was introduced complicated by development of entercoccal bacteremia. Clinical improvement was seen after three doses INX, however there was a lag of several weeks before an improvement in donor chimerism. Six months later her hematological, renal and liver parameters remained stable, chimerism study showed <5% T cells, CD8 cells and NK cells and a protocol renal biopsy showed no evidence of GVHD associated denovo glomerulonephritis.

Discussion: The non-specific presentation of GVHD with rash, cytopenias and diarrhea leads to delayed diagnosis and high mortality. Detection of donor chimerism through short tandem repeat sequences is used to establish diagnosis and monitor response through short tandem repeat sequences is used to establish diagnosis and monitor response.

PO2430
Kidney After Intestinal Transplantation, a Comparison with Combined Kidney Intestinal Transplant: A UNOS Database Analysis
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Background: There is limited data on outcomes for patients receiving a isolated kidney transplant (KAIT) after any prior Multi-organ or Isolated Intestinal transplant (IT). We compared the outcomes of such transplants with Combined Intestinal-Kidney Transplants (CIKT).

Methods: The KT database from 1992 through Sep 2017 was cross-linked with the IT database for all kidney transplants performed. Data was analyzed for incidence, demographics, risk factors and outcomes after KT.

Results: There were a total of 2,886 IT recorded from 1990 through Sep 2017. There were a total of 190 (6.6%) Kidney transplants recorded of which 54 (28.4%) were KAIT while the remaining 136 (71.6%) where Combined (CIKT). The Median Duration from Intestinal Transplant to Kidney transplant was 5.6 years (Range 0.47 to 18.9). One year KAIT graft survival was 87% as compared to CIKT 52%. 5 year graft survival was 74% vs 36%. Death censored KAIT graft survival at 1 year was 98% vs 87% and 5 years 83% vs 74% overall unadjusted kidney graft survival was significantly lower in CIKT as compared to KAIT p<0.009.

Conclusion: Our data shows that isolated kidney transplant after any prior Multi-organ or isolated Intestinal transplant has higher graft survival as compared to combined Intestinal Kidney Transplant. Higher CNI trough levels may be one common factor leading to lower graft survival.
PO2432
Renal Recovery After Liver Transplantation Alone in Patients with Liver Cirrhosis and Severe CKD with Normal Kidney Size

Background: Most guidelines recommend simultaneous liver-kidney transplantation (SLKT) in patients with liver cirrhosis (LC) and severe chronic kidney disease (CKD) over liver transplantation alone (LTA). CKD, however, is not irreversible. This study evaluates the reversibility of kidney disease after LTA based on kidney size.

Methods: In this single-center retrospective study, we classified 90 patients with LC and severe CKD into 3 groups: normal kidney-LTA (NK-LTA, n=39), small kidney [both <9 cm3] LTA (SK-LTA, n=46), and small kidney-SLKT (SK-SLKT, n=11). Baseline characteristics and renal recovery and survival outcomes were compared among 3 groups.

Results: The NK-LTA group had a lower percentage of hepatocellular carcinoma, a higher pre-LT eGFR, and a shorter duration of eGFR < 60 ml/min-pre-LT dialysis. This group, however, was older, received livers from a higher percentage of deceased donors and had a higher Child-Pugh score. Renal recovery, defined as no hemodialysis (HD) after LT, was found in 79% of those in the NK-LTA group, which was higher than 7.5% of those in the SK-LTA group. Renal survival, defined as patient survival without progression to HD or kidney transplant was found in 56% of patients in the NK-LTA group, which was higher than 2.5% of those of the SK-LTA group.

Conclusions: Patients with LC and severe CKD with normal kidney size may experience reversible kidney disease after LTA. Therefore, kidney after liver transplantation is recommended over SLKT for these patients.

Funding: Private Foundation Support

PO2433
Immediate Allograft Function After Liver Transplant (LT) Modifies the Effect of Pre-LT Renal Dysfunction (RD) on Post-LT Survival
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Background: Pre-LT RD is associated with higher post-LT mortality. It is unclear if immediate liver allograft function modifies this risk.

Methods: We retrospectively reviewed data on 2,856 primary LT performed in our center from 1998 to 2018. Pre-LT RD was defined as Cr ≥ 1.5 mg/dl or on dialysis at LT. Immediate liver allograft function was defined using the validated early allograft dysfunction (EAD) criteria (bilirubin t10 mg/dl, INR ≥1.6 or ALT/AST ≥2000IU/mL, on POD 7). Pre-LT RD was present in 591 (21%), of these 429 patients had Cr >1.5 and 165 were on dialysis. EAD developed in 784 (27%). The cohort was divided into 4 groups according to pre-LT RD and EAD. Group 1 (n=1,617): No RD and no EAD, Group 2 (n=643): No RD but had EAD, Group 3 (n=451): had RD and no EAD, Group 4 (n=140): had both RD and EAD. The unadjusted and adjusted post-LT survival was compared between the 4 groups.

Results: Results are presented in Figure 1. Group 1 had the best outcome with 1,3 and 5 year survival of 95%, 89% and 82%, respectively, and group 4 had the worst outcome with 1, 3 and 5 year survival of 79%, 70% and 60%, respectively, P < 0.0001. Group 2 and 3 had intermediate survival and comparable (P >0.5 between group 2&3) outcomes. Survival was better in group 2&3 compared to those in group 4 (P < 0.0001) but was worse than group 1 (P = 0.02). After adjusting for recipient age, female gender, DM, MELD score, cause of ESLD and DRI, group 4 had the highest risk of death (aHR 2.33, CI 1.69-3.21, P < 0.001). Patients in group 2 (aHR 1.16, CI 0.95-1.41, P=0.3) and group 3 (aHR 1.23; CI 0.96-1.58, P=0.09) had comparable adjusted risk of death to group 1 patients.

Conclusions: LT recipients with pre-LT RD who enjoy immediate liver allograft function have comparable adjusted survival to those with normal renal function at LT. Our results indicate that livers at higher risk of EAD should be avoided in LT recipients with RD.

PO2434
Sex and Equitity in Pediatric Kidney Transplantation

Background: Mortality in pediatric kidney failure (ESRD) is higher in girls than in boys, in contrast to the general population. In a recent report, correcting for access to transplantation partially ameliorated this risk, prompting an examination of equity in pediatric kidney transplantation.

Methods: USRDS files were used to examine incidence of pediatric ESRD (ages 18) and initial Rx modalities from 2000-15. UNOS data were used to evaluate pediatric kidney recipients between 2000-2019. Logistic regression was used to calculate an odds ratio (OR) for receiving a living donor kidney (LD). Hazard ratios (HR) of death, graft failure and death-censored graft failure (deCF) were obtained in Cox models stratified for LD/deceased-donor (DD). Models were adjusted for age, sex, and year of transplant and reported with 95% CI.

Results: Among 17,366 incident pediatric ESRD patients in USRDS, 42.8% were female. Mean and median age did not differ. Initial kidney treatment was transplantation in 17.9% of girls and 23.8% of boys, with more hemodialysis in girls (46.0 vs 40.5, P=0.001). Among 16,811 UNOS recipients, 41.0% were female. Changes in allocation policy were associated with a shift from parental donors to deceased-donors, which was more marked in female recipients (figure). 42.8% of boys and 39.7% of girls received LD (P>0.001); adjusted OR of receiving LD was 0.91 (0.85, 0.98, P=0.007) for girls. Compared to boys, girls had inferior outcomes with DD, with HRs: death 1.51 [1.30, 1.76], graft failure 1.31 [1.21, 1.40], and deCF 1.30 [1.20,1.40, P<0.001 for all]. LD outcomes did not differ by sex.

Conclusions: Female children have fewer early transplants and higher odds of receiving DD kidney transplants that are associated with inferior outcomes than their male counterparts. Attention to sex-specific disparities may improve ESRD outcomes in girls.

Living (LD) & Deceased-donors (DD) in male (M) and female (F) recipients

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PO2435
Outcomes of Emergency Department Visits of Children After Kidney Transplantation
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Background: Systematic data evaluating the postoperative Emergency Department (ED) care and outcomes of Pediatric Kidney Transplant (PKTx) recipients is limited. Our study objective is to identify the risk factors, disposition, and outcomes of PKTx recipients presenting to the ED.

Methods: We retrospectively reviewed the medical records of PKTx patients (<18 years of age) who presented to our University Children’s Hospital ED from 04/01/2015 to 06/30/2015. Data pertaining to patient demographics, chief complaint, evaluation, interventions, results, length of stay (LOS) and disposition were abstracted. Multiple logistic regression analysis was used to study the associations between admission, the presence of bacteremia, and multiple risk factors.

Results: During the study period, 60 of the 85 PKTx recipients (71%) presented to the ED for acute care (total of 210 visits, range 1-20; mean 3.5 per recipient). The majority (148/210, 70%) of the visits occurred in the first year following transplant. Fever (44%) and gastrointestinal complaints (27%) were the most frequent presentations. Mean ED LOS was 3.5 hours (range 0.22-10.8 hours). Most (109/210, 52%) visits resulted in hospital admission, for a mean inpatient LOS of 4 days (range 1-55 days). After adjusting for age and sex, the following risk factors were significantly predictive of hospital admission: shorter time since transplant (p<0.003), presence of fever (p<0.001), higher heart rate (p<0.001), higher white blood cell count (p<0.004), and presence of Systemic Inflammatory Response Status (SIRS) (p<0.001). Age adjusted systolic and diastolic blood pressure, type of transplant (deceased vs living donor), underlying primary kidney disease, the presence of a central line, or the number of immunosuppressant drugs were not predictive of hospital admission. Multivariate analysis of all significant risk factors found that shorter time since transplant and presence of SIRS were the only factors significantly associated with hospital admission (p<0.05). Only presence of SIRS was significantly associated with positive blood cultures (p=0.03).

Conclusions: Nearly-three quarters of all PKTx recipients presented to ED most frequently in the first postoperative year, with over half requiring hospital admission. Shorter time since transplant and presence of SIRS were significantly predictive of hospital admission.

PO2436
The First Increase in Live Kidney Donation in the United States in 15 Years
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Background: After more than a decade of decline, the first sustained increase in live kidney donation was observed in the US from 2017 to 2019. Understanding these trends in donation may provide opportunities to effectively sustain or even enhance this recent increase in donors.

Methods: We conducted a national registry study of 35,900 donors (70.3% white, 14.5% Hispanic, 9.3% black, 4.4% Asian) to understand the increase in 2017-2019 vs. 2014-2016 using Poisson regression stratified by donor-recipient relationship (biologically related, unrelated, and kidney paired donors).

Results: Among biologically related donors aged ≥35, 35-49, and ≥50 years, the number of donors did not change across race/ethnicity but increased by 38% and 29% for Hispanic and black ≥50; white donors increased by 42%, 50%, and 68%; Hispanic donors <35 and 35-49 increased by 18%, 14%, and 27%; Hispanic donors ≥50 did not change but increased by 22% and 33% for 35-49 and ≥50; black donors ≥50 declined by 23% and did not change for 35-49 and ≥50; Asian donors did not change. Among kidney paired donors ≥35, 35-49, and ≥50, white donors increased by 42%, 50%, and 68%; Hispanic donors ≥35 and 35-49 increased by 36% and 55% and did not change for ≥50; black donors did not change; Asian donors ≥35 did not change but increased by 107% and 82% for 35-49 and ≥50.

Conclusions: The increase in live kidney donation was driven predominantly by unrelated and paired white donors. Donation among unrelated black individuals should be promoted.

Funding: NIDDK Support, Clinical Revenue Support

PO2437
Safety and Effect of Alkali Therapy on Vascular Function in Kidney Transplant Recipients: A Pilot Study
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Background: Acid retention is a common feature of kidney transplant recipients (KTR). Studies have found that lower bicarbonate levels in KTRs are associated with an increased risk of mortality and cardiovascular disease. We tested the hypothesis that alkali therapy was safe and feasible in KTRs and would improve vascular function.

Methods: We performed an 18-week, randomized, double-blind, placebo-controlled crossover safety and feasibility pilot study of the use of sodium bicarbonate therapy in 16 KTRs. We recruited KTRs at least one year from transplant with an eGFR ≥ 45 ml/min per 1.73m2 and a serum bicarbonate level of 16-24 mEq/L. Patients received study drug therapy (sodium bicarbonate and placebo) at 0.5 mEq/kg/lean body weight for the entire 8-week treatment period. Each treatment period was 8 weeks in duration with a 2-week washout period between treatments. All patients had to be on stable immunosuppression and antihypertensive regimen for at least one month prior to randomization. Each patient served as his or her own control. During each treatment period, patients were assessed at 4 and 8 weeks for adverse events, weight, blood pressure, gastrointestinal symptoms and pill compliance. Brachial artery flow-mediated dilation (FMD) was obtained at beginning and end of each treatment period.

Results: The mean (SD) age, eGFR, and serum bicarbonate levels were 52 (19) years, 71 (21) ml/min/1.73 m2, and 23 (2) mEq/L, respectively. Serum bicarbonate levels increased by 0.4 mEq/L during treatment. Sodium bicarbonate therapy was not associated with worsening blood pressure, weight gain, or hypokalemia. 46% of patients experienced nausea and/or bloating on sodium bicarbonate therapy compared to 40% while on placebo. The study was not powered to detect differences in FMD, but there was a trend towards improved FMD in the sodium bicarbonate group compared to the control (mean difference 1.6%; 95% confidence interval, -0.39 to 3.6; p=0.1). Additionally, a trend towards decreased 24-hour urine albumin excretion (mean [SD] change -9.0 (17.1) mg/dL, p=0.07) and ammonium excretion (mean [SD] change +6.0 (12.1) mEq/d, p=0.08) was observed.

Conclusions: Sodium bicarbonate therapy is safe and feasible in KTRs. There was a trend towards improvement in FMD, strengthening the need for a larger randomized controlled trial.
Demographic Variability of Kidney Function in Live Donors: A Single-Centre Analysis

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Background: Live donation is encouraged as better outcomes in kidney transplant recipients. Donor assessment requires thorough evaluation but kidney function varies with demographics. We compare mGFR with the performance of eGFR formulas and creatinine clearances.

Methods: Analysis of 997 live donors between February 1995 and October 2019. Using pre-donation measured GFR (Te EDTA-GFR) as the gold standard, we compared the performance of CKD-MDRD, Cockcroft-Gault (CG) and Creatinine clearance by Cockcroft Gault (Cr CI) and Creatinine clearance by Cockcroft Gault (Cr Cl). We calculated the relative bias (mGFR-eGFR/mGFR), root mean square error and the accuracy (P30)(eGFR between +30% mGFR) of different eGFR equations.

Results: 424/42.32% male donors. 616/62% Caucasian, 228/23% South Asian, 114/11% Afro Caribbean and 39/4% of other ethnic groups. Cardio-metabolic risk factors in kidney donors contribute to liver dysfunction. The primary outcome was HCV transmission, defined as 2 consecutive positive HCV nucleic acid tests tested at Day 7 and 14-21 post-transplant. Confirmed HCV viremia triggered a 12-week course of DAAs.

PO2438

Direct Acting Antiviral Prophylaxis to Prevent Virus Transmission from Hepatitis C Viremic Donors to Hepatitis C-Negative Kidney Transplant Recipients

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Background: Studies have described a 12-week course of direct-acting anti-viral drugs (DAAs) for HCV transmission from infected donors to negative kidney transplant recipients. This strategy is limited by high cost and access to DAAs. A prophylactic strategy may be safer and cost-effective. We recently reported the results of our experience where a 2-4 day peri-operative DAA prophylaxis using sofosbuvir/velpatasvir (SOF/VEL) for D/R transplants prevented HCV transmission in a majority (88%) of cases. We report our entire experience based upon an adaptive iterative trial design where prophylaxis with SOF/VEL was initially extended to 7 days, and ezetimibe was added for a second cohort.

Methods: Wait-listed patients were eligible if they met the following: absence of living donor; panel reactive antibody ≤50; ≤1 prior transplant; absence of liver disease.

Results: 100 patients (mean age ≤56 years) received D/R transplants from November 2017 to April 2020. Mean wait time to transplant from enrollment was 34 days and the mean KDPI was 67%. At a median follow-up of 10 months (IQR: 1-30 months), graft survival was 99% and patient survival was 98% with no cases of liver dysfunction. In Group 1, 10 patients received one dose SOF/VEL immediately pre-transplant and a second dose on post-transplant Day 1. Viral transmission was 30% (3/10). In Group 2, 42 patients received two additional doses of SOF/VEL on Days 2 and 3 post-transplant. Viral transmission rate dropped down to 9.5% (4/42). All patients then achieved SVR with full graft survival was 99% and patient survival was 98% with no cases of liver dysfunction.

Conclusions: A 7-day DAA prophylaxis is effective in preventing donor-derived HCV transmission, can result in significant cost-savings and increase access to transplants. Adding ezetimibe to SOF/VEL did not provide an additional benefit in preventing viral transmission.

PO2440

Donor Hepatitis C Antibody Positivity Misclassifies Kidney Donor Profile Index in Non-Hepatitis C-Infected Donors: Time to Revise the Kidney Donor Profile Index

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Background: Kidneys from donors with hepatitis (CHCV) infection are traditionally excluded to be at risk for poorer graft outcomes, as reflected in the Kidney Donor Profile Index (KDPI). The KDPI defines an HCV positive donor based on HCV antibody (Ab) testing and/or nucleic acid amplification test (NAT), so not actively infected donor is also

Demographics & Comparative performances

PO2439

Assessment of Kidney Function at 3 and 6 Months in Kidney Donors with Cardio-Metabolic Risk Factors

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Background: Cardio-metabolic risk factors (CRFs) in kidney donors contribute to further deterioration of kidney function after donation, increase their post-donation cardiovascular risk. Objective: To assess the renal function of kidney donors with CRFs at 3 and 6 months after donation.

Methods: Cross-sectional, descriptive study, which included kidney donors who were admitted to the National Medical Center “Dr. Antonio Fraga Mouret” during the period from 2015 to 2019. Descriptive statistics were made, ANOVA with a 95% CI and a p-value of p ≤0.05. The CRFs' dyslipidemia, hypertension, hyperglycemia, body mass index (BMI) and hyperuricemia were evaluated.

Results: 153 donors were admitted, 34% with social security, 59% women, with a mean age of 42.7 ± 10.7 years. The clinical and biochemical characteristics at hospital admission were: mean SBP/DBP was 105 ± 7/70 ± 7 mmHg, Hb 14.3 ± 4.1 g/dL, Creatinine 1.21 ± 0.4 mg/dL, Albumin 3.8 ± 0.6 g/dL, Uric acid 4.1 ± 0.4 mg/dL, AST 45 ± 22 IU/L, ALT 53 ± 24 IU/L, Sodium 142 ± 3 mmol/L, Potassium 4.4 ± 0.5 mmol/L, Calcium 9.4 ± 0.6 mg/dL, Phosphorous 3.4 ± 0.4 mg/dL, Albumin 3.8 ± 0.6 g/dL, GFR 75 ± 30 mL/min/1.73 m².

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considered as HCV positive. The outcome of kidneys from HCVAb positive but NAT negative donors are unknown.

Methods: A national-registry-based retrospective cohort study was conducted using the SRTR data set. We identified all HCV negative recipients between April 1st, 2015 and March 2nd, 2018, who received kidney transplant from HCV Ab positive and NAT negative (D-HCVAb)-/NAT(-) patients, HCV Ab negative and NAT negative (D-HCVAb+)/NAT(-); n=25,574) donor kidneys. We then compared recipients' estimated glomerular filtration rate (eGFR) at 6 months in matched cohorts, using combined exact matching (based on KDPI) and propensity score matching. We created two separate matched cohorts to examine differences in outcomes based on how HCV positive status is defined: for the first cohort, we used the allocation KDPI (where HCV is considered positive in D-HCVAb+/NAT(-)/patients), while for the second cohort we used a modified KDPI, where the HCV component of KDPI was considered negative in D-HCV Ab(+) /NAT(-)/patients.

Results: The mean±SD age of the allocation KDPI matched cohort at baseline was 59±10 years, 69% were male, 61% and 30% of the patients were white and American, respectively. The baseline characteristics of the recipients were well-balanced in both matched cohorts. Recipients' eGFR at 6 months after transplantation was significantly higher in the D-HCVAb+/NAT(-) group compared to the D-HCVAb+/NAT(-)/group (61.1±17.9 versus 55.6±18.8 mL/min/1.73m², p<0.01) in the allocation KDPI matched cohort, while it was similar (61.8±19.5 vs. 62.1±20.1 mL/min/1.73m², p>0.9) in the modified KDPI matched cohort.

Conclusions: Recipients who received HCVAb positive, but NAT negative donor kidneys did not experience worse 6-month eGFR than correctly matched D-HCVAb+/NAT(-)/patients.

PO2443

Hepatitis C NAT-Positive Kidney Transplant into Hepatitis C-Negative Recipients: A Single-Center Experience


Background: Direct-acting antivirals (DAA) for Hepatitis (Hep) C have a 96-100% sustained viral remission (SVR) rate. This makes transplant of Hep C nucleic acid amplification testing (NAT)+ kidneys and treatment post-transplant feasible. We performed a prospective IBB approved trial at our center to validate the use and challenges of this approach.

Methods: Informed consent from eligible patients was obtained. Patients with chronic liver disease, dual organ transplants, HIV and active Hep B infection were excluded. Post-transplant, viral load was tested on day 3-5 and 7-10 and weekly thereafter until viremia was confirmed. All pts. were treated by hepatologist based genotype and insurance company preference. Standard of care immunosuppression protocols was used.

Results: 51 pts. got Hep C NAT+ kidney. The median age of the recipients was 58 years (range 29-72) and the mean wait time was 802 days (range 68-3073). Mean KDPI was 58.8 (range 27-94) with a median donor age of 38 years (range 21-56). Out of 16 implant biopsies, 13/16 (81%) had <5% of the donor's glomeruli, 14/16 (88%) had minimal interstitial fibrosis, and 15/16 (94%) had no arteriosclerosis. There was a 100% transmission rate of Hep C. As of now, 46/51 (90%) have completed a 12-week course of DAA, and 45/46 (98%) have become RNA negative with 34/46 (74%) achieving SVR. So far, there had been no insurance denials of DAA coverage. Among 18 for cause allograft biopsies, 1 showed tubuloreticular inclusion thought to be Hep C related and another showed recurrent CSGN thought to be triggered by Hep C and Hep B.

Conclusions: Transplantation of HepC NAT+ kidneys to Hep C negative recipients followed by treatment with DAA is a feasible option as a standard of care outside trials. Recipients should be monitored for Hep C related complications.
John Cunningham Virus (JCV) in Renal Allograft Recipients (RAR)
Bushra Z. Saleem, Sonitka Puri, Zahidul H. Mondal. Rutgers The State University of New Jersey, New Brunswick, NJ.

Introduction: Both JCV and BK virus belong to Polyoma virus (PV) family and can lead to opportunistic infection in RAR. BK nephritis in RAR is well described in literature (incidence 1- 10 %) in contrast to JCV nephropathy (JCVN) which is a rare entity. Here we describe two cases of JCV in RARs.

Case Description: Case 1: 44-year-old woman with PMH of HTN and ESRD received her first renal transplant in 2009 followed by antibody mediated rejection (AMR) as a result of graft dysfunction. She received preemptive second renal transplant in 12/2015 followed by multiple RA biopsies within first few months due to elevated serum creatinine (s.cr). The biopsies showed borderline CMRs, acute AMRs and eventually chronic active AMR. Treatment regimen included steroids, rituximab, IVIG and plasmapheresis. Despite repeated treatments, her s.cr remained elevated leading to another biopsy in 6/2016 showing viral cytopathic changes suspicious for PVN. SV40 stain was negative as was serum BK titer. Immunosuppression (IS) was reduced and a biopsy was repeated in 8/2016 that stained positive for SV40. Given repeatedly negative serum BK, serum JCV titer was sent, which was positive and peaked at 350699 copies/ml on 9/2016. Titer improved to 66153 after 2 doses of Cidofovir however, later deteriorated to 33420. She had no neurological involvement. Despite Cidofovir, her renal function deteriorated rapidly requiring bilateral RA nephrectomies with pathology showing JCVN. IS was discontinued following which JCV titer became undetectable. Case 2: 59-year-old man with PMH of HTN and ESRD who received renal transplant in 4/2013 followed by baseline s.c r of 1.6 mg/dl. He was on Myfortic, Sirolimus and Prednisone for IS. He presented with rising s.c r in 9/2019 (2.1mg/dl). He underwent RA biopsy in 11/2019 showing viral cytopathic changes, positive SV40 consistent with PVN. BK by PCR resulted negative x 2 but JCV titer returned at 3896 copies/ml. Myfortic was discontinued. Repeat JCV titer trended down to 2603 in 3/2020. Further follow up was delayed due to COVID-19 pandemic.

Discussion: The diagnosis of JCVN is challenging and easy to miss. Index of suspicion should be high with positive viral cytopathic changes (+/- SV40 stain) on allograft biopsy and negative serum BK. Currently there is no definitive therapy for JCV. Early diagnosis and reduction IS are critical. Cidofovir may be of utility.

PO2446
Disseminated Adenovirus Treated with Brincidofovir in a Kidney Transplant Recipient
Tiffany Truong, Thanh Cao, Santhi Voora, Thin Thin Maw. University of Southern California, Los Angeles, CA.

Introduction: Adenovirus is a common viral infection, with which immunocompromised patients have an increased risk of disseminated disease. It is less frequently described in solid organ transplant recipients and the optimal therapy for disseminated disease is unknown. We present a case of disseminated adenovirus in a kidney transplant recipient who was treated successfully with brincidofovir.

Case Description: A 56 year old female with ESRD of unknown etiology received her second kidney transplant from a deceased donor 2 years ago with thymoglobulin based immunosuppression and achieved levels of gross hematuria and right flank pain, anemia, 2 weeks of malaise and 5 days of fever, cough, sore throat, nausea and vomiting. She had acute kidney injury with creatinine of 1.75 mg/dl from a baseline of 0.8 mg/dl. She was found to have adenovirus on urine (Coombs) and serum. Other infectious etiologies were ruled out. Initial treatment consisted of reduced immunosuppression with discontinuation of mycophenolate mofetil and tacrolimus and increased prednisone from 5mg to 10mg daily due to leukopenia. Given disseminated symptoms, adjunctive treatment was also initiated with cidofovir 1mg/kg IV q48hr alternating with IVIG 500mg/kg q48 hr. She received 4 doses of cidofovir and IVIG, with resolution of hematuria and adenovirus level in urine. Although she received hydration before and after cidofovir, creatinine rose to 2.04 mg/dl. With 2 additional cidofovir doses, she continued to have AKI (peak 3.1 mg/dl) before brincidofovir was started at a dose of 100mg twice weekly. Creatinine peaked to 2.73 mg/dl when initiated on brincidofovir which decreased and stabilized to 2.2 mg/dl. Brincidofovir was discontinued when adenovirus was undetected in serum and <500 copies/ml in urine.

Discussion: The most commonly used adjunctive treatment to reduced immunosuppression of adenovirus infection is cidofovir. However, cidofovir is nephrotoxic and renally cleared. This may limit its use, particularly in kidney transplant patients. Brincidofovir is less nephrotoxic due to decreased accumulation in proximal tubules, and may be better tolerated in kidney transplant recipients. We report a case of well tolerated brincidofovir treatment of disseminated adenovirus infection in a kidney transplant recipient who demonstrated clearance of infection and improvement in kidney function.
BK Polyomavirus Nephropathy After Kidney Transplantation from HCV-Infected Donor to HCV-Uninfected Recipient

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Introduction: BK polyomavirus (BKPyV) is an important cause of renal allograft dysfunction. We previously published the potential association of an increased risk of BKPyV DNAemia/nephropathy in kidney transplant recipients receiving Hepatitis C (HCV) infected donor transplantation. Here, we report severe BKPyV DNAemia/nephropathy in a recipient who received HCV infected donor transplantation, which was temporally associated with initial HCV treatment failure.

Case Description: 62-year-old HCV negative African American male received a cadaveric kidney transplant from a HCV infected donor in January 2019, with immediate graft function. Laboratory results 4 weeks later indicated HCV PCR of 9,310,000 IU/mL, serum creatinine 1.62 mg/dL, and BKPyV DNAemia was negative. He received ganciclovir and foscarnet (March 2019) for a total of 12 wk. At completion of treatment, HCV PCR was negative. Evaluation 4 weeks later revealed HCV PCR level of 482,446 IU/mL, indicating initial treatment failure. While waiting for insurance approval for coverage of secondary direct acting antiviral (DAAs) regimen, he developed acute kidney injury 6 wk after HCV viremia, with serum creatinine peaking at 3.3 mg/dL along with a rapidly rising BKPyV DNAemia to >5,000,000 copies/mL. His immunosuppressive regimen was decreased. Allograft biopsy showed BKPyV nephropathy and proliferative glomerulonephritis (GN) with monoclonal IgG deposits. He was started on cidofovir, levofloxacin and intravenous immunoglobulin, followed by a course of sofosbuvir/glecaprevir and pibrentasvir (March 2019) for a total of 12 wk. At completion of treatment, serum creatinine gradually improved to 2.04 mg/dL.

Discussion: By inciting an inflammatory response due to direct cytotoxic endothelial cell damage, CMV infection may cause a procoagulant state. This can lead to potentially life-threatening end-organ infarction such as splenic infarction. To our knowledge, this is the first reported case of CMV infection in a KT recipient presenting with splenic infarction. A high index of suspicion for this association is warranted for early recognition and treatment of these potentially reversible conditions.

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PO2452

Early Increase in Urinary Exosomal BK Virus MicroRNA as a Predictive Marker of BK Virus Nephropathy: A Prospective Kidney Transplantation Cohort

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Background: Urinary exosomal bkv-miR-B1-5p was associated with BK virus (BKV) nephropathy (BKVN) in a cross-sectional study. However, its time-dependent post-transplantation changes and predictive value for BKVN have not been investigated.

Methods: We carried out a multicenter prospective cohort from which 83 kidney transplant recipients (KRTs) in South Korea (biopsy-proven BKVN [n=10], presumptive BKVN [n=12], and non-BKVN patients [n=61]) were selected for the measurement of urinary exosomal bkv-miR-B1-5p levels at 0.5, 3, 6, and 12 months posttransplant.

Results: At 2 weeks posttransplant, urinary exosomal bkv-miR-B1-5p levels showed an increasing trend (non-BKVN < presumptive BKVN < biopsy-proven BKVN), while plasma BKV DNA levels were undetectable in all groups. Thereafter, both urinary exosomal bkv-miR-B1-5p and plasma BKV DNA levels peaked at 3 months posttransplant and then decreased. Multivariable-adjusted Cox regression showed that urinary exosomal bkv-miR-B1-5p levels at 2 weeks and 3 months posttransplant independently predicted biopsy-proven BKVN development. In particular, the early increase in urinary exosomal bkv-miR-B1-5p makes its predictive ability for biopsy-proven BKVN superior to that of plasma BKV DNA at 2 weeks posttransplant.

Conclusions: Our results suggest that urinary exosomal bkv-miR-B1-5p can be used to identify the KRTs at high risk for BKVN at earlier time than plasma BKV DNA loads, enabling earlier intervention.

Table 1. Baseline characteristics of the study population

PO2453

Polyomavirus Nephropathy with Crescent Formation

Laura Binari, Meghan E. Kapp, Heidi M. Schaefer, Beatrice P. Concepcion. Vanderbilt University Medical Center, Nashville, TN.

Introduction: Polyomavirus reactivation in an immunosuppressed transplant patient may cause polyomavirus nephropathy (PVN). Classically seen as a pleomorphic tubulo-interstitial inflammatory reaction to the virally infected tubular epithelial cells, there are few reports of glomerular viral tropism. We present unique histopathologic findings of PVN including crescent formation with ultrastructural and immunohistochemical evidence of viral infection of glomerular epithelial cells in a kidney transplant recipient with acute kidney injury.

Case Description: A 52 y/o man s/p DDKT with well-controlled HIV presented with 2 weeks of worsening cough. He was diagnosed with multifocal pneumonia and disseminated CMV and VZV infection. His serum creatinine (SCR) and BK virus PCR were elevated to 3mg/dl (baseline 1.4-2.0 mg/dL) and 3.8M copy/mL respectively. He received ganciclovir and his immunosuppression was reduced. His pneumonia improved, but his BK PCR increased to 13.6M copy/mL and SCR remained elevated at 2.4 mg/dL. A renal biopsy showed a diffuse plasma cell-rich pleomorphic interstitial inflammatory infiltrate, tubulitis, and acute tubular injury. Viral cytopathic effect was evident and SV40 immunostain was positive in 60-70% tubular profiles, as well as parietal and visceral epithelial cells. EM revealed viral particles measuring 30 nm in diameter in tubular epithelial cells and a parietal epithelial cell. In addition, 7 of 21 total glomeruli had crescent formation with no GBM breaks or fibrinoid necrosis. There was no evidence of concomitant cellular or antibody-mediated rejection or CMV infection. These findings were indicative of PVN, with the rare finding of frequent crescents with glomerular epithelial cell infection.

Discussion: PVN is rarely described as having crescentic glomerular lesions, and if present, only one glomerulus per biopsy was affected. There are no reported cases of rapidly progressive glomerulonephritis in PVN. In our case, we found crescent formation more frequently in 33% of glomeruli. Additionally, viral cytopathic changes uncommonly affect glomeruli, typically only involving parietal epithelial cells when present. We demonstrated viral infection of both parietal and visceral epithelial cells. Our case highlights a pattern of kidney injury not commonly seen in PVN and supports that crescent formation can be caused by viral infection of the parietal epithelial cells.

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PO2455

A First-in-Human Study of MAU868, a Novel Neutralizing Antibody Against BK Virus

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Background: Reactivation of BK virus (BKV) infection can cause significant kidney and bladder disease in immunocompromised patients. BKV nephropathy is a leading cause of allograft loss in kidney transplant recipients. There are currently no effective or BKV-specific therapies. MAU868 is a novel monoclonal human IgG1 that binds to the BKV major capsid protein (VP1) with potent in vitro neutralizing activity against the 4 major BKV genotypes (IC50 ranging from 0.009 to 0.093 μg/mL).

Methods: MAU868 was administered i.v. (1, 3, 10, 30, and 100 mg/kg) or s.c. (3 mg/kg) to healthy adults in a randomized, placebo-controlled, blinded, single ascending dose design. Each i.v. cohort was 5 subjects (4 MAU868:1 placebo); the s.c. cohort was 8 subjects (6 MAU868:2 placebo). Subjects were observed for 24 h and followed for 106 days with routine safety monitoring and PK assessments. Ex vivo neutralizing activity of serum was measured before and 4 wk after dosing. The range of doses included and exceeded the predicted clinically efficacious dose.

Results: 33 subjects completed the study. Adverse events were mild and infrequent; those occurring in more than 1 subject included nasopharyngeal pain (3, 9.1%), and injection site hemorrhage (eczema after s.c. injection; 2, 6.1%). There were no infusion reactions. No subject discontinued the study due to an adverse event or developed anti-drug antibodies. MAU868 PK was typical of a human IgG with a half-life of 23 to 30 d. AUC and Cmax were dose-proportional, ranging from 9880 to 106000 μg·h/mL and 24.7 to 2740 μg/mL (ie, no evidence of FcRn saturation). Day 29 plasma MAU868 concentrations, adjusted for extravascular distribution to estimate parenchymal exposure, were approximately 7- to 751-fold higher than the highest in vitro EC50 (0.093 μg/mL). Maximum ex vivo neutralizing activity of serum was achieved for doses > 10 mg/kg. Bioavailability after s.c. injection was 57.6%.

Conclusions: MAU868 was safe and well tolerated with PK typical for a human IgG. The ex vivo neutralizing activity suggests where the therapeutic range may be for the treatment or prevention of BKV disease. These results warrant further clinical investigation of MAU868 in patients with or at risk for BKV disease.

Funding: Commercial Support - Novartis

PO2456

Induction with Alemtuzumab and Thymoglobulin in Kidney Transplant and the Risks of Leukopenia, Cytomegalovirus Infection, and BK Virus Nephropathy

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Background: Induction immunosuppressive therapy at the time of kidney transplantation reduces the risk of allograft rejection and improves graft outcomes. We compared the association between induction with thymoglobulin and alemtuzumab on the risks of leukopenia, CMV infection, and BK virus nephropathy.

Methods: We used TriNetX, a global federated research network that provides access to statistics on the electronic medical record (EMR). The Penn State Health TriNetX searchable database allows the analysis of approximately 1.7 million Penn State Health patient observations dating back to 1997. We analyzed the EMR of 1070 adult patients who had undergone kidney transplant between 1997 and May 10, 2020 (mean age: 60 ± 17; Male: 63%; White: 81%; Hispanic or Latino: 8%). We created two cohorts (19) in the alemtuzumab group. Leukopenia ± thrombocytopenia (BKV-specific therapies. MAU868 is a novel monoclonal human IgG1 that binds to the cause of allograft loss in kidney transplant recipients. There are currently no effective or BKV-specific therapies. MAU868 was safe and well tolerated with PK typical for a human IgG1. The ex vivo neutralizing activity suggests where the therapeutic range may be for the treatment or prevention of BKV disease. These results warrant further clinical investigation of MAU868 in patients with or at risk for BKV disease.

Funding: Commercial Support - Novartis

PO2457

Effects of Early Conversion to mTOR Inhibitors on Viral Infections in Renal Transplant Recipients: Eight-Year Single-Center Experience

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Background: Mammalian target of rapamycin inhibitors (mTORis) may decrease cytomegalovirus (CMV) and BK infection in renal transplant recipient. long-term effect on rejection rate deserves follow up.

Methods: This is a retrospective analysis of all patients who underwent living unrelated donor kidney transplant at Nasr city Insurance and Nile Badrawy Hospitals from 2011 to 2018, panel reactive antibody zero and no donor specific antibody. Uni- and multi-variate analysis were done to compare between mTORis based regimen and cyclosporin inhibitors (CNI)-based regimen.

Results: We identified 1458 patients who underwent living unrelated kidney transplant with intermediate risk for CMV. All patients received Induction with anti-thymocyte globulin then were maintained on mycophenolate mofetil (MMF)+CNI-prednisone for at least 6 months. They were classified into two groups: * Group I: 658 patients on mTORis (sirolimus or everolimus), who were shifted from CNI to mTOR-I due to different causes. Group II: 800 patients on CNI (cyclosporin or tacrolimus). The overall incidence of CMV infection and BK infection (Table 1) were statistically significant lower in mTORis group compared to CNI group with no statistical differences in incidence of rejections in the first 36 month but late higher rate of BPAR (Table 2).

Conclusions: mTORis/MMF is associated with low incidence of CMV and BK infection with no significant difference in rejection rate in the first 36 months. However, further regimen modification is required to reduce late rejections.

PO2458

The Utility of Procalcitonin in the Management of Kidney and Pancreas Transplant Recipients with Suspected Infection

Sarah Gilligan1, Fauad S. Shihab1, Divya Raghavan, Laith Al-Rabadi, Josephine E. Hall,1 Isaac Abraham, Isaac E. Hall. University of Utah Health, Salt Lake City, UT.

Background: Procalcitonin is used to differentiate between bacterial and viral infections to guide judicious use of antibiotics. It has not, however, been well studied in renal and pancreas transplant recipients. These patients are frequently exposed to antibiotics and are at risk for developing resistant infections. Thus, there is a need for reliable markers of bacterial infection. The purpose of this study was to compare procalcitonin levels in patients with and without bacterial infection to determine whether procalcitonin is a reliable marker of bacterial infection in the transplant population.

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Methods: Serum procalcitonin levels were measured on admission to all patients admitted to the Transplant Nephrology service with suspected infection as determined clinically by the on-call physician. We obtained all study data via chart review.

Results: Procalcitonin was measured in 154 patients. Demographics are included in the table. Forty-two patients (27%) had a positive bacterial culture. Mean procalcitonin for those with positive cultures was 5.36 ng/ml vs. 3.35 ng/ml in those without positive cultures, however this was not statistically significant (t = 0.642, p = 0.522). Patients with positive cultures were more likely to have procalcitonin levels >0.5 mg/ml (p = 0.003). Procalcitonin had a modest but significant correlation with WBC count (r = 0.249, p = 0.002). Receiver operating characteristic analysis demonstrated an area under the curve (AUC) of 0.679 (95% confidence interval: 0.590-0.768, p = 0.001) for predicting positive cultures with procalcitonin compared with an AUC of 0.584 (95% confidence interval: 0.474-0.694, p = 0.110) for WBC count.

Conclusions: In this cohort of hospitalized kidney and pancreas transplant recipients, serum procalcitonin concentration was associated with bacterial infection and was found to be a better predictor than WBC count. More information is needed to determine the utility of procalcitonin measurements in clinical decision making in this patient population.

Table 1: Baseline Characteristics and Outcomes of Elderly vs. Non-elderly

<table>
<thead>
<tr>
<th>Variable</th>
<th>Elderly (n=71)</th>
<th>Non-Elderly (n=78)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>74.6 ± 5.6</td>
<td>71.0 ± 5.3</td>
<td>&lt;0.05</td>
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<tr>
<td>Sex (male)</td>
<td>49.0%</td>
<td>58.7%</td>
<td>0.08</td>
</tr>
<tr>
<td>Time from transplant (years)</td>
<td>4.8 △</td>
<td>4.2 +</td>
<td>0.07</td>
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<tr>
<td>Pancreas or kidney transplant</td>
<td>17 △</td>
<td>19 +</td>
<td>0.07</td>
</tr>
<tr>
<td>Race - % (non)</td>
<td>75.1% (115)</td>
<td>71.1% (106)</td>
<td>0.59</td>
</tr>
<tr>
<td>Native Hawaiian or Polynesian</td>
<td>4.5% (7)</td>
<td>5.1% (8)</td>
<td>0.59</td>
</tr>
<tr>
<td>Other - % (non)</td>
<td>14.3% (22)</td>
<td>19.5% (29)</td>
<td>0.59</td>
</tr>
<tr>
<td>Ethnicity - % (non)</td>
<td>20.3% (31)</td>
<td>23.0% (35)</td>
<td>0.59</td>
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<td>BMI (kg/m²)</td>
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<td>Weight (kg)</td>
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<td>Height (cm)</td>
<td>169.2 ± 8.5</td>
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<td>Serum creatinine (mg/dl)</td>
<td>2.3 ± 0.5</td>
<td>2.4 ± 0.6</td>
<td>0.59</td>
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</table>

PO2459

Infection Rate at 1 Year of Deceased Donor Kidney Transplant in the Elderly

Wina Yousman, Nicole Low, Wei Xiang Wong, Venkatesh Kumar Aiyamuthu, Bekir Tantrrver. The University of Arizona, Tucson, AZ.

Background: There is limited publications about infection incidence rate in deceased donor kidney transplant (DDKT) recipients older than 65. The objective of this study is to examine our center specific infection incidence rate within one year of DDKT.

Methods: Retrospective chart review of DDK T (N=176) from July 2016 to December 2019 at Banner Medical Center in Tucson, AZ. Primary outcome was the infection incidence rate among recipients older than 65 year-old, including Cytomegalovirus (CMV) viremia and BK viremia (screened by monthly plasma PCR testing), or urinary tract infection (UTI) (diagnosed with positive urine culture and urinary symptoms within first year of transplant). We also fitted a multivariable logistic regression for the outcomes variables adjusted for demographics, KDPI, CIT, EPTS, and ePRA.

Results: The characteristics of the study cohort was shown in Table 1. Out of 176 patients, 63 patients (35.8%) were older than 65 year-old. There was no significant difference in the incidence rate of total infection, CMV viremia, BK viremia, and UTI in the elderly versus non-elderly patient (63.5% vs 51.3%, p = 0.11, 20.6% vs 11.5%, p = 0.010, 15.9% vs 11.5%, p = 0.41, 32.3% vs 28.3%, p = 0.59). The multivariable logistic regression analysis (adjusted for ethnicity, KDPI, EPTS, ePRA, and CMV mismatch) did not show increased odds of all types of infections among older recipients.

Conclusions: The infection rate of elderly versus non-elderly who received DDKT were similar.

PO2460

Two Deaths of Acute Transplant Patients from Strongyloides Hyperinfection Syndrome (SHS): Can We Prevent Harm with Screening and Prophylaxis at the Time of Transplantation?


Background: A 59 year old Vietnamese man presented with non-specific abdominal pain 8 weeks after a deceased donor kidney transplant. He was thoroughly investigated and no cause for the pain identified. On day three of the admission he became febrile and hypoxic. He died with multi-organ failure. Within three months a patient of Congolese origin presented nine weeks post transplant with abdominal pain. He became febrile with gram positive bacteraemia and was admitted to the ICU with type 1 respiratory failure where he unfortunately died. Autopsy findings revealed SHS. These cases were patients at a transplant centre in a non-endemic area albeit with an ethnically diverse population. A survey of other UK transplant centres showed that none did pre-transplant screening for strongyloides infection.

Methods: As a result of these cases we implemented and evaluated a program to screen for and prophylactically treat Strongyloides infection: Live donor patients were screened with Strongyloides serology in advance of transplantation. All recipients of deceased donor transplants were screened on admission for their transplant unless they had never travelled to an endemic area. At induction recipients received a weight adjusted dose of Ivermectin pending serology results. If positive a second prophylactic dose was administered at day 14. Travel histories and demographic data were recorded.

Results: Between July 2019 and March 2020, 135 patients were transplanted at our unit. Of those 125 had strongyloides serology testing; eight were positive at time of transplant. All patients reported as “borderline” drome. One further patient tested positive on a previous admission for a transplant which was cancelled; but was negative on the admission of the successful transplant. This indicates that at least 8% of our transplant listed patients are positive for strongyloides infection. By May 2020 there were no recorded deaths due to SHS, or morbidity associated with strongyloides infection in this group.

Conclusions: We have demonstrated that there is a significant level of sero-positivity within our pre-transplant population and that a relatively low-cost strategy may help prevent the potentially fatal Strongyloides Hyperinfection Syndrome.

PO2461

Infectious Complications and Malignancy After Kidney Transplant in the Elderly Population

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Background: Kidney transplantation improves quality of life and survival in all patients regardless of age. However, older patients are prone to development of side effects related to immunosuppressive medications including infections and malignancy. We aim to evaluate clinical outcomes in recipients >65 years of age.

Methods: We retrospectively reviewed all patients over the age of 18 who received an isolated renal transplant at our center from January 2013 to June 2017. We compared clinical outcomes including allograft and patient survival, as well as the development of infections and malignancy in patients > 65 compared to younger patients.

Results: Of 624 patients analyzed, 148 (24%) were > 65 years of age. There was no difference in terms of gender, race, immunosuppressive or induction therapy between the two groups. Older patients were more likely to receive a deceased donor kidney transplant (92% vs. 81%, p = 0.009). During a median 48 months (28, 70) of follow-up, as expected mortality was higher in older patients (16% vs. 6.5%, p = 0.0001) but there was
no difference in terms of death-censored graft loss (10.8% to 9%, p=0.52) compared to younger patients. Detailed analysis of infections revealed that there was no difference in terms of BKV and CMV viremia, pneumonia, bacteremia, influenza and c. diff between the two groups. However, older recipients had more fungal and urinary tract infections and malignancy. The most common infection in the elderly was PJP pneumonia (4%), candidemia (3%), and cryptococcal infection (2%). The most common malignancy in the elderly was skin cancer (6%) followed by prostate (2%), lung (1%), and colon (1%).

**Conclusions:** Recipients older than 65 had similar graft survival compared to younger patients, but had a higher incidence of fungal and urinary tract infections and malignancies.

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**PO2462**  
Risk of Active Tuberculosis Infection in Kidney Transplantation Recipients: A Matched Comparative Nationwide Cohort Study

Sooheon Park,1 Ji Eun Kim,2 Mi-yeon Yu,3 Yong Chul Kim,2 Dong Ki Kim,3 Kwoun Wook Joo,4 Yon Su Kim,4 Kyungdo Han,5 Hajeong Lee.3  
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**Background:** Although the risk of mycobacterium tuberculosis (TB) infection is high in both kidney transplantation (KT) recipients and dialysis patients, a large-scale evidence comparing the risk between the two groups in a nation with moderate or higher TB prevalence was rare.

**Methods:** We performed a nationwide retrospective cohort study based on the claims database of South Korea where moderate TB prevalence is reported. We included incident KT recipients from 2011 to 2015 and compared their active-TB risks with matched controls. The 1:1 matched general population group was matched for age, sex, and era, while the dialysis group was matched for age, sex, era, underlying hypertension, and diabetes. They excluded the matched pairs with age < 20 years old, a previous TB history, and those matched to a multi-organ transplantation case. The incident active-TB risk was assessed by the multivariable Cox regression analysis. Within KT group, associations between active-TB, as a time-dependent variable, and post-transplant death or death-censored graft failure was investigated.

**Results:** The number of matched 7,462 subjects (total 22,386) were included to each of the study groups. During median 3.57 years of follow-up duration, the incidence rate for active-TB was 3.92/1,000, 4.38/1,000, and 0.67/1,000 person-years in the KT, dialysis, and general population groups, respectively. The KT group showed a significantly higher risk of active-TB than the general population group [adjusted HR 3.59 (1.88-6.12)] but a similar to the dialysis group [adjusted HR 0.98 (0.73-1.31)]. Active-TB was a significant risk factor for death [adjusted HR 2.24 (1.19-4.42)] or death-censored graft failure [adjusted HR 2.21 (1.36-3.58)] in the KT patients.

**Conclusions:** In Korea with moderate TB prevalence and active surveillance strategies, KT patients may not have to burden additional risk of active-TB when compared to dialysis patients. Still, clinical attention for active-TB complication should not be overlooked in end-stage kidney disease patients, particularly for KT patients as active-TB was associated with worse post-transplant prognosis.

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**PO2463**

Hydroxychloroquine as an Alternative or Adjunctive Antimetabolite in Kidney Transplant Recipients: Analysis of Linked US Registry and Claims Data

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**Background:** Hydroxychloroquine (HCQ) is an antimalarial drug with immunomodulatory effects in patients with systemic lupus erythematosus (SLE) and scleroderma. The potential anti-viral effects of HCQ have raised attention in the context of BKV and CMV viremia, pneumonia, bacteremia, influenza and c. diff between the two groups. However, older recipients had more fungal and urinary tract infections and malignancy. The most common infection in the elderly was PJP pneumonia (4%), candidemia (3%), and cryptococcal infection (2%). The most common malignancy in the elderly was skin cancer (6%) followed by prostate (2%), lung (1%), and colon (1%).

**Conclusions:** Recipients older than 65 had similar graft survival compared to younger patients, but had a higher incidence of fungal and urinary tract infections and malignancies.

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**PO2464**

Bacillary Angiomatosis in a Kidney Transplant Recipient

Cleveland Clinic, Cleveland, OH.

**Introduction:** Bacillary angiomatosis (BA) is a vascular proliferative manifestation of Bartonella henselae (BH) or Bartonella quintana (BQ) that usually affects immunocompromised hosts. It usually involves the skin but may affect other organs. Few cases of BA in kidney transplant (KT) recipients have been reported, with most cases presenting years after KT. We describe a case of BA in a KT recipient that occurred early post-transplant.

**Case Description:** A 67-year-old male KT recipient from a deceased donor developed fevers, night sweats, and fatigue 1-month post-KT. He received antithymocyte
globulin induction, and maintenance tacrolimus, mycophenolate, and prednisone. Two months later, he presented with diffuse violaceous papules (Figure 1A). Biopsy of a papule with Warthin-Starry stain showed clusters of bacteria suggestive for BA (Figure 1B). Diagnosis was confirmed with a positive serum Bartonella polymerase chain reaction (PCR). He was treated with doxycycline with resolution of symptoms. BH and BQ Immunoglobulin G (IgG) were equivocal. A few weeks later, IgG for BH was 1:256 (reference range <1:128). Echocardiogram, abdominal computed tomography, and kidney biopsy were unremarkable. Recipient Bartonella PCR and antibodies on the day of transplant were negative. Donor Bartonella PCR and BH IgG were negative. Donor BQ IgG was equivocal. The recipient had a cat 8 years prior to KT with recent exposure. Allergist function remains intact, and the rash completely resolved. Bartonella PCR 6 months on treatment was negative.

Discussion: Our patient developed signs of BA with positive seroconversion within the first 3 months of KT which is rare. BA should be considered in the differential diagnosis of fever and cutaneous angioma-like lesions in KT recipients, even in the absence of exposures. Combined serology and molecular testing (PCR) is useful in diagnosing BA as serology alone may be unreliable. Early empiric treatment should be considered in transplant recipients while waiting for confirmatory results.

Figure 1. (A) Violaceous papules on the trunk. (B) Warthin–Starry stain showing bacteria (arrow).

PO2465
Isavuconazole as Consolidation Therapy for Disseminated Histoplasmosis in a Kidney Transplant Recipient
Samara Medani, Michael Kessler, Sandesh Parajuli. University of Wisconsin-Madison, Madison, WI.

Introduction: The diagnosis of systemic fungal infection may be elusive and requires a high index of suspicion with prompt evaluation, directed laboratory and radiological work-up and if necessary, histological examination. To our knowledge, this is the first case report of isavuconazole use as consolidation therapy for disseminated fungal infection in a kidney transplant recipient.

Case Description: A 76-year-old female with polycystic kidney disease presented 8 years post kidney transplantation with a painful tongue ulcer, anorexia, weight loss, progressive anemia and severe de-conditioning. She was on maintenance mycophenolate, prednisone and tacrolimus. A midline fissure on the dorsal tongue surface (image 1- left), and two non tender nodular masses in the left forearm and right buttock were noted. A diagnosis of disseminated histoplasmosis was made by biopsy of the tongue ulcer, and cultures of blood, tongue tissue and forearm nodule aspirate. Blood and urine histoplasma antigens were positive. The patient was treated with amphotericin for two weeks before transitioning to itraconazole due to QT prolongation. Mycophenolate was stopped. An outstanding clinical response with healing of the tongue ulcer (image 1- right), shrinking of the subcutaneous lesions, and substantial functional progress to prior independence was seen within 3 months. Histoplasma urinary and plasma antigen levels declined to undetectable levels. Isavuconazole was continued for a year with no adverse side effects reported.

Discussion: Infections with Histoplasma capsulatum are largely asymptomatic but progressive disseminated mycosis can occur in the immunocompromised. There is no specific agent selectively approved for second line maintenance therapy when itraconazole is not tolerated or is ineffective. Limited experience has been reported with other azoles, and even less so with isavuconazole. This case demonstrates an excellent outcome of treating disseminated histoplasmosis with isavuconazole in a kidney transplant recipient.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO2466
The Diagnostic Dilemma of Diffuse Lymphadenopathy in a Kidney Transplant Recipient
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Introduction: Immunological balance is critical for transplant recipients. An optimum amount of immunosuppression prevents rejection while avoiding infection and cancers. Constitutional symptoms and lymphadenopathy could be present in both scenarios and could pose a diagnostic challenge.

Case Description: A 36-year-old male immigrant from India (ten years ago) with PMH of ESRD secondary to IgAN received a DDKT (9/2019, EBV D+/R+, on tacrolimus and myfortic). He was admitted with extensive retroperitoneal and mesenteric lymphadenopathy and a hypodense structure in the left upper abdomen (3.8 x 3.1 cm) on CT scan along with constitutional symptoms of fevers, constipation, and abdominal pain for ten days three months after transplant. Vital signs and physical examination were unremarkable except for the low grade fever. Aside from mild anemia (Hb 10 mg/dL), laboratory analysis was normal. PET scan revealed hypermetabolic lymphadenopathy in the neck, abdomen, and pelvis and consolidative changes in the left lung base and a right-sided loculated pleural effusion. Extensive workup - CMV PCR, pan-culture, fungal infections, and flow cytometry – was negative. CT-guided retroperitoneal lymph node biopsy, incisional biopsy of the mesenteric mass, and an endobronchial ultrasound-guided transbronchial needle aspiration of subcarinal LN were non-diagnostic. Finally, exploratory laparotomy and resection of the mesenteric mass revealed granuloma formation with multinucleated giant cells concerning for TB. The AFB culture grew mycobacterium tuberculosis on day 24. He is currently on antituberculosis treatment with a good response.

Discussion: Our case highlights the importance of a high degree of clinical suspicion for infectious etiology in transplant recipients, especially those from countries with a high prevalence of TB. Our patient bore a distant immigration history and a negative tuberculin test and did not have a history of exposure. Still, he was at increased risk of activation of latent TB due to his immunocompromised state. Extra-abdominal TB, like abdominal TB, poses a diagnostic challenge as the presentation can be non-specific and the AFB stain and culture can be non-diagnostic. Thus, a tissue biopsy becomes key to diagnosis. PTLD was highly differential given the PET-avid LAP. PET-avid lesions imply a hypermetabolic state which can happen in both malignancies and infections.

PO2467
Post-Transplant Lymphoproliferative Disorder: Recurrence at an Unusual Site
Aditi Saha, Sohail Tariq, Lalitha Thiruvarukasur Murugan, Sunil Sapru, Miguel Conde. Saint Barnabas Medical Center, Livingston, NJ.

Introduction: PTLD includes a spectrum of clinical presentations due to lymphoid proliferation ranging from benign hyperplasia to aggressive lymphomas that occur after either a SOT or HSCT. PTLD can involve extra nodal sites like graft tissue, GI tract, and lungs. Skin and soft tissue involvement is very rare. We report a patient with PTLD who had relapsed with axillary lymphadenopathy and a soft tissue mass on the arm.

Case Description: A 59-year-old male was diagnosed with EBV negative PTLD involving retroperitoneal, mediastinal and supraclavicular lymph node, one year after renal transplant. He was treated R-CEOP (Rituximab, Cyclophosphamide, Etoposide, Vinristine, Prednisone). After 6 cycles of chemotherapy repeat PET showed complete resolution. 3 months later, he presented with LUE pain and swelling. Labs were significant for high LDH and Beta-2 microglobulin. CT LUE revealed 4.8 cm mass over left anterior arm and left axillary adenopathy. Biopsy and flow cytometry of axillary lymph node confirmed relapse. Immunohistochemical stains showed tumor cells positive for CD20, PAX5, BCL2, MUM1, BCL6 with K67 of 80-90%. Patient developed compartment syndrome and had to undergo fasciotomy. Patient was started on modified regimen with Rituximab, Gemcitabine and Oxaplatin (R-GEMOX) for poor performance status.

Discussion: The incidence of PTLD ranges from 1 to 25% with 90% of cases being EBV-associated, CD 20 positive, B cell neoplasms. EBV negative PTLD occurs only in 5-10% cases, appears late with worse prognosis than EBV positive PTLD. EBV negative PTLD is assumed to be related to Tp53 mutation caused by immunosuppressive agents like azathioprine or tacrolimus. Skin and subcutaneous lesions are extremely rare as sites of extra nodal presentation and may take the form of solitary or multiple papules, nodules, plaques with ulceration, comedo-like lesions, follicular keratotic papules, or localized alopecia. Our patient is interesting as he had a relapse of EBV negative PTLD in the form of a soft tissue fibro-adipose mass in the upper extremity. To the best of our knowledge, there have been three cases of PTLD presenting as soft tissue masses on head reported in the literature. Biopsy remains the gold standard for diagnosis. Treatment is includes reduction of immunosuppression and rituximab with additional chemotherapy.

PO2468
Post-Transplant Lymphoproliferative Disorder (PTLD) Presenting as Solitary CNS Lymphoma: A Rare Occurrence
Aditi Saha, Sohail Tariq, Lalitha Thiruvarukasur Murugan, Sunil Sapru, Israel R. Grossman. Saint Barnabas Medical Center, Livingston, NJ.

Introduction: PTLD associated lymphoma is the second most common malignancy in patients receiving SOT or HSCT with an incidence rate of 1%-3%. CNS involvement occurs in 7%-15% of all PTLD cases. We present a case of isolated PCNS lymphoma two years after renal transplant.

Ulcereated median sulcus of the tongue, before (left) and 8 months after (right) starting antifungal therapy.
Case Description: A 57-year-old woman with PMH of ESRD s/p kidney transplant (D = HLA EBV+) with chronic CClVI of 30-40% percutaneous presented with paresthesia and numbness over the right side of her body with mild ataxia 2 years post transplant. Physical exam revealed only numbness over the right side of body. MRI with contrast revealed a left thalamic lesion with moderate wasogenic edema, and MR spectroscopy confirmed high grade neoplasm involving left thalamus. Stereotactic biopsy showed polymorphic CD-20 and EBV positive PTLD. EBV PCR were elevated. Further evaluation ruled out systemic PTLD. Myelotoxic was stopped and oral steroids started with mild improvement in symptoms. Choice of systemic chemotherapy was limited due to reduced CCl and risk of graft failure. She received modified regimen with a newly adjusted high dose Methotrexate, Vincristine and Rituximab for 6 cycles with partial remission and then Tenofovir for 7 cycles with complete remission.

Discussion: The incidence of PTLD ranges from 1 to 25% with 90% of cases being EBV associated. EBV positivity in the host cell neoplasms. PCs-PTLD has a higher incidence in renal SOT, occurs late and is usually monomorphic unlike our patient. Median time of occurrence is 4.5 years after transplant. Risk factors include age, intensity of immunosuppression, time to transplant and EBV status of donor and recipient. Common presenting features include neurological deficits, seizure, and raised intracranial pressure. MRI of the brain is preferred imaging and shows multifocal, ill-defined, ring enhancing lesions usually in supratentorial and lobar regions. Positive CSF EBV PCR is highly suggestive but biopsy remains the gold standard for diagnosis. Treatment modalities include reduction of immunosuppression, rituximab, high dose methotrexate, cytarabine and cranial radiotherapy. Use of high dose methotrexate has shown improved outcomes with median survival of 26-47 months. Lack of response to first line therapy is considered the dominant prognostic factor. Early recognition and diagnosis remain crucial for improving outcome.

PO2469
National Trends in Kidney Transplantation Among Patients with ESKD from Plasma Cell Dyscrasias
Jia Hwee Ng,1,2 Stephanie Izard,1 Kenar D. Jhaveri,1,2 Vinay Nair.1 Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, 1Northwell Health, Great Neck, NY.

Background: Due to relapses and kidney involvement, plasma cell dyscrasias have been a relative contraindication for kidney transplantation. With newer medications and improved prognosis of plasma cell dyscrasias, kidney transplantation in this population is becoming more common. We aimed to describe national trends in the proportion of kidney transplants among patients who had ESKD from plasma cell dyscrasias (multiple myeloma, amyloidosis, and monoclonal gammopathy of renal significance).

Methods: We used data from the United Network for Organ Sharing/ Organ Procurement and Transplantation Network (UNOS/OPTN) database. Patients 18 years or older, BMI >15 or <45 kg/m2, received a first kidney transplant between January 1, 2006 to December 31, 2017 were eligible. Recipients of more than one organ transplant were excluded.

Results: A total of 160,966 patients received a first kidney transplant. Among these, 487 (0.3%) had ESKD from plasma cell dyscrasias, kidney transplantation in this population is becoming more common. We aimed to describe national trends in the proportion of kidney transplants among patients who had ESKD from plasma cell dyscrasias (multiple myeloma, amyloidosis, and monoclonal gammopathy of renal significance).

Table 1: National trends in kidney transplantation among recipients who had end-stage kidney disease from plasma cell dyscrasias (multiple myeloma, amyloidosis, and monoclonal gammopathy of renal significance)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number of transplants</th>
<th>Total plasma cell dyscrasias (%)</th>
<th>Multiple myeloma (%)</th>
<th>Amyloidosis (%)</th>
<th>Monoclonal gammopathy (%)</th>
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</thead>
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<tr>
<td>2006</td>
<td>12571</td>
<td>0.03</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
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<tr>
<td>2007</td>
<td>14244</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2008</td>
<td>15265</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2009</td>
<td>15779</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2010</td>
<td>16090</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2011</td>
<td>16328</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2012</td>
<td>15481</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2013</td>
<td>14243</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>2014</td>
<td>13550</td>
<td>0.02</td>
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<tr>
<td>2015</td>
<td>14069</td>
<td>0.02</td>
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</tr>
<tr>
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<td>15091</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusions: Despite improvement in the treatment of plasma cell dyscrasias, national trends show only a small rise in the proportion of kidney transplantation for patients with ESKD from plasma cell dyscrasias. Additional analyses are needed to assess the outcomes of these kidney transplant recipients.

PO2470
A Retroperitoneal Cyst of Pancreatic Origin in a Renal Transplant Recipient: Expect the Unexpected
Muhammad O. Saleem,1 Ambreen Chughtai,1 Imran Y. Gani,1 Muhammad I. Saeed,2 Rajan Kapoor.1 1Augusta University, Augusta, GA; 2FMH College of Medicine and Dentistry, Lahore, Pakistan.

Introduction: The immunosuppression required to maintain a renal allograft function puts the recipient at a higher risk of malignancy. We report a rare case that presented a diagnosis of a retroperitoneal hemorrhagic cystic mass turn out to be an adenocarcinoma of pancreaticobiliary origin.

Case Description: 43-year-old female with a history of End Stage Renal Disease due to IgA Nephropathy and two renal transplantations, first in 1999 from her sister and second in 2005 from a deceased donor, presented with complaint of left sided abdominal pain and distention for one month. Her graft function was stable with creatinine of 1.8mg/dl on immunosuppression with tacrolimus, mycophenolic acid, and prednisone.

On examination the abdomen was soft, flat and tender. There was a well defined area of tenderness in the left lower quadrant. There were no masses palpable. The CT scan showed a 1.7 cm well defined area of high density in the left lower quadrant. She subsequently underwent exploratory laparotomy which revealed a retroperitoneal 1.7L cystic hematoma with no association to native or transplant kidneys. The histopathology showed adenocarcinoma with mucinous and enteric features. Based on the morphology and immunoprofile, the differential diagnosis included an ovarian, gastrointestinal or peritoneal primary. Tumor markers showed elevated CA19-9, but normal CEA and CA-125. Given the positivity for both CK 7 and CK 20, colonic origin was unlikely but could not be completely excluded. Negative IEG and colonoscopy ruled out GI malignancy. PET scan was unremarkable. Molecular analysis predicted 90% probability of pancreaticobiliary adenocarcinoma. Subsequently patient was started on adjuvant chemotherapy with Gemcitabine. She failed first and second lines of chemotherapy with progression of cancer. Then she received PD-1 inhibitor, Nivolumab which could not prevent progression of disease but resulted in renal graft failure. Per last reports, patient was on palliative chemotherapy and in terminal phase of her life.

Discussion: Post-transplant malignancy is one of the most feared complications. It is the third leading cause of mortality and accounts for 8-10% of all deaths in United States and 30% in Australia in kidney transplant recipients. Compared with general population, the risk is increased 2-3 folds and mortality rates are higher. The occurrence of pancreatic cancer is high too. But finding a pancreaticobiliary cancer from a retroperitoneal cyst with negative pancreas imaging is rare.

PO2471
Secondary Malignancy in Kidney Transplant Recipients: University of Southern California Experience
Alexandra K. Wong, Tiffany Truong, Poorva Vaidya, Gino In, Thin Thinx Maw. Keck Hospital of USC, Los Angeles, CA.

Background: Kidney transplant recipients (KTR) on immunosuppressive therapy are at higher risk of developing secondary malignancy (SM). Although previous studies have demonstrated this increased risk, much remains to be elucidated regarding the spectrum of SM and the contributing factors to morbidity and mortality.

Methods: We conducted a retrospective review of all KTR from April 2005 to December 2017 at our institution. We then selected only those patients with SM, and collected demographics, variables related to kidney transplant, malignancy, and outcomes.

Results: Among 1414 KTR, 84 patients (pts) had post-tx SM. Forty-five percent of pts were Hispanic, 35% Caucasian, 11% Asian and 6% African American. Twenty four pts (28%), 11 pts (13%), and 51 pts (59%) developed cutaneous malignancy, hematological malignancy and solid organ malignancy (SOM) respectively. One patient developed both a secondary cutaneous and SOM, while another pt developed 2 different SOM. 46 (55%) pts were deceased by 1/1/20: 25 pts died from malignancy and 9 pts died from infection. Among those 46 pt, 37 pts (80%) had intact graft function at death. Eleven pts (13%) had malignancy prior to tx. The induction was rATG (36%) and basiliximab (41%). 20 pts had biopsy-proven acute rejection; of these 75% was prior to and 25% was post cancer diagnosis. 18 pts were switched to mTOR inhibitor from tacrolimus and cefepine was stopped in 22 pts.

Conclusions: We describe a wide range of SM among a diverse population of KTR, with nearly half of our patients being Hispanic. This highlights the need for further investigation of the impact of ethnicity on SM. Among our KTR, SM was the cause of death for 25 pts and infection was for 9 pts. Regardless of etiology, the majority of pts (80%) had intact graft function at death. Our findings illustrate the need for vigilant cancer screening and additional strategies to decrease cancer risk and death in KTR.

PO2472
Spectrum and Consistency of Cancer Outcomes in Randomized Trials in Kidney Transplant Recipients: A Systematic Review
Erica H. Ashford,1 Allison T. Law,1 Gemma Wong,1,2 Jonathan C. Craig,1 1The University of Sydney Faculty of Medicine and Health, Sydney, NSW, Australia; 2Children’s Hospital at Westmead Centre for Kidney Research, Sydney, NSW, Australia; 3Flinders University College of Medicine and Public Health, Bedford Park, SA, Australia.

Background: Cancer is an important cause of morbidity and mortality in kidney transplant recipients. Despite being identified as a critically important outcome by patients, caregivers and health professionals, inconsistency in how cancer outcomes are defined and reported in trials involving kidney transplant recipients may limit decision-making. The aim of this study was to assess the spectrum and consistency of cancer outcomes in trials involving kidney transplant recipients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: ClinicalTrials.gov was searched from inception to October 2019 to identify randomized controlled trials (RCTs) in adult kidney transplant recipients, which included cancer as a pre-defined outcome. We extracted the details of all primary and secondary cancer outcomes, including type, timepoint and definition of cancer (histology, grade and stage).

Results: Among the 71 RCTs included, there was a total of 87 cancer outcomes. The majority of trials (n = 61, 86%) included cancer as a secondary outcome only, with 8 trials (11%) including cancer as a primary outcome and 2 (3%) including cancer as part of a composite primary outcome measure. The most common descriptions of cancer in these outcomes were "malignancy" without specific reference to diagnostic criteria, histology, grade or cancer stage (40, 46%) or "cancer" without specific clarification (8, 9%). Some trials included mention of specific cancer types, with post-transplant lymphoproliferative disorder (13, 15%), non-melanoma skin cancer (10, 11%) and skin cancer (9, 11%) being the most common, but these were not defined. A range of timepoints were used, with a single timepoint at the end of the primary trial being the most frequent (38, 44%); 13 studies included measurement at several timepoints during the trial (15%). A range of metrics for measuring cancer outcomes were used, including cancer incidence (53, 61%), proportion with cancer (9, 10%), and time-to-event (5, 6%). No measurement metric was specified in 18 (21%) cancer outcome measures.

Conclusions: Cancer is one of the most important outcomes for patients post-transplantation, but cancer outcomes are very poorly defined and highly variable in RCTs. A core outcome for cancer for all trials in kidney transplant recipients should be developed that is consistent and meaningful to patients and clinicians.

Funding: University of Wisconsin School of Medicine and Public Health, Madison, WI.

PO2473
Acute Rejection and Graft Failure in a Kidney Transplant Recipient with Malignant Melanoma and Treated with Pembrolizumab: A Case Report
Annalise M. Panthofer, Kurits J. Swanson, Didier A. Mandelbrot, Neetika Garg. University of Wisconsin School of Medicine and Public Health, Madison, WI.

Introduction: Malignancy treatment with immunotherapy in renal transplant recipients is complicated by a very high risk of rejection. Immunochemotherapy increases immune recognition and destruction of immune-evading cancer cells. This can lead to an overly robust immune response leading to allograft injury and failure. Here we present a case of graft failure due to rejection within a week of starting immunotherapy.

Case Description: 73-year-old female with a history of end-stage renal disease attributed to hypertensive nephrosclerosis underwent live unrelated kidney donor transplant and presented 6 months post-transplant with a right foot lesion and was diagnosed with stage IIIIC malignant melanoma. Her maintenance immunosuppression was decreased from tacrolimus/prednisone to prednisone monotherapy and the lesion was excised. 14 months later, disease surveillance via PET scan revealed metastatic disease. After carefully weighing the risks of mortality without treatment versus graft rejection, pembrolizumab, a programmed death one (PD-1) inhibitor, was initiated. 5 days after administration of the first dose, the patient presented emergently with acute kidney injury with Cr of 4.3 mg/dL, increased from baseline Cr of 0.9-1.0 mg/dL. Ultrasound of her graft demonstrated significant edema and graft thrombosis. Allograft biopsy was consistent with 95% cortical necrosis with thrombotic microangiopathy and grade III acute cellular and antibody mediated rejection. Transplant nephrectomy was performed on day 7 and HD was re-initiated.

Discussion: Immune checkpoint inhibitors have been shown to be effective treatments for certain malignancies (melanoma, renal cell carcinoma namely); however, they can cause acute rejection and graft loss in transplant recipients. Though PD-1 inhibition has been a major scientific breakthrough in late-stage cancer treatment, its risk profile should be carefully considered in organ transplant recipients due to high risk on graft rejection. Prevention and management of rejection in a transplant recipient with an aggressive melanoma such as ours is not clear.

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Underline represents presenting author.
Hypercalcemia Associated with Pneumocystis jirovecii Pneumonia in Renal Transplant Patients

Introduction: Pneumocystis jirovecii pneumonia (PJP) is a common complication following solid organ transplantation with an estimated incidence of 5-15%. Although previously reported, hypercalcemia is not classically a sign of PJP. In the past 6 months at our institution, there have been six cases of PJP presenting with varying degrees of hypercalcemia.

Case Description: All patients in the table below presented with signs and symptoms concerning for pneumonia and were diagnosed with PJP by DFA and/or PCR from induced sputum or bronchoscopy. Patient demographics, labs, and calcium trends are outlined in the table. All patients were treated with Bactrim and prednisone for PJP (some had intravenous sulfamethoxazole/trimethoprim and intravenous meropenem and then trimethoprim. A follow-up MRI two months from diagnosis showed marked improvement in all lesions and he was transitioned to oral doxycycline to complete at least 12 months of therapy.

Discussion: Nocardiosis can present in unusual fashion in transplant recipients and is more likely to infect immunosuppressed patients. We report a case of a kidney transplant patient who presented with a tender lump of his right shoulder.

PO2478
Hypercalcemia: A Prodromal Feature of Pneumocystis jirovecii Pneumonia in Kidney Transplant Recipients
Joy C. Chen, Johann N. Isaac, Raviprasanna K. Parasaruman. University of Michigan, Ann Arbor, MI.

Introduction: Hypercalcemia in transplant recipients (KTRs) is frequently caused by persisting hyperparathyroidism. However, hypercalcemia can also be a prodromal feature of serious underlying infections and malignancy. We present 2 cases of parathyroid hormone (PTH) independent hypercalcemia that preceded Pneumocystis jirovecii pneumonia (PJP) diagnosis.

Case Description: Case1. A 21 y.o. male with end-stage kidney disease (ESKD) from FSGS presented with 3 weeks of dyspnea and cough 8 months after transplant (Tx). Chest x-ray (CXR) showed interstitial opacities. Lab revealed acute kidney injury and severe hypercalcemia. He was initially treated with IV fluid and calcium, and hypercalcemia improved (Figure 1). Workup showed significant elevation in 1,25 dihydroxyvitamin D (1,25(OH)2 VitD)and low PTH level, and his sputum was positive for PJP by DNA PCR. Case2. A 26 y.o. male with ESKD from nephronophthisis presented with 2 weeks of cough and dyspnea 10 yrs after Tx. He had severe hypercalcemia, and CXR showed nodular interstitial opacities. He was diagnosed with PJP by sputum DNA PCR. His hypercalcemia workup also revealed elevated 1,25(OH)2 VitD and low PTH.

Discussion: PJP occurs in 5–15% of KTRs without prophylaxis with significant morbidity and mortality. A timely diagnosis is challenging given its indolent presentation. Since hypercalcemia can occur in 20-30% of cases during early stages of PJP from increased production of 1,25(OH)2 VitD via 1α-hydroxylase from alveolar macrophages, its presence should alert clinicians of its diagnosis. In 2019, 2 out of 5 PJP cases at our center had hypercalcemia at least 2 weeks prior to PJP diagnosis with high 1,25(OH)2 VitD and low PTH. In both cases, hypercalcemia resolved after treatment of PJP. These 2 cases illustrate hypercalcemia could be a prodromal feature in PJP. Early recognition with appropriate treatment would significantly reduce its morbidity and mortality.

Clinical characteristics

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Normal Range</th>
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<tbody>
<tr>
<td>Hypercalcemia</td>
<td>Yes</td>
<td>Yes</td>
<td>&lt;10 mg/dL</td>
</tr>
<tr>
<td>Pneumocystis jirovecii pneumonia</td>
<td>Yes</td>
<td>Yes</td>
<td>Acute Kidney Injury</td>
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Underline represents presenting author.
Effect of UNOS Kidney Allocation System on Transplantation Rates for Veterans Waitlisted at Veterans Affairs Transplant Centers
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Background: Impact of new Kidney Allocation System (KAS) on kidney transplantation (KT) rates for patients waitlisted at Veterans Affairs Transplant Centers (VATC) is unknown. This study compares effect of KAS on waitlisted patients at VATC and non-VATC.

Methods: UNOS data on adult patients waitlisted for KT during January 2009 to December 2016 were obtained. Logistic regression was used to assess association between center type (VATC vs. Non-VATC), time period (pre-KAS 2009-2014 vs. post-KAS 2015-2016) and outcomes (receiving KT or death on waitlist) within 2 years of waiting. Odds ratio (OR) was calculated adjusting for demographic factors, comorbidities, calculated Panel Reactive Antibodies (cPRA) and Estimated Post-Transplant Survival (EPS) score.

Results: During study period, a total of 263,410 patients were listed at non-VATC (75% pre-KAS; 25% post-KAS) and 3,150 at VATC (68% pre-KAS, 32% post-KAS). VATC patients were significantly older (58.3 vs. 51.7 years), diabetics (55.4% vs. 42.5%), had lower cPRA, higher EPS (53 vs.39%) and longer duration of dialysis (762 vs. 727 days). Within 2 years of waitlisting, Veterans listed at VATC did not benefit from the new KAS like patients in non-VATC centers. Overall, independent of the era, Veterans tend to be transplanted lesser in this early waitlisting period. But waitlist death was 29% in VATC patients. (Results are shown in the table)

Conclusions: Benefit of new KAS did not extend to Veterans listed at VATC who are older, less immunogenic and have higher EPS score. Early benefit of KAS seen in non-VATC could be due to “bolus effect” from transplantation of younger, highly sensitized patients. However, risk of death is significantly lower in VATC waitlisted patients.

Outcomes of patients within 2 years of waitlisting for kidney transplantation

PO2480
Lend Me Your Ear: An Unusual Presentation of a Transplant Complication
Meredith McAdams, Kruti Yagnik, Swae-Ling Levea, Jeffrey Tessier, Reuben J. Arasaratnam. University of Texas Southwestern Medical School, Dallas, TX.

Introduction: Infections are a major complication in solid organ transplant (SOT) patients due to need for life-long immunosuppression. Incidence of fungal infections following solid organ transplant ranges from 5-20%. Cryptococcosis is an invasive fungal infection that can cause several types of infections including meningitis, pulmonary, cutaneous, and disseminated disease.

Case Description: A 66 yo F with past medical history of ESRD s/p deceased donor kidney transplant 15 months ago, DM, HTN presented to renal transplant clinic with right ear pain for the past 4 weeks after being evaluated in the emergency room. Her exam was notable for painful ear and cheek lesions (Figures A and C). Fungal serologies were taken and patient was sent to dermatology clinic for evaluation. Punch biopsies were taken from several lesions and cultures obtained. Serum cryptococcal antigen was positive with titer of 1:4096. fungal culture from lesion grew Cryptococcus neoformans. Skin biopsy showed cryptococcus (Figure B). Patient was admitted to the hospital and further testing revealed positive CSF cryptococcal antigen, CT chest with nodular involvement. Patient was admitted to the hospital

Discussion: Cryptococcal infection is the third most common invasive fungal infection in SOT patients and typically presents later in kidney transplant patients, 16-21 months, compared to other transplanted organs. Risk factors include type of immunosuppressive agent and comorbid conditions such as diabetes. The majority of transplant patients with cryptococcus present with CNS manifestations or disseminated disease, cutaneous involvement is less common. Our patient had risk factors including diabetes, older age, and use of induction immunosuppression. Initial presentation with skin lesions is atypical for cryptococcal infection. It is important to have a high suspicion for fungal infections in immunosuppressed patients even those with atypical presentations.

PO2481
Pegloticase for Uncontrolled Gout in Kidney Transplant Recipients: Early Data Report of a Multicenter, Open-Label Efficacy and Safety Study
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Background: Gout is common and more severe in US kidney transplant (KT) recipients, with prevalence >10% higher than in non-transplant patients. The management of gout can be challenging in KT patients due to decreased urate lowering therapy (ULT) clearance and drug-drug interactions. Recent reports suggest that pegloticase, a pegylated uricase approved for treating uncontrolled gout, has improved efficacy and safety when co-administered with immunosuppressive medications (IMM). We conducted the PROTECT trial (NCT04087720) to examine pegloticase use in KT recipients.

Methods: Patients with uncontrolled gout (sUA ≥7 mg/dL, intolerance of or contraindication to ULT, and a of the following: tophus, chronic gouty arthritis, a2 flares in past y) and functioning KT graft (eGFR ≥15 mL/min/1.73m2) are included (KT ≥1 yr earlier). Pegloticase (8 mg q2w for 24 wks) safety and efficacy are examined. Primary endpoint is ≥5% pegloticase responders during Month 6 (sUA <6 mg/dL for ≥80% of time).

Results: 7 patients were enrolled by Apr 30, 2020 (age: 52.0±11.2 yrs, KT 15.3±5.0 yrs ago, sUA: 10.0±1.4 mg/dL, gout duration: 5.9±4.3 yrs; all on stable doses of a2 IMM) and received 2-12 infusions. 1 patient discontinued. In the 1 completed and 5 ongoing patients, all central lab sUA levels were <1 mg/dL, indicating treatment response; no infusion reactions occurred. No notable eGFR changes were observed; 2 patients with baseline albuminuria of >300 mg/g showed >35% reduction in UACR by wk 14. 2 SAEs (stomach ulcer, cellulitis) unrelated to pegloticase were reported.

Conclusions: Early data of this ongoing clinical trial are promising and suggest pegloticase is safe and effective for treating uncontrolled gout in KT recipients. Additional efficacy and safety data are planned.

Funding: Commercial Support - Horizon Therapeutics

PO2482
Minoxidil-Induced Chylous Ascites in a Renal Transplant Recipient
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Introduction: Chylous ascites is generally associated with malignancies and surgical trauma and rarely secondary to administration of drugs.1 Pathak et al. JClinMed.2019;8:94. Calcium channel blockers related chylous ascites is more common is Asian ethnicity we could not find any published report of minoxidil causing chylous ascites.

Case Description: This patient is a 64 years old diabetic and hypertensive male who underwent kidney transplantation on 09.06.2009. He was HBsAg positive for last 9 years. He was taking multiple medications namely carvedilol, amplodipine, lasix, metformin and linagliptin and Entecavir. He came in May 2019 with ascites. Investigation revealed normal kidney function and ultrasound guided ascitic fluid tapping was done and it was found to be chylous. He underwent abdominal paracentesis and about 12 lt of ascitic fluid was drained but he came back within 10 days with ascites again. Portal hypertension was ruled out by transhepatic hepatic venous pressure gradient measurement and liver biopsy did not show any evidence of chronic liver disease. An upper GI endoscopy and duodenoscopy including duodenal biopsy were normal. Whole body PET scan did not show any active infection or disease. Meanwhile literature review suggested association of minoxidil with chylous ascites and it was stopped but he continued to develop recurrent ascites. An abdominal CT lymphangiogram was done which did not show any lymphatic leak.

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He also underwent diagnostic laparoscopy which also ruled out TB or any malignancy. This patient had bilateral chylous ascites for 6 months then we decided to discontinue minoxidil as it is known to cause fluid accumulation including pleural and pericardial. He showed immediate improvement after stopping minoxidil and never developed ascites again. He was fine even 6 months later on follow up.

Discussion: Minoxidil causes vasodilatation like calcium channel blockers though by a different mechanism so the mechanism of chylous ascites formation could be the same that it is also a lipophilic drug allowing it to pass rapidly into the lymphatic system and causes relaxation of smooth muscles of lymphatic vessels, interferes with lymphatic drainage, and increases the hydrostatic pressure in lymph vessels and causing it to leak in the peritoneum. Minoxidil must be considered as a probable cause of atrumatic drug induced chylous ascites.

PO2483
COVID-19 in Kidney Transplant Recipients: Experience from a Large Health System in Louisiana
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Background: Infections are an important cause of morbidity and mortality among kidney transplant recipients. The novel Coronavirus Disease 2019 (COVID-19) has affected all kinds of populations world-wide. However, the role of immunosuppression in the outcomes of these patients is not well understood.

Methods: We conducted a retrospective study in kidney transplant recipients from a single health system that were diagnosed with COVID-19 based on a positive real-time reverse transcription polymerase chain reaction test for SARS-CoV-2 RNA between March 2020 and October 2020. We compared them with a control case-matched group without a kidney transplant and without any kind of immunosuppressive medication (control). We examined the rates of hospitalization, intensive-care unit (ICU) admission, acute kidney injury (AKI) and mortality as outcome measures.

Results: A total of 8473 patients were diagnosed with COVID-19 within our Health System within the study period. Thirty-three (0.4%) were kidney transplant recipients. Sixteen of the 33 (48%) were admitted to the hospital (median age of 56, 68% males, 93% African American) vs 2201 admissions (25%) for the control group (median age 66, 48% males, 65% African American), i.e., a significantly greater risk for hospitalization for transplant recipients (p = 0.006). Percentage of patients with hypertension in the transplant group was numerically higher (93% vs 80%, p = 0.06), as well as the number of ICU admissions (43% vs 28%, p = 0.055). AKI was more common in transplant patients (81% vs 33.8% p<0.0001). No difference in mortality was observed (31 vs 24%, p = 0.34). Among transplant patients, those hospitalized were more likely to be on prednisone (75% vs 35%, p = 0.025) and had a post-transplant graft life of 7.9 years compared to 5.5 years for those not hospitalized, p=0.08.

Conclusions: Kidney transplant recipients affected with COVID-19 exhibited a greater incidence of hospitalization, AKI and a trend for more ICU admissions. Use of immunosuppression with prednisone was associated with greater risk for hospitalization.

PO2484
Recurrent Anemia due to Chronic Parvovirus B19 Infection in a Kidney Transplant Recipient: Can Everolimus Make a Difference?
Diana Rodriguez-Espinosa, Nuria Esforzado, Fritz Dickmann, Ignacio Revuelta. Hospital Clinic de Barcelona, Hospital Clinic de Barcelona, Barcelona, Spain.

Introduction: Parvovirus B19 (PB19) is a common infection among transplant recipients. Usually, it is asymptomatic, but some patients may suffer severe infections, often presenting with recurrent flares despite standard treatment. Relapses are usually managed by reducing immunosuppressive treatment (IST), potentially increasing graft rejection risk.

Case Description: 45-year-old woman with ESKD due to ADPKD, received a living-donor kidney transplant on May 2013. Maintenance IST consisted of mycophenolate mofetil (MMF), prednisone and tacrolimus. A month after transplantation, she presented with fever and anemia. A bone marrow aspirate revealed pure red blood cell aplasia (PRCA) which was attributed to PB19 after positive serum qualitative PCR. She was treated intravenous immunoglobulin (IVIG) at 2g/kg and MMF was stopped with good response. However 3 new relapses occurred (anemia and malaise with viral loads for PB19 over a million copies). A monthly prophylactic dose of IVIG was initiated to control the infection. In spite of this, episodes of anemia and a high PB19 viral load (over a half million copies) continued to happen at least 3 times per year. Finally, given the potential antiviral properties of mTOR inhibitors (mTORi), conversion from tacrolimus to everolimus was decided. Since November 2017 her maintenance IST consists of everolimus and prednisone alone, her last prophylactic IVIG was on December 2017, to everolimus was decided. Since November 2017 her maintenance IST consists of mTORi. A month after transplantation, she presented with fever and anemia. A bone marrow aspirate revealed pure red blood cell aplasia (PRCA) which was attributed to PB19 after positive serum qualitative PCR. She was treated intravenous immunoglobulin (IVIG) at 2g/kg and MMF was stopped with good response. However 3 new relapses occurred (anemia and malaise with viral loads for PB19 over a million copies). A monthly prophylactic dose of IVIG was initiated to control the infection. In spite of this, episodes of anemia and a high PB19 viral load (over a half million copies) continued to happen at least 3 times per year. Finally, given the potential antiviral properties of mTOR inhibitors (mTORi), conversion from tacrolimus to everolimus was decided. Since November 2017 her maintenance IST consists of everolimus and prednisone alone, her last prophylactic IVIG was on December 2017, and since then she has been non-anemic with serum viral loads below 1000 copies, and without IVIG treatment.

Discussion: Incidence of symptomatic PB19 infection is highest during the 1st year after transplantation, like in the case presented. Standard therapy consists of IVIG. However, early KR, often relapse after the IVIG effect wears off. In such cases, reduction of IST is needed to control the infection and avoid recurrences. There are multiple studies indicating that mTORi have antiviral properties although their effect on PB19 has not been specifically studied. In conclusion, conversion from tacrolimus to an mTORi, could be an interesting approach in difficult-to-manage cases similar to ours, moderating the reduction of IST and minimizing the risk of rejection. Further studies are needed to establish this approach as “treatment of choice” in relapsing PB19 infection.

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Racial-Ethnic Disparities in Preemptive Kidney Transplantation Among Incident ESKD Adult Patients, 2006 to 2018

Background: Preemptive kidney transplantation (PKT) is the preferred treatment for ESKD. Among kidney transplant recipients, black and Hispanics are less likely to receive PKT than whites, but less is known about disparities in PKT among the entire incident ESKD population. This is a critical gap in knowledge given the Advancing American Kidney Health goal of 80% of all new ESKD patients receiving transplant or home dialysis by 2025. This study assessed racial/ethnic disparities in initial treatment with PKT vs. dialysis among all incident ESKD failure patients aged 19-74 from 2006 to 2018.

Methods: Treatment modality for incident ESKD patients was identified using the CMS Medical Evidence Report Form. Linear regression models estimated PKT rates for dialysis by 2025. This study assessed racial/ethnic disparities in initial treatment with PKT among incident ESKD adult patients, black and Hispanics are less likely to receive PKT than whites, but less is known about disparities in PKT among the entire incident ESKD population. This is a critical gap in knowledge given the Advancing American Kidney Health goal of 80% of all new ESKD patients receiving transplant or home dialysis by 2025. This study assessed racial/ethnic disparities in initial treatment with PKT vs. dialysis among all incident ESKD failure patients aged 19-74 from 2006 to 2018.

Results: Among 1,133,326 incident ESKD adult patients, the age/sex adjusted PKT rate declined from 3.0% in 2006 to 2.5% in 2018, with varied trends in each racial/ethnic group (white: 5.0% to 4.0%, black: 0.3% to 0.7%, Hispanic: 1.3% to 1.3%, and Asians: 2.4 to 2.9%) (Figure). In age-sex adjusted analyses, whites had 3.9, 3.2, and 1.7 percentage points lower PKT rates than blacks, Hispanics, and Asians, respectively. These differences persisted after adjusting for clinical, geographic, socioeconomic, and access factors.

Conclusions: Among incident ESKD adult patients, racial/ethnic disparities in receipt of PKT are substantial, persistent, and not explained by differences in observed clinical factors and socioeconomic status. Efforts to increase preemptive transplantation must address disparities in access to this preferred treatment for ESKD.

Funding: NIDDK Support

PO2487

Lower Prevalence of Kidney Transplant Waitlisting in Micropolitan Areas, Small Towns, and Rural Areas

Background: The Percentage of Prevalent Patients Waitlisted (PPPW) measures the percentage of patients at a dialysis facility who were on the kidney or kidney-pancreas transplant waitlist. This measure joined the End Stage Renal Disease Quality Incentive Program in performance year 2020, with a weight of 4%. PPPW is adjusted for age, but not for other factors. Physical distance between residence and transplant center may influence PPPW. As an indirect test of this hypothesis, we assessed whether PPPW was associated with rural-urban commuting area (RUCA) levels.

Methods: We analyzed data in Dialysis Facility Compare (DFC), as of October 30, 2019. DFC included PPPW values that quantified waitlisting prevalence during 2018. According to ZIP code, we classified the location of each dialysis facility as metropolitan (RUCA values, 1-3), micropolitan (4-6), small town (7-9), or rural (10). We estimated weighted mean PPPW values in each location class, with the weight of each facility equal to the number of patients contributing to PPPW. We fit a linear regression model to test differences in PPPW values between the location classes.

Results: PPPW values were reported in 7086 (94%) of 7566 dialysis facilities, and RUCA values were identified in 6999 (99%) of 7086 facilities. The weighted mean PPPW value among all facilities was 17.5%. There were 5363 (77%) facilities in metropolitan areas, 954 (14%) in micropolitan areas, 550 (8%) in small towns, and 132 (2%) in rural areas. By location class, weighted mean PPPW values were 18.5% in metropolitan areas, 12.8% in micropolitan areas, 12.1% in small towns, and 10.8% in rural areas. Relative to the mean PPPW value in metropolitan areas, mean PPPW values were 5.8, 6.5, and 7.7 percentage points lower in micropolitan areas, small towns, and rural areas, respectively (P < 0.01 for each).

Conclusions: The PPPW measure takes significantly lower values in dialysis facilities located in micropolitan areas, small towns, and rural areas, relative to metropolitan areas. The physical distance between residence and transplant center may preclude many patients in non-metropolitan areas from completing the process of kidney transplant evaluation. New processes are needed to improve access to transplantation in outlying areas.

Funding: Commercial Support - Fresenius Medical Care

PO2489

Demonstrating Charitable Premium Assistance as a Mechanism for Overcoming the Cost Barrier to Transplant for Low-Income Patients in the United States

Background: The optimal treatment for patients with end-stage renal disease (ESRD) is kidney transplantation. Adequate insurance coverage is one requirement for transplant eligibility. Many low-income ESRD patients cannot afford insurance coverage. Patients on dialysis are eligible for Medicare. Because Medicare covers only 80% of healthcare costs, most patients require supplemental insurance, often Medigap. Although Medigap

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plans reduce out-of-pocket spending on healthcare services by almost 50%, spending on burberry products more than doubles compared to Medicare premiums alone. For low-income patients who cannot afford such premiums, inadequate insurance coverage can become an insurmountable barrier to qualifying for a kidney transplant (KT). We evaluated a premium assistance program designed to help low-income ESRD patients maintain insurance coverage and the impact on KT access.

Methods: We performed a descriptive analysis of self-reported patient data collected from paper and digital applications submitted to American Kidney Fund’s (AKF) Health Insurance Premium Program (HIPP) between November 15, 2018 and December 31, 2019.

Results: HIPP provided financial assistance grants to 1,357 (5.8% of all) kidney patients transplanted in the United States during the study period so they could maintain their health coverage in 2019. Of the 1,357 grants, 36% of grants issued helped patients pay Medigap. Average monthly recipent recipients’ per month were to be $62 (78% vs. 12%), more likely to be African American (38% vs. 34%), and had lower median income ($23,622 vs. $27,168 respectively) compared to the overall transplant population.

Conclusions: KT candidates face financial barriers to transplantation. Premium assistance significantly reduced the barrier to transplant among KT candidates who rely on Medigap for ensuring adequate coverage.

PO2490
“Some Person Behind a Desk Is Going to Be Looking at My File”: Thematic Analysis of the Health Records of a National Sample of Patients with Advanced Kidney Disease Evaluated for Kidney Transplant

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Background: To be considered for kidney transplant, patients with advanced kidney disease must participate in a formal evaluation and selection process. Little is known about how this process unfolds in real-world clinical settings.

Methods: We conducted a thematic analysis of clinician documentation related to the kidney transplant evaluation in the VA-wide electronic medical records of patients who were referred to a transplant center among a random sample of 4,000 adults with advanced kidney disease between 2004 and 2014 who were followed through 2019.

Results: We identified 211 patients (5.2%) who were referred to a VA transplant center during follow-up. Four dominant themes emerged from qualitative analysis of clinician documentation in the electronic medical records of these patients: 1) far-reaching and inflexible medical evaluation: patients were expected to complete a demanding evaluation that could take a substantial physical and emotional toll on them and their family members, made little accommodation for their individual needs, and impacted many other aspects of their care; 2) psychosocial valuation: the psychosocial transplant assessment could be subjective and intrusive and placed substantial demands on patients’ family members; 3) surveillance over compliance: clinicians monitored patients’ adherence to a wide range of medical recommendations; 4) disempowerment and lack of transparency: patients had a strong desire to receive a transplant, but neither they nor their local clinicians had a clear understanding of what to expect from the evaluation process or the rationale for selection decisions, which left patients and their clinicians with little choice but to adhere to the transplant center’s recommendations.

Conclusions: To be considered for kidney transplant, patients had little choice but to engage in an extensive, demanding, opaque evaluation over which neither they nor their local clinicians had much control. These findings call for a more evidence-based, transparent, and individualized approach to the kidney transplant evaluation process.

Funding: Veterans Affairs Support

PO2491
Implicit Bias in Recipient Selection

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Background: The decision to place or exclude a candidate from the waitlist is not exclusively based on medical criteria. Scarl literature exists regarding the intergroup dynamics within selection committees that influence decision making. This study attempts to clarify how the composition of selection committee meetings may affect listing outcome of kidney transplant candidates.

Methods: We performed a single-center retrospective study of kidney transplant selection committee attendance sheets and minutes from January 2012 to December 2015. We sought to determine if candidates who were evaluated by the same providers in attendance at selection committee are more likely to be listed for kidney transplant.

Results: 5205 (48.4%) of 6630 donor and recipient candidates presented during 91 selection committee meetings from 2012 to 2015 were listed. 8 nephrologists, 9 surgeons and 3 social workers comprised the clinicians that both evaluated potential candidates and attended recipient selection meetings. Table 1 describes the frequency with which clinicians who were in attendance at selection meetings had previously evaluated the candidates being listed and the number of times over which neither the nephrologists nor the surgeons who had evaluated the patient was significantly associated with a greater likelihood of the candidate being listed (OR 4.443 and 3.952 respectively, p=0.006, see Table 2). White race was also associated with an increased propensity to list, OR 1.202, p=0.006. Interestingly, the presence of both the nephrologist and surgeon who evaluated the patient, or the presence of both physicians and the social worker, were associated with reduced likelihood of listing (OR 0.267 for both, p=0.000 ; OR 0.715, p=0.001 for all three, see Table 2).

Conclusions: The composition of attendees at recipient selection meetings may influence listing outcomes of potential kidney transplant candidates.

PO2492
Predictors of Kidney Transplant Evaluation Non-Attendance

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Background: We examined which medical and socio-cultural factors predict kidney transplant evaluation (KTE) non-attendance, because missing a KTE appointment precludes access to transplantation, and having empty clinic slots impacts access to care for other patients.

Methods: We collected patient characteristics in an interview prior to KTE, covering demographics (e.g., income, education), medical factors (e.g., on dialysis, co-morbidities), cultural factors (e.g., medical mistrust), psychosocial characteristics (e.g., social support, knowledge of kidney transplantation), and knowledge and attitudes (e.g, knowledge class analysis (LCA)) to determine if we could identify meaningful classes (groups of patients with patterns across variables) that were associated with KTE non-attendance.

Results: Our sample (N=1119) was 37% female, 76% non-Hispanic White, median age 59±4 years (IQR= 49.2-67.5), 25% had income below federal poverty line, 47% were ≤ high school graduate, 48% were married, 44% had public insurance only, and 142 (13%) did not attend KTE appointment. LCA analyses indicated that a two-class solution consisting of a (1) high burden and (2) low burden group was optimal. Relative to the low burden group, the high burden group was less likely to be married, more likely to be on dialysis, less likely to have potential living donor, had higher kidney disease burden, more experiences of healthcare discrimination, higher medical mistrust, less social support, more depression, less knowledge about transplant, and more worry about kidney transplant harm. Belonging to the high burden group was associated with approximately twice greater odds of KTE non-attendance (OR=1.92, p<0.001, 95% CI 1.57, 2.34).

Conclusions: Medical and socio-cultural factors predict KTE non-attendance. Transplant teams should consider targeting patients with characteristics indicating high burden for additional support (e.g., exploring motivation and barriers with patients, assisting with resources to attend appointment, and providing additional reminders or notifications). Given the association of clinic non-attendance with being on dialysis, a treatment with significant patient burden, future research should also focus on the benefits of referring patients for transplant evaluation prior to initiating dialysis.

Funding: NIDDK Support, Clinical Revenue Support

PO2493
Racial Disparities in Receipt of Medications for Secondary Prevention of Cardiovascular Disease in Kidney Transplant Recipients in the FAVORIT Trial

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Background: Cardiovascular disease (CVD) is the most common cause of death with a functioning graft in kidney transplant recipients. Black patients have been shown to have higher prevalence of cardiovascular (CV) risk factors and less intensive risk factor modification. We evaluated racial disparities in receipt of HMG-CoA reductase inhibitors (statins) and aspirin for secondary prevention of CVD in kidney transplant patients in the Folic Acid for Vascular Outcome Reduction in Transplantation Trial (FAVORIT) trial.

Methods: FAVORIT was a multicenter international trial of vitamin therapy to lower low density lipoprotein (LDL) CV outcomes in kidney transplant patients. We identified FAVORIT trial participants from US and Canada who had a self-reported

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Underline represents presenting author.
Long-term kidney graft survival may be affected by factors other than biologic, including social determinants of health such as food scarcity and psychosocial stress. Methods: A face-to-face survey was conducted in a random convenience sample of 31 pts in transplant clinic: The Stress and Social Support survey and the Perceived Stress Scale were used. Dietary intake was assessed using 24-hr recall and analyzed with ASA-24 software. All comparisons are by Chi square or t-test.

Results: There were 11 women(36%), 20 men(65%), 22 Black(71%). Mean age was 55.2±1.9 yrs, time since transplant 63.9±14.1 mos. 24 (77%) reported income <$40K, with 12 (39%)<$20K.12 (39%) received SNAP benefits (SNAP+). Income or employment rate did not differ for SNAP+ vs SNAP-. SNAP+ had significantly worse kidney function(creatinine 2.17±0.24 vs 1.44±0.11 mg/dL=p<0.01) and eGFR(37.9±3.8 vs 53.8±7.5 mL/min,p<0.01). SNAP+ also did not differ for time since transplant, gender, race, BMI, tacrolimus level or age. SNAP+ also were more likely to disagree with the statement “I feel I am in control of my health and it doesn’t control me” (33% vs 0%, p=0.017), to report never or almost never feeling confident about handling personal health problems (33% vs 16%, p<0.018), and to be unable to control irritations in their lives(67% vs 16%, p<0.043,p<0.043). No difference in caloric or macronutrient intake existed, but SNAP+ ate less macronutrients(11.1±3 vs 16.7±1.8 gmp, p=0.023)and fewer servings of fruits/vegetables(1.5±0.28 vs 3.75±0.85, p<0.021). When asked about missed medication they did not report more missed doses.

Conclusions: In our patient population: 1. Pts receiving SNAP had worse kidney function than those who did not despite similar time since transplant, tacrolimus level, income, and employment status. 2. They ate less fiber and fewer servings of fruits/vegetables despite similar caloric intake, which should be investigated further as higher intake of fruit/vegetables is associated with delayed progression of kidney disease in non-transplant pts. 4. They also reported feeling less control over their health and less ability to handle daily stress. 4. These findings suggest that special attention should be paid to this population who have issues with social determinants that may affect kidney function.

Impact of Ethnicity Matching on Kidney Transplant Outcomes Among African Americans: A Mate Kidney Analysis
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Background: Transplantation of kidneys from African American (AA) donors is associated with poorer outcomes compared to transplants from white Americans. Unmeasured variables such as APOL1 renal risk variants and sickle cell trait could contribute to the heightened risk. We used a mate kidney model to test the hypothesis that enhanced genetic risks associated with AA donor kidneys could be counterbalanced by favorable immunologic matching when AA donor kidneys are transplanted into AA recipients.

Methods: We identified AA deceased donors in OPTN/UNOS database from 2000 to September 2019 in which both kidneys were transplanted into first-time kidney-eligible recipients only, and both recipients received induction therapy followed by tacrolimus/mycophenolic acid maintenance. Marginal models for hazards of graft failure, death censored graft failure (DCGF) and death were constructed, with adjustments for recipient and transplant variables. Outcomes of AA, Hispanic, and Asian recipients were compared, using white American recipients as reference. Results were compared to a parallel analysis of 41,886 recipients of white American donor kidneys.

Results: Median follow up of the study was 3.3 (IQR 1.1-6.5) years among 8194 paired recipients of AA donor kidneys. Despite donor ethnicity matching, DCGF was higher for AA recipients compared to recipients with white donor kidneys. These findings were consistent across all recipient types. Outcomes of AA recipients were compared to a parallel analysis of 41,886 recipients of white American donor kidneys.

Conclusions: Our data indicate an increased risk of DCGF in AA recipients of AA donor kidneys, despite the potential benefits of favorable immunologic matching and does not support an ethnicity-matching strategy to improve outcomes and reduce disparities. Our observations suggest that other recipient factors predominantly influence graft outcomes. Improved outcomes in Hispanic and Asian patients merit further study.

Funding: Private Foundation Support
PO2498

Cardio-Metabolic Risk Factors in Kidney Donors at a Third-Level Hospital of Care in Mexico

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Background: Living donor kidney transplantation is the treatment of choice for chronic terminal kidney disease. A high prevalence of cardio-metabolic risk factors (CRFs) in the general population implies challenges when choosing the best candidate for kidney donation. Knowing the frequency of CRFs will allow us to make timely interventions in order to reduce cardiovascular complications after donation.

Methods: Cross-sectional, descriptive study, which included kidney donors who were admitted to the National Medical Center “Dr. Antonio Fraga Mouret” during the period from 2015 to 2019. Descriptive statistics were made, with a 95% CI. CRFs were included; systolic hypertension (SBP) higher than 120mmhg, diastolic hypertension (DBP) higher than 80mmhg, anemia hemoglobin less than 13 g/dl in men and less than 12 g/dl in women; impaired fasting glucose ≥110 mg/dl, body mass index (BMI)>25, 28% of donors smoked, 7% had SBP risk and 27% DBP risk, 60% had BMI>25, 4% had anemia and 13% hyperalumunemia; 10% with impaired fasting glucose. Figure 1 shows the prevalence of CRF. More than 25% of kidney donors had 2, 3 and 4 CRFs on admission to hospital for donation. 72% presented acute kidney injury (AKI) after surgery, none required renal replacement therapy. The highest AKI frequency was observed in subjects who had from 1 to 3 CRFs with frequencies of 26-34%.

Results: 153 donors were included, 59% were women, 33% were siblings and 31% were the patient’s mother; 34% had no social security. The mean age was 42 ± 10.7 years; the mean BMI 26 ± 5.4, with a mean GFR 101.9 ± 13.6 (61-133) ml/min. 28% of donors smoked, 7% had SBP risk and 27% DBP risk, 60% had BMI>25, 4% had anemia and 13% hyperalumunemia; 10% with impaired fasting glucose. Figure 1 shows the prevalence of CRF. More than 25% of kidney donors had 2, 3 and 4 CRFs on admission to hospital for donation. 72% presented acute kidney injury (AKI) after surgery, none required renal replacement therapy. The highest AKI frequency was observed in subjects who had from 1 to 3 CRFs with frequencies of 26-34%.

Conclusions: A BMI higher than 25 was the most prevalent CRFs; associated with AKI when more than 1 CRF was observed. Timely detection of CRFs will allow for timely interventions that will reduce post-donation cardiovascular risk and decrease the risk of AKI.

PO2499

The Effect of Anemia Correction with ESA and Cholecalciferol Supplementation on Post-Transplant Malignancy Among Kidney Transplant Recipients: A Prespecified Analysis of a Randomized Clinical Trial

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Background: Kidney transplant recipients (KTRs) are at increased risk of cancer, and post-transplant malignancy (PTM) is among the leading causes of death with functioning allograft. Aggressive anemia correction with ESA shows the rate of decline in kidney allograft function but may increase the incidence of PTM. Vitamin D is proposed to exert anti-tumoral effects including anti-cancer properties and may prevent the development of PTM.

Methods: We enrolled 153 KTRs with anemia and ≥1-year history of transplantation across 23 facilities in Japan and conducted a multicenter, two-by-two factorial, open-label, randomized clinical trial. Patients were randomly assigned to either a high or low hemoglobin (Hb) target (>12.5 g/dl or ≥10.5 g/dl) or to either cholecalciferol 1000 IU/day or control. PTM was a prespecified secondary outcome.

Results: Patients were 51±12 years old, among whom 54% were male. The median (IQR) of transplant vintage was 8 (5, 12) years. Their baseline eGFR, Hb, and serum 25(OH)D levels were 30.6±11.0 ml/min per 1.73 m², 10.7±1.2 g/dl, and 14.5±5.2 ng/mL, respectively. There was no between-group difference in the prevalence of prior malignancy in either arm. The mean Hb level was 11.4±0.6 g/dl and 10.6±0.6 g/dl in the high and low Hb target groups, respectively. The mean serum 25(OH)D level exceeded 30 ng/mL.

Conclusions: ID, low ferritin and low TSAT are consistently associated with poor performance on neurocognitive tests measuring verbal memory, executive functioning, and ID with neurocognitive scores are presented in the table.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

PO2500

Association Between Elevated Ferritin and Graft Survival During the First Year After Kidney Transplant

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Background: Both iron deficiency and iron overload are associated with adverse outcomes in patients with end stage kidney disease on chronic hemodialysis. In contrast, the effect of iron metabolism markers on kidney transplantation has not been thoroughly evaluated. In this study we aimed to evaluate the association between serum ferritin and transferrin saturation during the first year post transplantation on patients and graft survival.

Methods: Retrospective cohort study, using the Rabin Medical Center (RMC) kidney transplant registry. We included adults (>18 years) patients transplanted between 1/1/2006 and 31/12/2017 that had at least one available iron, transferrin and ferritin value during the first year post transplantation. Serum ferritin and transferrin were measured at baseline and at 6 months. Two iron metabolism markers were used for the primary composite outcome of patients’ and graft survival.

Results: Seven hundred and twenty-six patients were included in the study, of whom 219 (30.2%) had serum ferritin above 500 mg/dl. Patients with high serum ferritin were older with more diabetes mellitus (DM) and heart disease and tended to have deceased donors. Graft survival was delayed for high ferritin. In the univariate analysis, high ferritin and transferrin saturation were associated with increased risk of death and graft loss (Hazard Ratio (HR) 2.38, 95% Confidence Interval (CI) 1.69-3.35, p<0.001). In a multivariate model ferritin was still highly associated with increased rate of graft loss (HR 1.87, 95% CI 1.29-2.72, p=0.001). High ferritin was also associated with increased risk of the secondary outcome of death censored graft loss (HR 2.09, 95% CI 1.26-3.48, p<0.005).

Conclusions: High ferritin during the first year post transplantation was associated with reduced graft survival. Further research is needed to evaluate whether this association is due to inflammation, iron overload or combination of the two.

PO2501

Iron Deficiency in Kidney Transplant Recipients: Impact on Cognitive Functioning

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Background: Cognitive function impairment is common in kidney transplant recipients (KTRs). Brain functioning requires energy, for which iron is essential at the level of oxygen delivery and mitochondrial function. Iron deficiency (ID) has been linked to compromised cognitive functioning in premenopausal women. We aimed to investigate whether ID could be a potentially modifiable risk factor for cognitive function impairment in KTRs.

Methods: In a prospective study among KTRs participating in the TransplantLines Biobank and Cohort study, we analyzed KTRs ≥1 yr post-transplant with data on iron status. All participants underwent neurocognitive testing to measure memory (Digit Span Forward, Digit Span Backward, and Delayed Recall of the 15 Word Test), attention and mental speed (Symbol Digit Modalities Test, Trail Making Test-A) and executive functioning (Trail Making Test-B, Digit Span Backward). ID was defined as ferritin <100µg/L or 100-299 µg/mL with transferrin saturation (TSAT) ≤20%. We used multivariable linear regression models to assess associations between ID and neurocognitive outcomes. Analyses were adjusted for hemoglobin, CRP, age, sex, eGFR, BMI, smoking, alcohol intake, time since transplantation, dialysis duration, donor type, educational level and immunosuppressives.

Results: We included 398 KTRs (age 56±14 yrs, 62% male, eGFR 52±14 ml/min/1.73m²). ID was present in 289 (73%). ID with neurocognitive scores are presented in the table.

Conclusions: ID, low ferritin and low TSAT are consistently associated with poor performance on neurocognitive tasks measuring verbal memory, executive functioning,
mental speed and attention in KTRs, independent of hemoglobin and other potential confounders. Future studies should address whether ID correction restores cognitive function.

Discussion: SV use may have more serious GI adverse effects in CKD patients than noted in the original clinical trials. Preexisting GI disease and/or abnormalities may increase the risk of adverse GI effects related to SV. Recent use of SV prior to kidney transplantation or use of SV for control of hyperphosphatemia in the context of DGF can be associated with GI morbidity in the early post transplant setting. Need for higher doses of phosphate binders and severity of hyperparathyroidism may be contributing factors to this risk.

PO2504
C-Terminal and Intact FGF-23 in Kidney Transplant Recipients and Their Associations with Kidney Transplant Loss and Mortality
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Background: Increased fibroblast growth factor 23 (FGF23) is a risk factor for mortality, cardiovascular disease, and progression of chronic kidney disease. Limited data exist comparing the association of either c-terminal FGF23 (cFGF23) or intact FGF23 (iFGF23) in kidney transplant recipients (KTPs) with graft loss and all-cause mortality.

Methods: We conducted a prospective observational cohort study in 562 stable kidney transplant recipients. Patients were followed for graft loss and all-cause mortality for a follow-up of 48 months.

Results: During a median follow-up of 48 months, 94 patients had adverse outcome (graft loss or died). Both cFGF23 and iFGF23 concentrations were significantly higher in patients who had adverse outcome than those without adverse outcome (24.59 [11.43-87.83] vs 14.56 [5.99-22.73] pg/mL; P=0.001 and 45.24 [18.63-99.03] vs 29.04 [15.20-66.65] pg/mL; P=0.002 for cFGF23 and iFGF23, respectively). cFGF23 and iFGF23 measurements correlated well (rho=0.54, P<0.0001). ROC analysis of cFGF23 and iFGF23 yielded AUC of 0.69 (p<0.0001) and 0.61 (p=0.002) for prediction of the composite endpoint, respectively. Cox regression analyses adjusted for confounding factors, showed that cFGF23 (HR for one unit increase of log transformed cFGF23: 1.35; 95% CI, 1.03-1.77; p=0.028) but not iFGF23 (HR for one unit increase of log transformed iFGF23: 1.03; 95% CI, 0.81-1.31; p=0.827) was associated with the composite endpoint (Figure 1).

Conclusions: Elevated cFGF23 levels at baseline are independently associated with an increased risk all-cause mortality or graft loss. iFGF23 measurements were not independently associated with the study endpoint. The iFGF23 ELISA might detect bioactive FGF23 fragments that are not detected by the iFGF23 ELISA.
blood type O recipients decreased by 3.4 years from 2015-2019 (Figure 1). We observed a decrease in disparity between African Americans and Hispanics versus Caucasians, with average waiting times decreasing from 2.5 years to 1.2 years and 1.6 years to 0.5 years, respectively. There were no type B recipients who received A2 donors in this cohort.

**Conclusions:** Waiting time at our center decreased significantly across all blood types with a disproportional benefit in blood group B recipients despite not utilizing the benefits of A2 donors transplanted into B. Thus, this reflects our increase in volumes by utilizing extended criteria donors such as acute kidney injury and high kidney profile index donors (KDPI). These efforts have reduced the disparities in waiting time particularly in African-American and Hispanic populations.

**Funding:** Clinical Revenue Support

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**PO2507**

A Randomized Trial of Vitamin D Supplementation on Skeletal Muscle in Patients Early Post Kidney Transplantation

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**Background:** Developing strategies for managing skeletal muscle weakness and loss in kidney transplant recipients (KTRs) is an important clinical challenge. Little is known about the effect of native vitamin D (ViD) supplementation on skeletal muscle in KTRs.

**Methods:** We conducted a 11-month, double-blind, randomized, controlled trial to assess the efficacy of ViD for improving skeletal muscle weakness and loss in KTRs receiving kidney transplantation within one month. Eligible patients were randomly assigned to a Vitamin D (cholecalciferol, 4000 IU / day) group or a placebo group in a 1:1 ratio. A prespecified secondary endpoints in this study included a percent (%) change in handgrip strength (HGS), and leg strength (LS) for skeletal muscle strength, and skeletal muscle index (SMI) for skeletal muscle mass.

**Results:** A total of 193 KTRs were randomized, but 6 KTRs were lost before taking the medication. We analyzed 92 KTRs in Vitamin D group and 95 in Placebo group. Dropout during this study were 3 KTRs in Vitamin D group and 2 in Placebo group. In Vitamin D group, at baseline the mean age was 52.2 ± 12.5 years old and the number of males was 28 (30.4%), and in Placebo group, 53.7 ± 11.4 years old and 30 (31.5%), respectively. The mean changes in serum 25 hydroxyvitamin D levels from baseline to the end of this study was 11.2 ± 4.1 to 39.8 ± 13.0 ng/mL in Vitamin D group (p < 0.001) and 11.2 ± 4.1 to 14.5 ± 5.0 ng/mL in Placebo group (p < 0.001). In this study, there were no difference in % changes in HGS, LS, or SMI between those groups, respectively.

**Conclusions:** ViD supplementation alone appears not to be effective in improving skeletal muscle weakness and loss among KTRs early post-transplantation. Larger-scale trials are warranted to confirm these findings.
PO2509

Recurrent Cardiovascular Events After Kidney Transplant Are Associated with Increased Risk for Graft Failure and Mortality
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Background: Cardiovascular (CV) disease is prevalent after kidney transplant (KTx). The objective of this study was to describe patients with recurrent CV events in association with allograft function and mortality.

Methods: 1148 consecutive adults that received a KTx between 2011-2013 at a single center were evaluated. CV events were defined as: cardiac: myocardial infarction, heart failure, cardiac arrest requiring resuscitation, and vascular, any stroke, or peripheral vascular disease requiring intervention. Recurrent events were defined as more than one event (either cardiac or vascular).

Results: Mean age was 56.0 years (SD 14.2), 500 (44%) were female, 403 (35%) had diabetes, 1083 (94%) had hypertension, 127 (11%) had prior history of CV events, 98 (8%) had coronary artery disease (CAD), 26 (2%) had cardiac arrest. Mean follow-up of 74 months there were 229 (20%) deaths and 217 (19%) CV events, of which 602 (53%) required dialysis, and 867 (76%) received living donor KTx. After a median of 7 years post KTx heart failure, 38% had diabetes, 1083 (94%) had hypertension, 127 (11%) had prior history of CV events, and 87 (7%) had CAD.

Conclusions: Prevalence of recurrent CV events after KTx was 8.5%. Patients with recurrent CV events are at increased risk for mortality and graft failure. Decreased graft function was the primary predictor of recurrent CV events.

PO2510

Mitril Regurgitation and Aortic Stenosis After Kidney Transplantation
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Background: Valvular heart disease (VHD) is highly prevalent in patients with end stage kidney disease and has been associated with poor outcomes. The 5-year mortality rate among patients with at least mild aortic stenosis (AS) or mitral regurgitation (MR) is more than 50% greater than in persons without kidney disease (Samad et al, JAHA 2017). Current knowledge of VHD in patients after kidney transplantation (KT) is scarce.

Methods: This is an ongoing single center retrospective study. In our center, all KT recipients have echocardiograms within one year prior to KT. We included KT recipients at our institution between Jan 2016 and Dec 2016 who had underlying MR and/or AS of any severity. Participants had to have an echocardiogram (Echo) around one year post KT. Our primary objective was to compare the severity of MR and AS at one year post KT to the baseline severity. The secondary objective was to describe changes in left ventricle hypertrophy (LVH).

Results: Two hundred subjects were initially screened. The number of patients that met our inclusion criteria was 22 (Table 1). Mild MR was present in 10 recipients pre KT. MR improved in 4, remained stable in 4, and worsened in 2 out of these 10 recipients at one year post KT. Moderate MR was present in 7 recipients pre KT and all 7 had improvement in severity of MR at one year post KT. Two and three recipients had mild AS and moderate AS respectively pre KT and all of them were observed to have worsening of aortic valve area (AVA) at one year post KT (mean AVA 1.36 versus 1.15 cm2, p < 0.07). Nine out of the total 22 recipients included had mild LVH pre KT and all the 9 continued to have mild LVH post KT.

Conclusions: Our study showed that most KT recipients with pre-existing MR had improvement in the severity of MR at one year post KT. However, recipients with AS prior to KT were observed to have worsening in severity of AS at one year post KT. Larger studies are needed to confirm these findings and identify factors that influence progression.

Table 1. Clinical Characteristics

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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**PO2512**

Utility of the 6-Minute Walk Test in Coronary Artery Disease Screening Before Kidney Transplant

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**Background:** Coronary artery disease (CAD) screening is a cornerstone of kidney transplant (KTx) evaluation, but existing approaches result in excessive testing and low intervention rate. We hypothesize that aerobic performance, based on a simple office test (the 6-minute walk test, 6MWT), may help risk stratify KTx candidates.

**Methods:** We performed 6MWT in waitlisted patients who were nearing KTx. Results were used for frailty counselling and not for cardiac evaluation. CAD screening was done according to our center protocol: invasive angiogram for patients with long-standing diabetes mellitus (DM) and non-invasive testing for other patients with risk factors and at the evaluating transplant nephrologist’s discretion. We used subdistribution Cox regression and time-dependent receiver operator curve to evaluate time to CAD event (revascularization, myocardial infarction, waitlist removal for CAD, or cardiac death), treating waitlist removal for non-CAD and non-cardiac death as competing events.

**Results:** Of the 360 patients, 200 and 161 patients had 6MWT results <400 meters and ≥400 meters (<4 metabolic equivalents), respectively. Patients with lower 6MWT results were older (59±10 vs 50±12 years) and more likely to be female (54% vs 34%), have DM (61% vs 33%) or known atherosclerotic disease (44% vs 22%), and have had prior cardiac evaluation (72% vs 61%). They were also more likely to exhibit cardiac symptom during 6MWT (36% vs 6%) and more likely to be censored due to waitlist removal for non-CAD reasons (follow-up 391±337 vs 541±277 days). 6MWT was not associated with CAD event (subdistribution hazard ratio 1.00 [0.90-1.10], 1-year area under the curve [AUC] 0.54). 196 patients had invasive (52%) or non-invasive (48%) CAD testing within 6 months of 6MWT: 6MWT did not predict the CAD test result (odds ratio 0.96 [0.81-1.14], AUC 0.54). Of the 94 patients who had concurrent non-invasive CAD testing, the 1-year AUC of 6MWT, symptom (at rest or during 6MWT), AST guidelines, or non-invasive testing for CAD event were 0.64, 0.52, 0.46 and 0.66 respectively.

**Conclusions:** The 6MWT did not perform better in risk stratification for CAD events compared to a symptom- or risk factor-based approach.

**Funding:** Private Foundation Support

**PO2514**

Abstract Withdrawn

**PO2515**

A Devastating Complication of Encapsulating Peritoneal Sclerosis (EPS) In Two Renal Transplant Recipients

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**Introduction:** EPS is a rare complication of peritoneal dialysis (PD) which carries great morbidity and mortality. The risk of EPS may be higher in PD patients who undergo renal transplantation as compared to PD patients who do not receive a transplant. Pre-transplant EPS, progressive peritoneal remodeling, cessation of PD and use of calcineurin inhibitors are potential etiologies. We present two unique cases of post-transplant EPS requiring surgical intervention with devastating outcomes.

**Case Description:** Case #1 A 47-year-old female with end stage renal disease due to congenital kidney disease on PD for 8 years transitioned to hemodialysis due to peritonitis, underwent a deceased donor kidney transplant (DDRT) presented 4 weeks post operatively with nausea, vomiting, and abdominal pain. Imaging showed dilated loops of small bowel concerning for partial small bowel obstruction treated non-operatively with bowel rest. One month later she presented with similar symptoms and small bowel obstruction. Due to failure to improve, she was taken to surgery and was found to have a frozen abdomen with dense adhesions. Lysis of adhesions was complicated by enterotomies and small bowel resection. Multiple enterocutaneous fistulas prohibited wound closure. She is being evaluated for a small bowel transplant and remains on parenteral nutritional support. Case #2 A 39-year-old African female with history of ESRD secondary to Lupus on PD for 11 years received a DDRT. Eighteen months post-transplant, she presented with nausea, vomiting and abdominal pain. Imaging showed a small bowel obstruction treated non-operatively with bowel rest. Three weeks later she required emergent surgery for an acute abdomen undergoing lysis of adhesions, bowel resection and end ileostomy. She required parenteral nutrition for five months.

**Discussion:** We report two cases of EPS after DDRT who required surgical intervention with devastating outcomes. Fluid and nutritional support have complicated management and affected quality of life. Given the multifactorial etiologies and potential devastating outcomes of EPS, the pre-transplant evaluation should include a detailed assessment. Furthermore, long term PD patients and those with a history peritonitis should be monitored closely post-transplant.
When a Peritoneal Dialysis Catheter Should Be Removed Post-Kidney Transplantation?

Background: Approximately 15% of patients on the kidney transplant (KT) waiting list in the US receive peritoneal dialysis (PD), a growing home dialysis therapy for end stage renal disease (ESRD) patients. European guidelines recommend keeping the peritoneal dialysis catheter (PDC) in-situ during KT, due to the potential risk for delayed graft function (DGF). With this approach, a 10% risk for post-PTPRTD PDC exit-site infections has been reported. In the US guidelines for PD removal timing are lacking, and determine by transplant center and operating surgeon’s preferences.

Methods: We retrospectively reviewed the electronic medical records of all patients transplanted between 4/2017-7/2019 at our kidney transplant center. We studied basic donor and recipient characteristics, presence of DGF (defined as dialysis in the first week following KT), time interval between KT and PD removal, and wound related complications.

Results: Of 259 patients received a KT during the study period, 28 were on PD prior to KT. Of those 10 patients underwent a living donor transplant, 166 a deceased donor, and 2underwent a simultaneous kidney-pancreas transplant. Sixteen were female, 9were non-Hispanic blacks, and 4were aged ≥65 years. Three received induction with basiliximab (per center’s protocol for recipients aged ≥70 years) and the rest received antithymocyte globulin. PDC was removed at time of KT in 17 patients while in the other 11 recipients PDC was removed 22 days (median) post transplantation. For patients developed DGF, with modality switched to hemodialysis. Three of these had their PDC removed at the time of KT. The 4th patient with DGF who had his PD catheter left in place, received hemodialysis due to hemodynamic instability. Readmission rates (excluding planned hospitalization for PDC removal) and wound infections were similar between those who had their PDC removed at surgery, and those who did not.

Conclusions: Kidney transplant centers that do not routinely use PD for DGF should remove the PDC at time of kidney transplant to reduce costs and prevent patient and healthcare provider burden of additional surgery. As the prevalence of PD and KT is expected to grow in the near future with the new kidney health initiatives, kidney transplant centers should consider a protocol for optimal care for PDC removal.

Could Targeting Dry Weight on Hemodialysis Patients Before Kidney Transplantation Leave Them Too Dry?
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Background: Delayed graft function (DGF) after kidney transplantation is associated with inferior kidney and patient outcomes. Studies suggest that avoidance of hypovolemia peri-kidney transplantation is associated with a reduced risk of DGF. Hemodialysis (HD) patients that have HD prior to transplant targeting their usual dry weight may be volume contracted pre-transplant and at increased risk for DGF. By definition the dry weight is the state of near maximal volume contraction for most HD patients. The objective of this study is to examine the proportion of HD patients who have a pre-transplant post-HD weight at or below their usual dry weight.

Methods: This is a retrospective study of sequential kidney transplants in HD patients at our center from Jan 2015 to Dec 2019. The primary outcome was the proportion of patients who had an HD session before transplantation that resulted in a post-HD weight equal to or less than their prevalent set target dry weight. Data was extracted from the electronic medical record and chart review. Recipients on home therapies and pre-emptive transplants were excluded.

Results: Of 68 kidney transplants done in the study period, 40 were in-center HD patients with available HD data. They were mean age 54.8±14.5 years, 12 (30%) female, and majority were Caucasian. Twenty-five (62.5%) patients had a pre-transplant post-HD weight equal to or less than their prevalent set target dry weight (mean ± 0.2±0.25 kg). The other 15 (37.5%) patients achieved post-HD weights higher than their usual targets (+0.7±0.41 Kg).

Conclusions: The results of this study suggest that a high proportion of HD patients are at below dry weight after their dialysis and may be hypovolemic before kidney transplantation. This may represent at potentially avoidable increased risk for DGF. Further studies are planned to examine possible associations of achieved post-HD weight prior to transplant with perioperative central venous pressure, IV fluid administration, and graft function. There may be strategies to optimize volume status pre-transplantation to mitigate this risk of DGF including targeting a higher weight on HD or administration of IV fluid to raise weight above the prevalent target dry weight before transplantation when feasible.

Does the Timing of Dialysis Initiation Affect Peak Calculated Panel Reactive Antibody in Waitlisted Kidney Transplant Candidates?
Adam Price, Mohamed A. Mohamed Ahmed, Zemin Su, Maria Aurora C. Posadas, Karim M. Soliman, Vinaya Rao, Michael Casey. Medical University of South Carolina, Charleston, SC.

Background: Higher calculated panel reactive antibody (cPRA) restricts access to kidney transplantation, but it’s unclear how the timing of dialysis initiation after listing might affect cPRA. We hypothesized that patients with earlier dialysis initiation would have higher cPRA scores.

Methods: This was a retrospective SRTR database study of adults listed for a solitary kidney transplant from 10/1/09 to 11/30/18. Waitlisted patients were stratified by dialysis initiation: prelist, 0-1 year after listing, 1-2 years after listing, or no dialysis within 2 years after listing. The outcomes studied were mean peak CPA at 0-1 year and 0-2 years after listing. One-way ANOVA was used for statistical analysis.

Results: A total of 173,964 patients were identified who were waitlisted for 1-2 years. With later dialysis initiation, there was a stepwise decline in mean peak CPA between those who initiated dialysis prelist, 0-1 year after listing, and 1-2 years after listing (Figure 1). There was no difference in mean peak CPA between the dialysis initiation groups “1-2 years after listing” and “no dialysis 2 years after listing.” A similar stepwise decline in mean peak CPA was seen with patients who were waitlisted for 1 year (Table 1).

Conclusions: Our data suggest that waitlisted patients with earlier dialysis initiation may be at risk for developing higher cPRA scores. If verified with further studies, then this may be an incentive for early predialysis referrals for transplant evaluation.

Funding: Commercial Support - Dialysis Clinic Inc.
Elaine
Variations in Practice Patterns in Eligibility Assessments Across Kidney
PO2520
Poster
Tabel 1: Mean Peak cPRA Data

Patients

outcomes.

these variations may be associated with access to transplantation and post-transplantation
of eligibility for kidney transplantation. Further studies are needed to understand how
Centers differed in the kidney function threshold at which transplant evaluation was
begun, and age and body mass index limits for transplantation also varied considerably
52% of programs did not prioritize the evaluation of patients with a self-identified living
and 7% by other providers. The majority of programs (58%) screened referrals for
candidate evaluation, and determination of eligibility for kidney transplantation. We
not been well described in the contemporary era.

differences in national practice patterns related to transplant eligibility assessments have
been well described in the contemporary era.

Methods: We conducted a survey of kidney transplant programs in the US to assess
current practice patterns as it relates to criteria for prioritizing transplant referrals, candidate
evaluation, and determination of eligibility for kidney transplantation. We distributed our
survey to 171 adult kidney transplant programs in the US.

Results: 89 (52%) of programs invited to participate in the survey completed it, 45%
of which were completed by the Medical Director, 48% by a Transplant Nephrologist, and
7% by other providers. The majority of programs (58%) screened referrals for
contraindications to transplantation before scheduling an in-person evaluation (Figure 1).
52% of programs did not prioritize the evaluation of patients with a self-identified living
donor candidate when scheduling patients referred for eligibility assessments (Figure 1).
Centers differed in the kidney function threshold at which transplant evaluation was
canceled, and age and body mass index limits for transplantation also varied considerably
(Figure 1).

Conclusions: There is wide variation across transplant programs in the assessment of
eligibility for kidney transplantation. Further studies are needed to understand how
these variations may be associated with access to transplantation and post-transplantation
outcomes.

Funding: NIDDK Support

PO2520
Variations in Practice Patterns in Eligibility Assessments Across Kidney
Transplant Programs in the United States

Background: Kidney transplant programs are known to vary in terms of their practice
generally lack of consensus surrounding many aspects of pre-transplant workup. The
differences in national practice patterns related to transplant eligibility assessments have
been well described in the contemporary era.

Methods: We conducted a survey of kidney transplant programs in the US to assess
current practice patterns as it relates to criteria for prioritizing transplant referrals, candidate
evaluation, and determination of eligibility for kidney transplantation. We distributed our
survey to 171 adult kidney transplant programs in the US.

Results: 89 (52%) of programs invited to participate in the survey completed it, 45%
of which were completed by the Medical Director, 48% by a Transplant Nephrologist, and
7% by other providers. The majority of programs (58%) screened referrals for
contraindications to transplantation before scheduling an in-person evaluation (Figure 1).
52% of programs did not prioritize the evaluation of patients with a self-identified living
donor candidate when scheduling patients referred for eligibility assessments (Figure 1).
Centers differed in the kidney function threshold at which transplant evaluation was
canceled, and age and body mass index limits for transplantation also varied considerably
(Figure 1).

Conclusions: There is wide variation across transplant programs in the assessment of
eligibility for kidney transplantation. Further studies are needed to understand how
these variations may be associated with access to transplantation and post-transplantation
outcomes.

Funding: NIDDK Support

PO2521
Post-Transplant Diabetes Mellitus in a Single Pediatric Kidney
Transplant Center: Risk Factors, Outcomes, and Characterization of
Clinical Course
Aamli Khanna,1 Jee-Young N. Ham,2,3 Margret Kamel,1 Kathryn M. Ngo,1 Amanda S. Thomas,3 Rachele Liverman,2 Roubia Garro,2,3 1Emory University School of Public Health, Atlanta, GA; 2Children’s Healthcare of Atlanta Egleston Hospital, Atlanta, GA; 3Emory University School of Medicine, Atlanta, GA.

Background: The prevalence and outcomes of post-transplant diabetes mellitus (PTDM) in pediatric kidney transplant (KT) recipients vary among studies due to the
lack of a consistent definition. Risk factors for and pathogenesis of pediatric PTDM are incompletely understood.

Methods: PTDM prevalence, risk factors and disease course was evaluated at a high
volume, tertiary care pediatric hospital. We performed a retrospective review of pediatric KT recipients between 2006-2016 to evaluate PTDM prevalence. PTDM was defined as persistent hyperglycemia with serum glucose ≥200 mg/dl, HbA1C ≥6.5%, and requiring antihyperglycemic treatment for a 30 days. Full data were available on all patients
transplanted between 2010-2016 and were used to compare demographic and clinical characteristics between PTDM (n=9) and non-PTDM patients (n=173) using Chi-square and Wilcoxon rank sum tests.

Results: Between 2006-2016, 312 patients received KT. Five patients with pre-
existing DM were excluded. Fifteen developed PTDM with a prevalence estimate of
4.89 % (95% CI: 3% - 8%) and median time from transplant to DM was 17.6 months
(25%-75%: 3 – 83). The majority of PTDM patients had a family history of DM in 1st
degree relatives (81%) and were maintained on tacrolimus at diagnosis (67%). PTDM
prevalence and outcomes of post-transplant diabetes mellitus (PTDM) in pediatric kidney transplant (KT) recipients vary among studies due to the
lack of a consistent definition. Risk factors for and pathogenesis of pediatric PTDM are incompletely understood.

Methods: PTDM prevalence, risk factors and disease course was evaluated at a high
volume, tertiary care pediatric hospital. We performed a retrospective review of pediatric KT recipients between 2006-2016 to evaluate PTDM prevalence. PTDM was defined as persistent hyperglycemia with serum glucose ≥200 mg/dl, HbA1C ≥6.5%, and requiring antihyperglycemic treatment for a 30 days. Full data were available on all patients
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existing DM were excluded. Fifteen developed PTDM with a prevalence estimate of
4.89 % (95% CI: 3% - 8%) and median time from transplant to DM was 17.6 months
(25%-75%: 3 – 83). The majority of PTDM patients had a family history of DM in 1st
degree relatives (81%) and were maintained on tacrolimus at diagnosis (67%). PTDM
diagnosis and insulin initiation occurred in the context of active rejection episode in
only two patients. Despite a more stringent definition of PTDM, insulin therapy was
discontinued in 3/15 (20%) patients who continued to be normoglycemic. Comparing
patients with and without PTDM during the period 2010-2016 revealed that PTDM
patients had higher BMI-Z scores at transplant (p=0.053) and higher average blood
glucose during the first week post KT (p=0.095), with no difference in age, gender, race,
donor status, or dialysis modality.

Conclusions: A more consistent definition of PTDM and larger studies are warranted
to better understand the prevalence, risk factors, and pathogenesis of hyperglycemia and
PTDM in children. Detailed patient-level data can provide nuance that may be missed
with larger registry studies.

Funding: Private Foundation Support

PO2522
Diabetic Nephropathy: Is It All About Hyperglycemia?
Iyad Alabulh Bazza,1 Lois J. Arend,2 Sami Alanfar2 1Alfaisal University, Riyadh, Saudi Arabia; 2Johns Hopkins University, Baltimore, MD.

Introduction: Diabetic nephropathy (DN) is the most common cause of end
stage renal disease (ESRD). Hyperglycemia has been suggested to be necessary for the
development and maintenance of DN. Simultaneous pancreas and kidney transplantation
(SPK) has revolutionized the treatment of type 1 diabetic patients with end-stage renal
disease (ESRD), and prevention of recurrent DN is one of the main proposed benefits.
We present a case of recurrence of DN after SPK despite normal endocrine pancreas
allograft function

Case Description: A 47-year-old man with past medical history of ESRD due to
diabetes type I who underwent a SPK transplant from a deceased donor in December
2003. His nadir serum Creatinine was 1.5 mg/dl and baseline urine protein creatinine
ratio (UPC) is 110-250 mg/g. Maintenance immunosuppression consisted of tacrolimus,
mycophenolate, and prednisone. His home medications also included benazepril for
typhemia. Sixteen years after transplant, he was noted to have increase in UPC to
2100 mg/g and serum Creatinine to 1.9 mg/dl. Trough tacrolimus levels in the preceding
6 months ranged between 4.8 and 10.9 ng/mL. Donor specific antibodies were negative.
He underwent renal allograft biopsy which showed early nodular mesangial matrix
expansion and thickened glomerular basement membranes on electron microscopy.
consistent with diabetic nephropathy (Figure 1), early chronic transplant glomerulopathy, and severe arteriolar hyalinosis. Additional laboratory findings showed serum lipase 34 (Normal 7-60 U/L), amylase 103 (Normal 21-101 U/L), fasting glucose 79 (Normal 65-99 mg/dL), hemoglobin A1c 5.3, and C peptide was 2.03 (Normal 0.80 - 3.85 ng/mL). Despite increasing Benazepril dose to 40 mg daily, UPCR and Cr continued to increase but stabilized in a range of 3800-4500 mg/g and 2.5 mg/dL respectively.

Discussion: Our case suggests that development of DN can be linked to mechanisms independent of hyperglycemia and the usual metabolic disturbances seen in patients with diabetes. A comprehensive restudying of the pathophysiology of DN could further enhance our existing knowledge of the factors implicated in DN, and possibly our ability to develop a more targeted therapy.

PO2523

Use of Weight-Altering Diabetes Medications to Address Obesity as a Barrier to Kidney Transplant Evaluation in Patients with Type 2 Diabetes and Stage 4-5 CKD or ESKD

Kiran Chintam, Prince Mohan, Jamie A. Green, Alex R. Chang. Geisinger Health, Danville, PA.

Background: Many patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) are ineligible for kidney transplant due to high body mass index (BMI). Some medication classes are associated with weight loss (glucagon-like peptide-1 receptor agonists [GLP1-RAs]), neutral-weight (dipeptidyl peptide-4 inhibitors [DPP4is]), or weight gain (sulfonylureas and insulin).

Methods: We examined the relationship between BMI and use of weight-altering diabetes medications in patients with type 2 diabetes mellitus and stage 4-5 CKD or dialysis-dependent ESKD at Geisinger (1/18-3/20). In addition, we examined whether access to kidney transplant evaluation varied by BMI in patients on dialysis.

Results: Out of 4200 patients with T2DM and stage 4-5 CKD or ESKD, 30% had BMI ≥ 35 kg/m² and 15% had BMI ≥ 40 kg/m². Overall, use of T2DM medications with favorable weight effects was low, similar to use of sulfonylureas (Table). Patients with severe obesity had higher GLP1-RA use (BMI ≥ 35 vs. <35 kg/m²: 11%, 5%), higher insulin use (69%, 53%), and lower DPP4i use (9%, 13%). Similar findings were noted in the subset of patients on dialysis: GLP1-RAs (BMI ≥ 35 vs. <35 kg/m²: 6% vs. 2%), DPP4is (3% vs. 6%), sulfonylureas (5% vs. 8%), insulin (77%, 74%). In unadjusted analyses, transplant clinic attendance was highest in ESKD patients with BMI 30-34.9 kg/m² (23%), followed by BMI 35-39.9 (17%), BMI 25-29.9 (15%), BMI 18.5-24.9 (13%), BMI ≥ 40 (7%), and BMI < 18.5 (5%).

Conclusions: The vast majority of patients with T2DM and advanced CKD are taking obesogenic rather than weight loss-promoting diabetes medications. Those with BMI ≥ 40 kg/m² were 3.6x less likely to have been evaluated in transplant clinic than those with class 1 obesity (BMI 30-34.9 kg/m²). Consideration of the differential impact of certain diabetes medication classes on weight may help improve access to kidney transplantation and long-term outcomes.

Funding: NIDDK Support

Table. Diabetes Medications Use by BMI

<table>
<thead>
<tr>
<th>Table, Diabetes Medications Use by BMI</th>
<th>BMI ≥35 (n=1103)</th>
<th>BMI &lt;35 (n=3097)</th>
<th>Overall (n=4200)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight gain-associated meds</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intulin</td>
<td>758 (68.7%)</td>
<td>1650 (53.3%)</td>
<td>2408 (57.3%)</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>152 (13.8%)</td>
<td>476 (15.4%)</td>
<td>628 (15%)</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>28 (2.5%)</td>
<td>101 (3.3%)</td>
<td>129 (3.1%)</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>17 (1.5%)</td>
<td>45 (1.5%)</td>
<td>63 (1.5%)</td>
</tr>
<tr>
<td><strong>Weight-neutral meds</strong></td>
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<td></td>
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</tr>
<tr>
<td>DPP4 inhibitor</td>
<td>95 (8.6%)</td>
<td>387 (12.5%)</td>
<td>482 (11.5%)</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitor</td>
<td>0</td>
<td>8 (0.3%)</td>
<td>8 (0.2%)</td>
</tr>
<tr>
<td><strong>Weight loss-associated meds</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GLP1-RA inhibitor</td>
<td>119 (10.8%)</td>
<td>142 (4.6%)</td>
<td>261 (6.2%)</td>
</tr>
<tr>
<td>Biguanides</td>
<td>85 (7.7%)</td>
<td>203 (6.6%)</td>
<td>288 (6.9%)</td>
</tr>
<tr>
<td>SGLT inhibitor</td>
<td>4 (0.4%)</td>
<td>15 (0.5%)</td>
<td>19 (0.5%)</td>
</tr>
</tbody>
</table>

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2525

Health System Encounters in Kidney Transplant Recipients Converted from Immediate-Release Tacrolimus Capsules to Extended-Release Tacrolimus Tablets

Yoonle H. Pa,1* Jamal Rashidi,2 Mary Putt,2 Yu Bin Na,2 Chelsea Sammons,2 Maxwell Norris,2 Gregory Malat,1,3 Brendan Steiner,1 John H. Holmes,1 Roy D. Bloom,1 Peter P. Reese,1,3 Jennifer Trofe-Clark,3,1 Department of Epidemiology, Biostatistics and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; 2Department of Pharmacy, Hospital of the University of Pennsylvania, Philadelphia, PA; 3Renal Electrolyte and Hypertension Division, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; 4Drexel College of Medicine, Philadelphia, PA.

Background: Kidney transplant recipients (KTRs) converted from immediate-release tacrolimus capsules (IR-TAC) to extended-release tacrolimus tablets (ER-TAC) may benefit from reduced dosing frequency and improved bioavailability. However, few studies have characterized health system encounters in these KTRs. Study aims were to (1) determine if conversion to ER-TAC decreased number of dose changes, TAC troughs, and transplant clinic visits and (2) characterize number of dose changes and days to achieve two consecutive therapeutic troughs (5-12 ug/L) under ER-TAC.

Methods: Retrospective review of KTRs at our center transplanted between 2/2010-3/2019, on IR-TAC for ≥90 days, and converted to ER-TAC for ≥90 days. Random-coefficient Poisson regression was used to compare number of dose changes, troughs, and clinic visits during the 90-day periods pre- and post-conversion.

Results: 64 KTRs met inclusion criteria. Mean (SD) age was 52.8 (13.7) years, 38 (59%) were male, 28 (44%) were Black, and 8 (13%) were on an IR-TAC financial assistance program. Median (IQR) time since transplant was 333 (211-1,483) days. KTRs were on IR-TAC for a median of 26 (41%) non-adherence, 12 (19%) high IR-TAC dose, 2 (3%) sub-therapeutic troughs, 2 (3%); and other/unknown, 22 (34%). The incidence rate of dose changes but not troughs or clinic visits decreased significantly post-conversion (Table). For the 24 (38%) KTRs with two consecutive therapeutic troughs within 90 days, median (IQR) number of dose changes was 2 (0-3) and days to achieve two consecutive therapeutic troughs was 33.5 (23.5-63).

Conclusions: The incidence rate of dose changes decreased significantly under ER-TAC, but most KTRs did not achieve two consecutive therapeutic troughs within 90 days of conversion. Closely follow up may be beneficial for these KTRs. Future research should determine if reasons for conversion resolved with use of ER-TAC.

PO2526

Looking Beyond the Allograft Survival: Long-Term, Five-Year Renal Outcomes in Lung Transplant Recipients

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Background: With the increase in incidence and overall survival of lung transplant recipients, the risk for chronic sequelae in terms of CKD is on the rise. However, the data on long-term effect on kidneys in this population is scarce. Our study is the first to assess the five-year renal outcomes in Lung transplant recipients. Future research should determine if reasons for conversion resolved with use of ER-TAC.

Methods: We did a retrospective chart review of 171 adults with lung transplants performed between 1st January 2014 - 1st January 2019 and meeting inclusion/exclusion criteria. Primary outcomes were - the prevalence of CKD/ESRD (requiring RRT), risk of development of CKD in patients with AKI during index hospitalization, and all-cause mortality in recipients with CKD when compared to the non-CKD group. Secondary outcomes were calculation of the frequency of utilization of modalities for CKD (urinalysis, renal USG, biopsy, nephrology consults).

Results: 86% of patients were white, with a median age of 61 years, median BMI 27.3 kg/m² and 60% were males. Hypertension was present in 55% of patients at baseline. COPD and IPF were the commonest etiology for lung failure, and 66% received a double lung transplant. Baseline median creatinine and eGFR were 0.8 mg/dL and 54 mL/min/1.73 m² respectively, 6% (n=171), 60% (n=161), 67% (n=155), 79% (n=147), and 86% (n=7) had CKD at baseline, 6, 12, 36, 60 months respectively. Eighty percent received dialysis during the index hospitalization. The odds ratio of development of CKD in patients with an AKI episode during index hospitalization versus no AKI was 6.22 (2.87 to 13.06, p < 0.0001). Whereas, the odds ratio of all causes mortality in patients with CKD when compared to no CKD was 1.14 to 8.64, p< 0.005. Hematocrit and proteinuria were monitored during the index hospitalization. Renal biopsy done in 1.1% with renal USG abnormal in 22%, normal in 21 % and never performed in 57%. Sixteen percent of recipients were on dialysis, 3% received a renal transplant, and 27% of mortality noted over a five-year follow up period.

Conclusions: There is a high prevalence of CKD in lung transplant recipients, and increase in the patients who had an AKI during index hospitalization. With increased lung transplant nowadays, early involvement of nephrologists is prudent to prevent and manage CKD effectively in the future. Large prospective trials to delineate the problem is warranted.

PO2527

Incidence, Risk Factors, and Outcomes of Post-Transplant Erythrocytosis After Kidney Transplantation

Byeun Alzoubi, Abish Kharel, Fauzia Osman, Fahad Aziz, Neetika Garg, Maha A. Mohamed, Arjung Djamalai, Didier A. Mandembrot, Sandesh Parajuli. University of Wisconsin School of Medicine and Public Health, Madison, WI.

Background: Post-transplant erythrocytosis(PTE) is a common condition after kidney transplantation. PTE is known to increase the risk of stroke, pulmonary embolism, and deep vein thrombosis, commonly seen in vascular thromboembolism(VTE). In the current era of immunosuppressive medication and management, the incidence, risk factors, and outcomes of PTE among kidney transplant recipients(KTR) is unknown.

Methods: This was a retrospective study among all adult KTRs transplanted at our university hospital between 01/2001 and 12/2016. All recipients in the PTE group had at least 2 consecutive Hct levels of >51 within the first 2 years of transplant. Controls were selected in a ratio of 5:1 using event density sampling. Patient survival, graft survival, and VTE incidence were outcomes of interest.

Results: Of 4317 kidney transplants during the study period, 214(5%) had PTE and were compared with 1035 controls. While comparing baseline characteristics between PTE and control, KTRs in the PTE group were more likely to be younger, male, have lower BMI, higher prevalence of diabetes as the cause of ESRD and receive a non-deceased donor kidney. Similarly, looking at donor characteristics, the PTE group was likely to receive the kidney from a younger donor and have lower KDPI. The median interval from transplant to the diagnosis of PTE was 9.9 months (IQR 5.89), 13 (6.1%) in the PTE group and 7 (6.9%) in control had VTE events. In the multivariable analysis, patients with older age (HR: 0.98, 95% CI 0.97-0.99) and lower BMI (HR: 0.97, 95% CI 0.93-0.99, p<0.05) were less likely to develop PTE, while non-preemptive transplant (HR: 3.95, 95% CI 1.74-8.99, p<0.001) was significantly associated with increased risk of PTE. After adjustment for the multiple confounding factors, PTE was not associated with patient mortality (HR: 1.0, 95% CI 0.70-1.43, p=0.99), graft failure (HR: 1.13, 95% CI 0.69-1.83, p=0.61) or VTE (HR: 1.07, 95% CI 0.59-1.96, p=0.81). In a subgroup analysis among PTE with Hct >55 (n=39) compared with controls, similar findings were observed.

Conclusions: In this era, the prevalence of PTE is lower at 5% compared to around 15% in various previous studies. Similarly, there were no detrimental effects of PTE on patient survival, graft survival, or the risk of VTE in the current era.

PO2528

Post-Transplant Outcomes Among Kidney Transplant Recipients with Intentional and Unintentional Weight Loss

Meera N. Harhay,1 Xiaomeng Chen,2 Nadia M. Chu,2 Mara McAdams-DeMarco.2 Drexel University, Philadelphia, PA; 3Johns Hopkins University, Baltimore, MD.

Background: Research has shown that kidney transplant (KT) recipients who lose weight before KT are at increased risk for post-KT weight gain, all-cause graft loss (ACGL), and mortality. No studies have examined whether these associations differ between recipients with intentional and unintentional weight loss.

Methods: Among 366 KT recipients from a prospective cohort study of frailty and KT, we used adjusted mixed effects models to estimate differences in post-KT BMI trajectories, ACGL, and mortality by 1-year pre-KT weight change, defined as stable weight, intentional weight loss, unintentional weight loss, and weight gain.

Results: Mean age was 53 years, 39% were black, and 39% were female. The majority (64%) had stable pre-KT weight, 12% had weight gain, 14% had unintentional weight loss, and 10% had intentional weight loss. By 3 years post-KT, BMI increased by 0.05 kg/m² (95% CI 0.02, 0.08 kg/m²) among those with stable pre-KT weight; the increase was similar among those with pre-KT weight gain and intentional weight loss. Those with pre-KT unintentional weight loss had larger increases in post-KT BMI than those with stable BMI (BMI change difference 0.15 kg/m² [0.04, 0.25 kg/m²], p<0.01). Unadjusted cumulative incidence of mortality was similar across weight change categories (Figure). Adjusted for age, sex, race, BMI, and donor type, only unintentional weight loss was associated with higher mortality (aHR 2.31 [1.24,4.31], p<0.008) and ACGL (aHR 2.62 [1.24,3.31], p=0.005) relative to stable weight.

Conclusions: In this study, pre-KT unintentional weight loss was associated with higher post-KT BMI increases, ACGL and mortality than pre-KT intentional weight loss, stable weight, and weight gain. These results suggest that unintentional weight loss should be identified and addressed in KT candidates, independent of BMI.

Funding: NIDDK Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
*Adjusted for age, sex, race, financial assistance, conversion reason, time since transplant, and achievement of two consecutive therapeutic troughs
PO2529
Obesity and Poorer Renal Allograft Function: Analysis of Longitudinal Data
Ekamol Tantisattamo,1,2 Busara Songtain,2 Natmisea Leelavat,1 Sakdita Sarawapa,2 Possawat Vuthikraivit,3 Chawit Lopimphisut,4 Natchaya Polpichai,4 1Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California Irvine School of Medicine, Orange, CA; 2Multi-Organ Transplant Center, Section of Nephrology, Department of Internal Medicine, William Beaumont Hospital, Oakland University William Beaumont School of Medicine, Royal Oak, MI; 3Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; 4Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; 5Phramongkutklao College of Medicine, Mahidol University, Bangkok, Thailand; 6Faculty of Medicine Songklanagarin Hospital, Prince of Songkla University, Songkhla, Thailand.

Background: Obesity is associated with worsened allograft function, but its effect on allograft function after established baseline allograft function at a 12-week post-KT transplant (KT) is unclear.

Methods: All 105 KT recipients were divided into obese (BMI ≥ 30 kg/m2) and non-obese groups. Longitudinal data were analyzed by linear mixed model to examine association between obesity and eGFR during the 1st year post-KT.

Results: Mean age was 54±11 years and 64 patients (61%) was female. Seventy-one patients (68%) were obese. Generalized estimating equation revealed that eGFR increased 0.16 ml/min/1.73 m2 (95%CI 0.09 to 0.23) for every 1 week after KT. Excluding eGFR at 4-week post-KT when baseline allograft function is generally not established, mean eGFR at 12-week post-KT was the lowest and assigned as the baseline allograft function. Given unequal spreading of time when eGFR were measured, a 1-year follow-up period was categorized into every 4 and 12 weeks if eGFR were measured before and after a 12-week post-KT, respectively. Spline interaction term was created at the 12-week post-KT as well as categorized time-spline interaction term. By using a linear mixed model and after adjusted for age, gender, type of KT (deceased vs living donor KT), obesity category and its interaction team with categorized time and spline interaction term, obese group had a higher rate of eGFR decline of 2.9 ml/min/1.73 m2 every 4 weeks prior to 12-week post-KT, and the rate declined to 1.1 ml/min/1.73 m2 every 12 weeks after 12-week post-KT. At the 12-week post when baseline eGFR was established, eGFR were 74.1±20.5 and 78.0±20.5 ml/min/1.73 m2 for obese and non-obese groups, respectively (random intercept); whereas, rate of increase in eGFR of those corresponding groups were 69.3±0.2 and 70.3±0.2 ml/min/1.73 m2 every 12 weeks (random slope).

Conclusions: Although population-based estimated eGFR was significantly increased overtime, obese KT recipients had lower baseline eGFR at the 12-week post-KT and slower rate of increased eGFR than those of non-obese group when individual baseline eGFR at the 12-week post-KT and rate of eGFR change were taken into the consideration. Pre-KT obesity remains one of the associated factors of poor allograft outcomes, which may be mitigated by pre-KT weight loss.

PO2530
A Call to Action: Finding the Right Kidney for All Potential Recipients

Background: The burden of dialysis among ESRD patients is a huge driver of morbidity, mortality, and cost. Thousands of deceased-donor (DD) kidneys that almost certainly have better outcomes than dialysis are discarded each year. Our center sought to find and transplant kidneys that would reduce waiting time for our patients while preserving post-transplant outcomes consistent with nationally expected results.

Methods: We reviewed 1119 consecutive DDKT recipients transplanted between 1/1/2016 and 12/31/2019 at our center. Endpoints were eGFR by MDRD death-censored graft survival using Kaplan-Meier survival estimation and the Cox Proportional Hazards Model. We reviewed on additional year (2015) for waiting time impact.

Results: DD KT volumes doubled from 2016 to 2019 (191 ± 384). Growth was attributable to increased acceptance of hard-to-place imported kidneys, including kidneys with AKI (413% increase) and KDPI > 85 (296% increase). In 2016, 46.6% of DD kidneys were imported from outside our DSA and by 2019, 77.3% were imported. Overall one-year patient survival was 96.6% (CI: 95.4-97.6%) and death-censored one-year graft survival was 95.8% (CI: 94.4-97.6%). Recipients with any stage of AKI saw no additional risk vs. donor not affected by AKI (HR 0.94, p=0.854) while death-censored graft survival at one year was 91.9% for recipients of kidneys with KDPI >85% vs 96.7% with KDPI ≤85%, representing significant additional risk (HR: 1.91; p=0.017). This significantly decreased waiting time at transplant across all blood types (6 years in 2015 to 3.9 years in 2019). This benefit was even greater for blood group B (10.7 to 4.3) and significantly reduced the disparity in accrued waiting times for African-American and Hispanic populations. Kidney function was good at 1 year in all groups among those surviving with followup. Mean eGFR by MDRD formula was 60.0 (SD 23.2) in recipients with non-AKI donors and 61.9 (SD 26.1) in recipients with AKI donors (p=0.4384). Mean eGFR 49.0 in the KDPI >85% group vs 62.3 in the <= 85% KDPI group (p=0.0001).

Conclusions: Transplant centers can answer the growing demands of patients enduring dialysis to better utilize kidneys that have previously been discarded. Our center demonstrated that it is possible to reduce waiting time, and maintain outcomes using kidneys previously discarded.

Funding: Clinical Revenue Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Table 1. Hazard ratios of death-censored graft loss according to BMI and presensitization status

<table>
<thead>
<tr>
<th>BMI Status</th>
<th>Unadjusted HR</th>
<th>95% CI</th>
<th>Adjusted HR</th>
<th>95% CI</th>
<th>P-value</th>
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<tr>
<td>Low BMI (&lt; 25)</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
</tr>
<tr>
<td>Medium BMI (25-29)</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
</tr>
<tr>
<td>High BMI (&gt; 29)</td>
<td>2.40</td>
<td>1.43-4.03</td>
<td>2.77</td>
<td>1.52-5.10</td>
<td>&lt; 0.05</td>
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</table>

Multivariate regression model was adjusted with parameters showing significant difference among the 4 groups according to BMI and pre-sensitization status. Parameters were as follows: Age, Sex, DM, HTN, Fasting glucose, Triglyceride, HDL-cholesterol, Hemoglobin A1c, ESRD causes, Dialysis modality, and Prior KT history.

PO2532
Association Between Post-Transplant Visit-to-Visit Pulse Pressure Variability and Late Transplant Systolic Blood Pressure in Non-Elderly Kidney Transplant Recipients

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Background: Visit-to-visit blood pressure variability is associated with vascular stiffness and cardiovascular outcomes, particularly in elderly. Association between visit-to-visit pulse pressure variability (VVPPV), which takes SBP and DBP into account, and late post-kidney transplant (KT) blood pressure (BP) in different age groups is unknown.

Methods: VVPPV was examined by average successive variability (ASV), which is the average absolute difference between successive BP measured at 4, 12, and 24 weeks post-KT. Since the slope of the linear plot between VVPPV and SBP at 48 weeks post-KT abruptly changed when VVPPV was 15 mmHg, VVPPV was then categorized into <15 and ≥15 mmHg (Figure 1A). Association between the categorized VVPPV and systolic and diastolic hypertension (SHTN, DHTN) at 48 weeks defined by SBP and DBP ≥130 and ≥80 mmHg, respectively was examined by multivariate logistic regression and stratified into age <60 and ≥60 years old.

Results: Of all 105 KT recipients from a single KT center, mean age was 54±12 years and 64 patients (61%) was female. Mean VVPPV was 13±9 (range 2 to 50). Mean post-KT SBP and DBP at 48 weeks post-KT were 133±16 and 77±11 mmHg, respectively. In the whole population studied adjustment by gender, donor type (deceased vs. living), and types of induction immunosuppressive medications, patients with VVPPV ≥15 mmHg had 3.36 times higher risk of developing SHTN (OR 3.36, P≤0.001, 95%CI 1.17, 9.65). However, after additional adjustment by age and interaction term between age and ASV, the association was persist only in patients whose age ≥60 years old (OR 3.80, p = 0.04, 95%CI 1.04, 13.91 vs. OR 1.28, p = 0.40, 95%CI 0.36, 13.31 (Figure 1B)). There was no association between VVPPV and DHTN in the whole study and age-stratified populations.

Conclusions: Higher VVPPV is associated with late post-KT SHTN in younger age group (< 60 years old), but not in elderly. Further studies are required to elucidate the mechanisms.

PO2534
Middle Cerebral Artery Hemodynamics Is Blunted in Kidney Transplant Recipients

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Background: Kidney transplant (KT) recipients have a higher risk of dementia and cerebrovascular events than the general population. Cerebrovascular hemodynamic response (CVR) to constant-load moderate-intensity exercise marks the ability of the brain to respond to increased oxygen requirements with exercise. Blunted CVR seen with vascular disease and aging can increase risk of dementia and stroke. We evaluated the middle cerebral artery blood velocity (MCV) dynamic response in KT recipients and compared it to age matched non-CKD controls.

Methods: 35 KT recipients and 35 healthy controls completed a 90-second rest followed by a 6-minute moderate intensity exercise on a recumbent stepper at a prescribed step rate and workload. We used transcranial doppler (TCD) monitoring for MCAV while continuously monitoring heart rate and beat-to-beat mean blood pressure during rest and exercise. Baseline resting MCAV and steady state response during exercise was recorded. Outcome measures included resting MCAV and CVR (MCAV during steady state exercise – baseline MCAV) and workload needed to achieve target heart rate. Statistical analysis employed independent t-test.

Results: KT recipients were 52.4 ±0.8 cm/s compared to 12.9 ± 4.9; last follow-up 47.3±21.1 vs 57.5±14.8 mL/min/1.73m². Only 2 patients had oxalate crystals on protocol allograft biopsy, both with RYGB, and one with DGF and died 22 months after KT. GFR at 1 year was 34±23.8 ±0.73m²/1.73m² for these 2 patients.

Conclusions: RYGB is the most common cause of enteric oxalosis in KT recipients. DGF is common and graft outcomes are inferior compared to deceased donor KT among our institution. The lower GFR in RYGB patients raise concern for enteric hyperoxaluria as an unrecognized risk for allograft dysfunction.

Funding: Commercial Support - ALLENA pharmaceutical

PO2533
Kidney Transplant Outcomes for Patients with Enteric Oxalosis

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Background: Patients with enteric disorders associated with hyperoxaluria and systemic oxalate burden (enteric oxalosis) are at increased risk for calcium oxalate deposition causing ESRD. The objective of this study is to evaluate kidney transplant (KTx) recipients with enteric oxalosis at our institution.

Methods: KTx recipients with suspected oxalosis due to any of the following: inflammatory bowel disease, bariatic surgery, or pancreatic insufficiency from 2015 to 2019 were included. At our institution, pre-KTx serum oxalate>30mcml/L is the threshold for treatment.

Results: 31 patients were identified. Mean age was 58.5 years, 55% were female, 81% white, and 94% first KTx. Most common cause of ESRD was diabetes (45%), and 84% were on dialysis prior to KTx (median 30.5 months). The most common enteric cause was Roux-en-Y gastric bypass (RYGB, 77%) with surgery 11 year (median) prior to KTx. 39% had history of nephrolithiasis. Median peak serum oxalate (SOx) pre-KTx was 24mcml/L. 87% received deceased donor KTxs and 52% had delayed graft function (DGF). Post-KTx, 36% received calcium with meals for oxalate bind, and 39% had low oxalate diet education. 5 patients had pre-KTx SOx >30mcml/L at the time of KTx, of whom 4 had DGF and required either longer dialysis (up to 5 hours long) or increased dialysis sessions (up to 6 per week) to reduce SOx levels post-KTxs. The median duration of dialysis after KTx was 13.5days. After median follow up of 27 months, (mean SD) estimated glomerular filtration rate (GFR) was 47.6 ±21.2 mL/min/1.73m² and 68% of patients had GFR ≤60. One-year KTx was 48.4±2.4 mL/min/1.73m² which is lower than expected 1-year GFR for our Transplant Center (mean GFR 58±20.6±0.73m²). RYGB patients (n=24) had lower GFR vs patients with other EH causes (n=7) (1 year: 48.7±20.4 ±5.6±4.9; last follow-up 47.3±21.1 ±57.5±14.8 mL/min/1.73m²). Only 2 patients had oxalate crystals on protocol allograft biopsy, both with RYGB, and one with DGF and died 22 months after KTx. GFR at 1 year was 34±23.8 ±0.73m²/1.73m² for these 2 patients.

Conclusions: RYGB is the most common cause of enteric oxalosis in KTx recipients. DGF is common and graft outcomes are inferior compared to deceased donor KTxs at our institution. The lower GFR in RYGB patients raise concern for enteric hyperoxaluria as an unrecognized risk for allograft dysfunction.

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Underline represents presenting author.
PO2535

Longitudinal Physical Performance Following Kidney Transplant
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Background: Frailty and poor physical performance are strongly associated with poor outcomes in kidney transplantation (KTx). However, the effect of KTx on physical performance remains poorly understood.

Methods: We measured 6-minute walk test (6MWT, meters) and 1-minute sit-to-stand test (STS, number of repetitions from standing to sitting position) performances within 1 year prior to KTx. Physical performance indices were re-measured at 3 and 6-months, and 1-year post-KTx. Multivariable linear regression was used to assess which baseline characteristics were associated with 6MWT and STS. Trajectories of 6MWT and STS were assessed by baseline performance using a generalized estimating equation.

Results: Among 85 patients who performed baseline assessments, 39, 33 and 40 completed 3, 6, and 12-month evaluations, respectively. Average age was 53 and average diaylsis vintage was 7 years. 49% had diabetes mellitus, 18% had coronary artery disease, 5% had cerebrovascular disease, and 10% had peripheral arterial disease (PAD). In the multivariate model, age, female sex, and the presence of PAD were associated with lower 6MWT and STS. Trajectories of 6MWT and STS were assessed by baseline performance using a generalized estimating equation.

Conclusions: Walking ability did not improve appreciably after KTx. STS, a measure of lower body strength, improved progressively post-KTx, but was mostly observed in patients with higher baseline STS. Results must be interpreted with caution, since all patients, even those with lower physical performance, were selected to proceed with KTx.

PO2536

Outcomes of Kidney Transplantation in Fabry Disease: A Meta-Analysis
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Background: Fabry disease (FD) is a rare X-linked lysosomal storage disorder with progressive systemic deposition of globotriaosylceramide, leading to life-threatening cardiac, central nervous system, and kidney disease. Current therapies involve symptomatic medical management, enzyme replacement therapy (ERT), dialysis, kidney transplantation, and more recently gene therapy. The aim of this systematic review was to assess outcomes of kidney transplantation among patients with FD.

Methods: Comprehensive literature review was conducted utilizing MEDLINE, EMBASE and Cochrane Database, from inception through February 28, 2020 to identify studies that evaluate outcomes of kidney transplantation including patient and allograft survival among kidney transplant patients with FD. Effect estimates from each study were extracted and combined using the random-effects, generic inverse variance method of DerSimonian and Laird.

Results: Eleven studies including 424 kidney transplant recipients with FD were evaluated. The post-transplant median follow-up time ranged from 3 to 11.5 years. Overall, the pooled estimated rates of all-cause graft failure, graft failure before death, and allograft rejection were 32.5% (95%CI: 23.9%-42.5%), 14.5% (95%CI: 8.4%-23.7%), and 20.2% (95%CI: 15.4%-25.9%), respectively. A sensitivity analysis limited to the recent studies (year 2001 or newer when ERT became available), the pooled estimated rates of all-cause graft failure, graft failure before death, and allograft rejection were 28.1% (95%CI: 20.5%-37.3%), 11.7% (95%CI: 8.4%-16.0%), and 20.2% (95%CI: 15.5%-26.0%), respectively. The pooled estimated rate of biopsy proven FD recurrence was 11.1% (95%CI: 3.6%-29.4%), respectively. There was no significant difference in the risk of all-cause graft failure (P = 0.01) nor mortality (0.48) among recipients with vs. without FD.

Conclusions: Despite possible FD recurrence after transplantation of 11.1%, allograft and patient survival are similar among kidney transplant recipients with vs. without FD.

PO2537

Urinary Supersaturation in Patients with Kidney Transplant Nephrolithiasis
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Background: Urine supersaturation (SS) has not been reported for kidney transplant (KTx) recipients with de novo transplant-derived nephrolithiasis. The objective of this study was to evaluate supersaturation studies, treatment, and stone and allograft outcomes in KTx recipients with allograft nephrolithiasis.

Methods: Retrospective review from 2009-2019 of KTx recipients with nephrolithiasis at Mayo Clinic was completed. Stone event was defined as radiologic evidence.

Results: Fifty six transplant nephrolithiasis cases were identified. Mean transplant age was 56.5 ± 12.1 years, 32 (57.1%) were male, 46 (82.1%) received first KTx, 41 (75.9%) received living related donors, 27 (48.2%) had diabetes mellitus. Baseline stone size was 6 mm, and most common location was the lower pole (n=20 [41.7%]). Median time from KTx to stone event was 1 year. Thirty four (60.7%) had a 24-hour SS study at a median of 2 years after KTx. Select results are shown in Table 1. Of the 34, 14 (41.2%) had a stone event prior to KTx, and 6 (17.6%) had donor-derived stone. Thirty one (91.2%) had increased SS of calcium oxalate, 17 (50%) calcium phosphate, and 9 (26.5%) uric acid. Thirty two (94.1%) had urine citrate <450mg/24hrs. Management of the initial 56 included potassium citrate in 13 (23.2%), calcium citrate in 10 (17.8%), and dietician referral in 18 (32.1%). Forty five (80.8%) were seen by urology, 28 (50%) needed surgical management, and 14 (27.5%) passed the stone. At median follow-up of 4 years after KTx, 37 (66.1%) had persistent stone disease in the allograft, 3 (5.4%) had graft failure, and 2 (3.6%) had died.

Conclusions: This is the first study of urine SS in patients with transplant-derived nephrolithiasis. Profound hypocitraturia was the most prevalent risk, and increased supersaturation for calcium oxalate crystals predominated. Allograft stone clearance was rare, and many required surgical intervention.

Funding: Clinical Revenue Support

Table 1

PO2538

Exposure to Tacrolimus Trough Levels Below 6 ng/mL During the First Year Is Associated with Inferior Kidney Graft Survival
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Background: Accumulating data indicates that sub-therapeutic levels of calcineurin inhibitors are associated with long-term graft loss. However, while tacrolimus (TAC) was shown to provide adequate immunosuppression with lower acute rejection rate, its optimal maintenance dose for long term graft survival is still unknown. The aim of our study was to determine the minimal TAC trough level, which is associated with improved kidney graft survival.

Methods: We conducted a retrospective cohort study based on the RMC registry. We defined five TAC trough level intervals: 3-4, 4-5, 5-6, 6-7, and 7-8ng/ml. We compared allograft and patient survival among recipients with various TAC trough levels using the Kaplan-Meier survival analysis. Cox proportional hazards model was used to assess the independent association between TAC trough level and allograft and patient survival.

Results: Of 156 patients with functional allografts, 66 patients (42%) had allograft failure, and 33 patients (21%) died during follow-up (median follow-up: 36 months). The median time on TAC was 5 years (range: 0.1-18 years). The median TAC trough levels were 5 (range: 1-7.5) ng/mL, and the 1-year survival rates were 89%, 79%, 79%, 77%, and 77% for patients with TAC trough levels of 3-4, 4-5, 5-6, 6-7, and 7-8 ng/mL, respectively. The unadjusted hazard ratio for allograft failure at 1 year was 1.16 (95%CI: 0.72-1.87) for TAC trough levels 3-4 ng/mL compared to 5-6 ng/mL. After adjusting for age, gender, and diabetes, the hazard ratio remained the same (HR: 1.16, 95%CI: 0.72-1.87). The 1-year cumulative incidence of allograft failure was significantly lower for patients with TAC trough levels of 5-6 ng/mL compared to those with TAC trough levels of 3-4 ng/mL (P = 0.04).

Conclusions: Exposure to TAC trough levels below 6 ng/mL during the first year is associated with inferior kidney graft survival.
was adjusted to the exposure time below a given interval-level, allowing us to define the threshold for optimal TAC trough level as the upper limit of the interval. We then determined the association between the adjusted exposure time at each TAC level-interval and our primary outcome, death-censored graft survival.

Results: We included 1417 patients with a median follow up of 5.3 years (IQR 2.9-8.5 years). TAC through level interval of 5-6 ng/ml was the highest interval which demonstrated a statistically significant association between exposure time and increased risk of graft loss, even after adjustment to the exposure time below 5 ng/ml (HR 1.58 per log days, p<0.001). These results remained consistent in an extensive multivariable analysis (HR 1.44, p<0.004) and were not significantly changed when we analyzed for death- or included graft survival (HR 1.2, p<0.026) or the first three months and the subsequent nine months separately (HR 1.93, p<0.001, HR 1.56, p<0.001 respectively). Cumulative exposure time above 14 days to TAC trough level 6 ng/ml, was significantly associated with increased risk of graft loss in most studied subgroups including age, gender, low and high immunologic risk recipients, except for the subgroup of recipients with diabetes.

Conclusions: Prolonged exposure time to TAC trough level between 5-6 ng/ml within the first-year post-transplant was independently associated with increased risk of long-term graft loss. These results imply that keeping TAC trough levels above 6 ng/ml during high immunologic risk recipients, except for the subgroup of recipients with diabetes.

Impact of Renal Transplantation on Functional Status in Tacrolimus Era

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Background: Despite a large body of literature describing survival’s outcome after renal transplantation, little is known about the progress of functional capacity post-transplantation. Our aim is to assess the effect of renal transplantation and various factors on functional capacity.

Methods: From the United States Organ Procurement and Transplantation Network files, we identified a total of 19,704 renal transplant recipients (RTR) maintained on tacrolimus-based immunotherapy, who had Karnofsky Performance Status Scale (KPSS) defined functional capacity assessment at the time of transplant evaluation with five-years data follow up. Age, gender, ethnicity, functional status, diabetes, body mass index, cold ischemia time, number of previous transplants, panel reactive antibodies, donor type, donor age, HLA-mismatches, number of acute rejection episodes, induction therapies, maintenance immunotherapy, and recipient characteristics were collected. According to KPSS, RTRs at time of transplant evaluation were divided into 3 groups (A: 13,701 RTRs with mild impairment: >80%; B: 5,557 RTRs with moderate impairment: 40-80%; C: 446 RTRs with severe impairment: <40%). The outcome measured was KPSS functional status five-years post-transplant. Multiple logistic regression analysis was used to assess factors affecting functional status post-transplant.

Results: In group A, 86.45% of patients showed improvement in functional capacity, 65.5% in group B, while 88.56% improved in group C (64.57% improved from severe to mild and 23.99% improved from severe to moderate functional capacity). Furthermore, multiple logistic regression analysis showed that steroid withdrawal protocol was associated with significant improvement in functional capacity (OR=1.28, 95% Confidence Interval (95 CI): 1.1 - 1.49, P<0.007), while dialysis duration before transplantation was associated with abnormal functional capacity post-transplant (OR=0.74, 95% CI: 0.61 - 0.89, P<0.003).

Conclusions: Renal transplantation is associated with substantial improvement in all stages of functional capacity in RTRs. Steroid withdrawal as well as the duration of dialysis are the most important novel determinant factors of functional capacity post-transplant and merit considerations during transplant selection and subsequent immunosuppressive therapeutic planning.

Calcineurin Inhibitor-Based Immunosuppression Has Negligible Negative Effects on Pregnancy Outcomes After Renal Transplantation in the Netherlands

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Background: Pregnancy among renal transplant recipients (RTR) has increased over the past years, also in patients with compromised renal function and/or proteinuria. Immunosuppressive regimens may influence pregnancy outcomes and it is not yet clear whether replacing a calcineurin inhibitor (CNI) by a CNI-free (CNI-) regimen has a favorable effect.

Methods: We therefore retrospectively compared the effect of CNI-based (CNI+) and CNI- immunosuppression in the first trimester of pregnancy on maternal and fetal outcomes in Dutch pregnancies between 1986-2017 in RTR. We identified 129 CNI+ and 125 CNI- single-pregnancies. Demographics did not differ except for higher BMI in CNI+ (median 25.3 vs 23.7 kg/m2, p<0.01), year of renal transplantation (2000 in CNI+ vs 1989 in CNI-, p<0.01), year of pregnancy (2006 in CNI+ vs 1998 in CNI-, p<0.01) and interval of transplantation to pregnancy (69 in CNI+ vs 96 in CNI-; p<0.01). In the third trimester creatinine levels were significantly higher in CNI+ (127 vs 105 μmol/L in CNI-; P<0.01) but this difference had disappeared 6-18 months postpartum. The percentual change in creatinine from preconceptional level to the third trimester level was slightly different (+3.1% in CNI+ vs 2.2% in CNI-, p<0.05).

Conclusions: Our data indicate that CNI do not negatively influence the course of renal function up to 18 months postpartum, but only lead to a more pronounced increase in serum creatinine levels towards the end of pregnancy. However, the substantial short term loss of renal function and the high rates of premature birth rate and low birthweight classify them as high risk pregnancies that should be followed carefully in tertiary obstetric/ nephrologic care programs. Our data do not exclude possible long term negative effects of CNI on overall health, renal function or hypertension in the offspring of these women.
PO2542
The Natural History of Waitlist Candidates in the United States
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Background: Estimates of time to deceased-donor transplantation (DDKT) generally fail to take into account the competing risks of mortality. Understanding the natural history of KT registrants - their chance of DDKT/LDDT/death based on individual characteristics - can inform referrals for transplantation, counseling for transplant candidates, and allocation policy.

Methods: Using SRTA data on 186,174 waitlist registrants 12/2014-12/2019, we modeled time to DDKT, LDDT, or waitlist mortality in a competing-risks framework, overall and for clinical subgroups of patients (based on candidate age, sex, race, ABO blood type, PRA). Competing-risks regression was used to model individual n-year chance of DDKT/LDDT/mortality based on candidate characteristics.

Results: Among all candidates, 5-year cumulative incidence of LDDT/DDKT/mortality other removal was 17.3%/34.4%/15.7%/18.1% respectively. 85% of LDDT recipients received LDDT within 2 years of listing. Pediatric registrants had substantially higher incidence of DDKT than waitlist mortality (61.7% vs 1.1%), but adults had higher combined of waitlist mortality/other removal DDKT, particularly patients above age 65 (44.4% vs 32.3%) (Figure). Center-level 5-year incidence of LDDT (DDKT) 1.3%/44.8% (4.4%/82.6%) (Figure 2).

Conclusions: Despite a focus in the transplant community on small differences in one-year posttransplant outcomes and a reluctance to transplant kidneys with slightly worse expected outcomes, most adult patients wait >5 years for a kidney, incurring substantial waitlist mortality risk. High incidence of waitlist mortality will only be remedied through aggressive efforts to increase the living and deceased donor organ pool.

Funding: NIDDK Support

PO2543
Unusual Cause of Calcium Oxalate Nephropathy in a Renal Allograft
JoBeth McCoy, Anthony J. Langone. Vanderbilt University Medical Center, Nashville, TN.

Introduction: Crystal nephropathy is a well-known cause of acute kidney injury that is often overlooked. We present a case of oxalate nephropathy in a renal allograft that led to a rare diagnosis.

Case Description: A 63-year-old female with a kidney transplant for end-stage kidney disease (ESKD) caused by acute interstitial nephritis (AIN) presented with acute kidney injury. Her creatinine on presentation was 2.0mg/dL from her baseline of 1.0mg/dL and increased to around 3.0mg/dL despite hydration. It was decided that she would benefit from allograft biopsy. The biopsy was devoid of any rejection but did have many foci of calcium oxalate crystal deposition with tubular injury. She was planned for a 24-hour urine collection for stone evaluation that showed an elevated urine oxalate level, 140mg. She changed her diet and the 24-hour urine collection was repeated in 3 months with no change. With the continued elevation, genetic testing was sent for primary hyperoxaluria which revealed that she has homozygote mutation in the AGXT gene, confirming that she has type 1 primary hyperoxaluria. Reevaluation of her biopsy diagnosing AIN before transplant was found to have interstitial multinuclear infiltrate with some crystallization consistent with oxalate. Her particular mutation responds well to pyridoxine (vitamin B6) so she was started on 600mg per day. Since treatment, her creatinine has stabilized at 3.0mg/dL. Her 24-hour urine evaluation has shown improvement in urine oxalate to 79mg, a 43.5% reduction.

Discussion: This case report is a rare diagnosis of primary hyperoxaluria type 1 (PH1) is described by recurrence in a renal allograft in only 10% of cases. Delay in the diagnosis is common and results in a significant number of patients who have end-stage kidney disease (ESKD) at initial presentation. The rapidity of progression is determined by the residual enzyme activity and response to pyridoxine (vitamin B6). The definitive cure for PH1 is a liver transplantation that carries significant mortality risk. Medical management includes large fluid intake of greater than 3L/day to decrease tubular fluid oxalate concentration, potassium citrate-citric acid to increase the solubility of calcium oxalate and prevent precipitation, avoidance of oxalate in diet, and high dose pyridoxine to promote the conversion of glyoxylate to glycine rather than to oxalate. A trial of 5mg/kg of pyridoxine is suggested in all PH1 patients to see how they respond.

PO2544
Secondary Oxalosis with Enteric Oxalate Nephropathy in a Transplant Recipient: Is Mycophenolate the Culprit?
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Introduction: Secondary oxalosis causing acute kidney injury has been widely reported in native kidneys but its occurrence in allograft kidneys is relatively uncommon. Intestinal malabsorption can be present in transplant recipients as a result of factors beyond the general population such as immunosuppressive medications and some enteral infections. We present a case of enteric oxalate nephropathy as a result of mycophenolate toxicity.

Case Description: A 66-year-old male status post kidney transplant 3 years back for ESKD due to DM and HTN with a baseline creatinine of 1.5 mg/dL presented with a 2-month history of GI symptoms of vomiting, diarrhea and 22 lbs weight loss. He was on tacrolimus, mycophenolate and prednisone for immunosuppression. The patient denied any recent infection or antibiotic use, any medication change, supplements or OTC drug use. He denied any ESKD, and the physical examination on admission showed no lab findings showed Na 139, K 5.5, CI 117, Bicarb 11, AG 22, Ca 9.6, BUN 71 and creatinine 3.5. Lactate and serum osmolar gap were normal. Lipase, amylase, Vit B1 and B6 were normal. UA showed trace ketones and blood with no protein or bacteria. Serology for CMV and BK virus was negative. Tacrolimus level was at goal. MPA level was noted to be elevated at 9.7 at an office visit 1 month prior to admission with no recent adjustment in dosing. Plasma oxalate was elevated at 3.9. The stools studies and GI panel were negative. CT scan showed a 3mm non-obstructing stone. The renal biopsy showed interstitial fibrosis, tubular atrophy and calcium oxalate deposits with birefringence within the tubules. MMF was discontinued. The patient was given iv fluids and citrate to alkalize the urine. At discharge, his Cr improved with resolution of symptoms.

Discussion: Medication-induced malabsorption should be considered among potential causes of secondary oxalosis. The MMF metabolites indirectly affect lymphocytes in the GI tract leading to mucosal damage with malabsorption and enteric oxalosis. The hyperoxalosis causes saturation of oxalate crystals creating an interstitial nephritis, macrophage recruitment and inflammation leading to tubular atrophy. The transplant recipients with chronic diarrhea and no infection should be suspected for MMF toxicity. The oxalate and MPA levels must be checked and MMF dose should be adjusted accordingly.

PO2545
Prophylactic Use of Eculizumab and Grant Loss in Kidney Transplant Recipients due to Hemolytic Uremic Syndrome in the United States
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Background: Among kidney transplant recipients (KTRs) with end-stage kidney disease (ESKD) due to hemolytic uremic syndrome (HUS), recurrence is associated with poor allograft outcomes. We examined the prophylactic use of eculizumab, a monoclonal antibody that binds complement protein C5, and graft loss among HUS KTRs.

Methods: We conducted a retrospective cohort study using the United States Renal Data System. Out of 123,624 ESKD patients transplanted between January 1, 2008 and June 1, 2016, we identified 348 (0.28%) patients who had HUS as the primary cause of ESKD. We then linked these HUS patients to datasets containing the Healthcare Common Procedure Coding System (HCPCS) code for eculizumab infusion. We calculated crude incidence rates of overall graft loss and death-censored graft loss and conducted exact logistic regression, adjusted for recipient age and sex. Patients who received eculizumab prior to or within 30 days of transplant represented the exposure group.

Results: Our final study cohort included 335 HUS KTRs (23 received eculizumab, 312 did not). There were no significant differences in baseline demographic and clinical characteristics between the eculizumab vs. non-eculizumab group. For those who received eculizumab, the median number of infusions per patient was 42 (IQR 16, 66). The median payment amount per patient was $706,518 (IQR 241,237, 1,306,453). Eculizumab was discontinued in 9 out of 23 patients (39%), after a median prophylactic duration of 329 days (IQR 127, 791). As shown in the Table, the eculizumab group had no graft loss vs. 20% in the non-eculizumab group, with an adjusted odds ratio of 0.13.

Conclusions: Prophylactic use of eculizumab in HUS KTRs was significantly associated with a lower risk of graft loss. Given the high cost of eculizumab, randomized controlled trials are much-needed to guide prophylactic strategies to prevent graft loss.
PO2546

Post-Kidney Transplant Serum Magnesium Exhibits a U-Shaped Association with Subsequent Mortality

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Background: Hypomagnesemia is common in kidney transplant recipients (KTR), likely due, at least in part, to renal magnesium (Mg) wasting related to calcineurin-inhibitor (CNI) use. The association of serum Mg levels and KTR outcomes may provide insight into the optimal serum Mg levels in this population.

Methods: KTRs between 01/2000 and 2016 at a large US transplant center who were alive with a functioning graft at 6 months post-transplant were included. Mean of the outpatient serum Mg levels in the baseline period, i.e. 6 to 18 months post-transplant, was used. Cox proportional-hazards regression was used to analyze the association between Mg and all-cause mortality, cause-specific mortality, and risk of new-onset cardiovascular events post-transplant.

Results: 2,131 KTRs met our inclusion criteria. Mean number of Mg measurements per patient in the baseline period was 2.76. A U-shaped association between the mean baseline Mg level and all-cause mortality was observed in both unadjusted analysis and after adjusting for baseline characteristics, including eGFR and CNI levels. A mean Mg of 1.5 – 1.8 mg/dL was associated with the lowest incidence of death (Figure). Compared with Mg of 1.5 – 1.8 mg/dL, Mg level ≤ 1.5 mg/dL was also associated with higher incidence of mortality due to infection and arrhythmia but not ischemic heart disease or heart failure.

Conclusions: The relationship between serum Mg levels and mortality in KTRs is U-shaped. Interestingly, the risk is lowest with Mg levels 1.5 – 1.8 mg/dL, which represents the lower end of normal (1.6 – 2.6 mg/dL). Mg supplements for levels ≤ 1.5 mg/dL may be beneficial, but may cause increased renal wasting and diarrhea. Further studies are needed to understand why Mg > 1.8 mg/dL but well within the normal range was associated with higher risk despite adjustment for eGFR.

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PO2548

Virtual Reality, a New Vision Becoming Our New Actuality: A Retrospective Study Comparing Virtual Crossmatch vs. Physical Crossmatch at Tampa General Hospital

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Background: A crossmatch (XM) is required prior to kidney transplantation to ensure immunological compatibility between recipient and donor. This test is prone to false positive reactivity and can increase cold ischemic time (CIT) especially for organs procured outside the region of the transplanting hospital. Advances in HLA antibody testing and donor HLA antigen typing facilitate the use of a virtual XM (VXM) based on pre-transplant testing results to accurately predict a physical XM (PXM) result. Frequent antibody screening and an accurate history of sensitizing events further ensures that the VXM can predict immunological compatibility, even without retrospective PXM.

Methods: We compared the 6 mo. clinical outcomes of kidney recipients who proceeded to transplant with only a VXM (without retrospective PXM) to those receiving a PXM. 182 recipients with 6 mo. follow-up were reviewed for biopsy data, serum Cr and UPCR. Patients were grouped according to the transplant type (living donor (LD) vs. deceased donor (DD)) and XM type (PXM vs. VXM). LD recipients had a PXM (n=42). Patients with a VXM (n=76) were donor-specific antibody (DSA)-free and had a current tested sample within 30 days. DD recipients had PXM (n=64) due to the presence of DSA (current or historic) or the absence of a current tested sample within 30 days. All patients with PXM had an acceptable flow cytometric XM.

Results: Patients proceeding to transplant with a VXM tended to be less sensitized (32% with PRA >0%) compared to DD-PXM (66%) and LD-PXM (49%). For DD recipients, CIT was significantly reduced in patients receiving a VXM (727 vs 871 min; p=0.011). Within the first 6 mo. of follow-up, 67 for cause biopsies were performed. Rejection (T-cell or antibody mediated) was observed in 15 patients (7 DD-VXM, 6 DD-PXM and 3 LD-PXM). Interestingly, antibody mediated rejection was only observed in DD-PXM (n=3) or LD-PXM (n=1) groups.

Conclusions: In our cohort, kidney transplantation with an acceptable VXM was beneficial in reducing CIT and rejection was similar to DD recipients needing a PXM within the first 6 mo. post-transplant. Utilizing VXM helps facilitate kidney transplantation, permits entertaining offers from greater distances, and reduces laboratory burden with similar outcomes to when a PXM is performed.

PO2547

A Case of Subretinal IgA Deposition in a Patient with IgA Nephropathy and Early Allograft Recurrence

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Introduction: IgA Nephropathy (IgAN) has variable clinical manifestations and a 30% recurrence, which is typically a late complication in renal transplant recipients. Occular involvement in patients with IgAN is extremely rare. Thus, eye findings as a predictor of worse prognosis, including higher risk of recurrence, remains unexplored.

Case Description: A 66 year old Caucasian male with end-stage renal disease secondary to a 10 year history of IgAN complicated by retinal detachment and optic neuropathy with recent decline in visual acuity, underwent living related renal transplant from his twin sister with Basalimab induction. A month prior, Optical Coherence Tomography (OCT) had revealed bilateral macular edema and subretinal pigment deposits with central foveal sparing, consistent with IgA maculopathy. Post-operative course was uneventful with immediate allograft function and normalization of creatinine. 4 months later, repeat OCT showed improved retinopathy and occular edema. However, renal function declined 2 months later, with persistently elevated

PO2549

Reassessing Renal Transplantation in Light-Chain Deposition Disease


Background: Light chain deposition disease (LCDD) is a systemic rare condition that usually leads to end stage renal disease. Treatment with a bortezomib-based regimen, followed by autologous stem cell transplantation (ASCT) has been increasingly used with improvements in the response rates and the renal graft outcomes in kidney transplant recipients.
Methods: Retrospective study of 6 patients diagnosed of LCDD with complete response but not renal response after hematologic treatment that underwent kidney transplant in our institution between 2010 and 2019.

Results: A total of 6 patients (5 women) were analyzed, with mean age at diagnosis of 47 years, mean eGFR of 18 mL/minute and mean proteinuria of 5.5 g. Deposit was kappa type except in 1 case (heavy and light lambda type chains). In all of them there was an absence of monoclonal component in blood and urine but positive immunofixation in 5 cases (2 only in urine). 3 started chronic hemodialysis during admission and the others at 3, 5 and 44 months after diagnosis. As hematological treatment, all received bortezomib followed by ASCT, being under complete hematological response at the time of kidney transplant, which was performed at 28 months on average from ASCT. Mean kappa/lambda ratio was 2.6. 3 patients received induction with thymoglobulin and 3 with basiliximab, followed by triple therapy with tacrolimus+prednisone+mTOR inhibitor (4 patients) or mycophenolate (2 patients). After 36 months of mean follow-up after kidney transplant, 3 patients have suffered an hematological relapse, one of them including kidney involvement with graft loss at 46 months post-transplant. The remaining 5 continue with a functional graft with a mean creatinine of 1.54 mg/dL.

Conclusions: When sustained complete hematologic response is achieved but renal impairment with dialysis requirement persists, patients could benefit from a kidney transplant with good results.

PO2550
Granulomatous Interstitial Nephritis and Allograft Failure Secondary to Adenovirus Reactivation

Introduction: With an incidence of about 4% in renal transplant recipients, the typically self-limited adenovirus renders an infrequent propensity to cause allograft failure and life-threatening opportunistic infection in severe cases.

Case Description: A 29 year old female with history of living donor kidney transplant due to Henoch Schonlein Purpura (HSP) Glomerulonephritis with subsequent allograft failure underwent deceased donor re-transplantation with Anti-Thymocyte globulin induction. Post-op course was uneventful. Creatinine was 0.8 mg/dL on 4 month follow up. 6 months post-transplant, patient developed gross hematuria with clots, fever and acute kidney injury with creatinine of 2.82 mg/dL. Biopsy revealed granulomatous tubulointerstitial nephritis, extensive intra-nuclear viral inclusions with positive adenovirus immunohistochemistry (IHC). Mycophenolate Mofetil was discontinued and creatinine improved to 1.1 mg/dL. 3 months later, she was admitted for renal failure with creatinine of 7.2 mg/dL. Adenovirus was detected in the serum and urine. Repeat biopsy revealed markedly reactive tubular epithelium, widespread viral inclusions with negative adenovirus IHC, consistent with adenovirus nephropathy. Following a decrease in immunosuppression with improvement in renal function, adenovirus viral load became undetectable in both plasma and urine. The use of Cidofovir was considered for treatment but not renal response after hematologic treatment that underwent kidney transplant in our institution between 2010 and 2019.

PO2551
Phospholipase A2 Receptor Antibody Level Directed Management of Membranous Glomerulopathy After Transplant
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Introduction: MN can recur after transplantation. Patients with high PLA2R Ab are at higher risk. There is equipoise on how to manage these patients. We present two cases to highlight PLA2R Ab level directed approach to management.

Case Description: Case 1: 35 YO AA female with MN diagnosed in 2013. Failed cytotoxic therapy and started RRT. Received a DD kidney transplant in Sep 2018. Given Thymoglobulin, tacrolimus, mycophenolate and prednisone. Pre-transplant PLA2R titer 1:2560 by IIF. Titer serially monitored. After an initial decline, titer increase with precipitation of proteinuria noted. Biopsy confirmed early recurrent MN. Treated with 2 doses of Rituximab. Subsequent titters dropped with complete remission. Case 2: 65 YO W male with biopsy demonstrated MN (2015), on RRT since 2017 underwent DD kidney transplant in May 2019. Given Thymoglobulin and maintained on tacrolimus, mycophenolate and prednisone. Pretransplant PLA2 R Ab level was 164 RU/ml by EIA with 3.5 g/g of protein. His PLA2R Ab levels dropped and proteinuria rapidly & durably resolved after transplant. One year out, his PLA2R Ab is at 24 RU/ml with 0.11 g/g protein in the urine and a creatinine of 1.2 mg/dL.

Discussion: High PLA2 R Ab at the time of transplant is a significant risk factor for recurrent MN. PLA2R Ab levels should be monitored to direct care: decreasing PLA2R Ab should be followed conservatively. If Ab levels increase or proteinuria develops, perform biopsy to confirm diagnosis and initiate therapy expeditiously. PLA2R Ab levels should be monitored post transplant to ensure resolution. This approach allows stratification and directed therapy of patients with MN undergoing transplantation and avoids overt treatment.
PO2552

De Novo Membranous Nephropathy and Donor-Specific Allotubodies: A Path to the Pathophysiology?
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Introduction: While pathophysiology of post-transplant membranous nephropathy due to recurrence of primary disease is established, less is known about the development of primary de novo membranous nephropathy (dnMN). We report a case of dnMN associated with antibody-mediated rejection in a transplant recipient with end-stage kidney disease secondary to focal segmental glomerulosclerosis (FSGS).

Case Description: A 20-year-old African American female with FSGS status-post deceased donor transplant eight years ago presented with acute lower extremity edema and acute kidney injury concerning for acute rejection. She has no history of prior rejection or medication non-adherence. Ultrasound showed mild hydronephrosis. Biopsy showed Banff Type IB acute cellular mediated rejection (6, 21, 2) and Stage 1 membranous glomerulopathy. Serum phospholipase A2 receptor (anti-PLA2R) antibodies were negative. Donor specific antibodies (DSA) testing revealed the presence of DQ5, DQ7, and DRB1*1501. Diagnosis of coexistence of Banff Type IB acute-cell mediated rejection, positive de novo DSA, and dnMN was made. She was treated with five doses of antithymocyte globulin (1.5 mg/kg/dose) and plasma exchange (PLEX) followed by rituximab. Repeat DSA showed negative. Donor specific antibodies (DSA) testing revealed the presence of DQ5, DQ7, and DQ8. She was treated with high dose steroids, 10 sessions of plasmapheresis with intravenous immunoglobulin (IVIG), and Rituximab. His Cr improved to 1.2 mg/dL but DSA remained positive. Later on he was restarted on Etanercept which was withdrawn again in March 2019. Accordingly, in September 2019, he developed acute kidney injury with Cr up to 1.7 from baseline of 1.3-1.5 mg/dL associated with nephrotic range proteinuria. He had a rise in DSA to DQ7, and developed new DSA to A2 and B60 with positive cytotoxicity crossmatch. Donor derived cell free DNA was elevated at 4.4%. Allograft biopsy showed glomerulitis, peritubular capillaritis with positive c4d, consistent with ABMR. He was treated with high dose steroids, 10 sessions of plasmapheresis with IVIG and Rituximab. Repeat DSA showed reduction in A2, but no change in DQ7. His serum Cr improved but his proteinuria remained at nephrotic range.

Discussion: Despite the use of Etanercept in the treatment of graft versus host disease among transplant recipients, it hasn’t been studied as a potential immunosuppressive drug. In our patient, Etanercept seemed to provide anti-rejection effect as shown by two episodes of ABMR with de-novo DSA after the drug’s withdrawal. Close monitoring of renal function and DSA may be warranted once Etanercept or other TNF inhibitors are withheld.

PO2553

Histological Predictors of Graft Failure in Kidney Transplant Recipients
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Background: We aimed to identify the predictors of allograft failure in a large cohort of kidney recipients who underwent clinically indicated graft biopsies. We aimed to explore the importance of interstitial inflammation in biopsies with interstitial fibrosis and tubular atrophy (IFTA).

Methods: We retrospectively evaluated 516 patients who underwent transplant biopsy between 1/2009 and 1/2018. Acute and chronic allograft injury scores of Banff classification were used. We sub grouped the patients with chronic allograft injury score (cic/cic/tcv) ≥ 3 or < 3 and sub grouped per interstitial inflammation (i score=0 and > 0) and compared to biopsies with both cic/cic/tcv=0 and i=0.

Results: Biopsies were done at a median 12.5 months after kidney transplantation. The histopathological diagnosis were as following: acute antibody-mediated rejection (AMR) (6%), acute T-cell mediated rejection (9.3%), chronic AMR (6.7%), transplant glomerulopathy without donor-specific antibody (DSA) (10.2%), recurrent de novo glomerular disease (20.8%), BKV nephropathy (2.5%), and the rest 54.2% had other diagnosis (normal, acute tubular necrosis, or non-specific IFTA). During a median follow up of 59.3 months after kidney biopsy, 36 %recipients lost their graft. In univariate analysis, the following factors were significant for graft loss: Black race (p=0.005), previous rejection (p=0.001), DSA at the time of biopsy (p=0.014), cic/cic/tcv ≥ 3 (p=0.0485), cic/cic/tcv ≥ 3 with interstitial inflammation > 0 (p=0.0001), microvascular inflammation (p=0.0052), C4d positivity (p=0.008), serum creatinine at time of biopsy.

PO2554

A Case of Antibody-Mediated Rejection (ABMR) After Withdrawal of Etanercept in a Renal Transplant Recipient
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Introduction: Etanercept is a tumor necrosis factor (TNF) receptor fusion protein that is used to manage several forms of inflammatory arthritis and psoriasis. Herein, we present a renal transplant recipient who was concomitantly treated with Etanercept for psoriasis and subsequently developed two episodes of ABMR after the drug’s withdrawal.

Case Description: A 41-year-old man with history of psoriasis and end stage renal disease due to hypertensive nephrosclerosis and interstitial nephritis who underwent living related kidney transplant from his brother in December 2008. He was being treated for psoriasis with Etanercept which was withdrawn in September 2012. Subsequently he developed rising serum creatinine (Cr) from baseline of 1.3-1.5 mg/dL. Developed de-novo donor specific antibodies (DSA) to DR1 and DQ7 with positive cytotoxicity crossmatch. Renal allograft biopsy showed evidence of Banff 2A acute cellular rejection, ABMR, chronic glomerulonephritis and interstitial nephritis. He was treated with high dose steroids, 10 sessions of plasmapheresis with intravenous immunoglobulin (IVIG), and Rituximab. His Cr improved to 1.2 mg/dL but DSA remained positive. Later on he was restarted on Etanercept which was withdrawn again in March 2019. Accordingly, in September 2019, he developed acute kidney injury with Cr up to 1.7 from baseline of 1.3-1.5 mg/dL associated with nephrotic range proteinuria. He had a rise in DSA to DQ7, and developed new DSA to A2 and B60 with positive cytotoxicity crossmatch. Donor derived cell free DNA was elevated at 4.4%. Allograft biopsy showed glomerulitis, peritubular capillaritis with positive c4d, consistent with ABMR. He was treated with high dose steroids, 10 sessions of plasmapheresis with IVIG and Rituximab. Repeat DSA showed reduction in A2, but no change in DQ7. His serum Cr improved but his proteinuria remained at nephrotic range.

Discussion: Despite the use of Etanercept in the treatment of graft versus host disease among transplant recipients, it hasn’t been studied as a potential immunosuppressive drug. In our patient, Etanercept seemed to provide anti-rejection effect as shown by two episodes of ABMR with de-novo DSA after the drug’s withdrawal. Close monitoring of renal function and DSA may be warranted once Etanercept or other TNF inhibitors are withheld in transplant recipients.

PO2556

Molecular Analysis of Renal Graft Biopsies: Comparing the Edmonton Molecular Microscope with the NanoString Human Organ Transplant Panel
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Background: The renal transplant biopsy is the diagnostic gold standard and usually evaluated with the continuously expanded and updated Banff classification which is based on descriptive, empirically-derived criteria and thus lacks precision. High-resolution determination of the graft status by NanoString analysis, which was developed for formalin-fixed paraffin-embedded (FFPE) RNA, should be a sufficient approach for objective molecular diagnosis of renal transplant biopsies and may improve our understanding of graft biology.

Methods: We used well-annotated surveillance and indication biopsies from 63 patients whose time-matched second biopsy core had been frozen and analyzed by microarray in the INTERCOM/INTERCOMEX study. After reevaluation according to recent Banff consensus, RNA isolation of the FFPE biopsy was performed and led to 774 RNA yields in 53 samples which were further processed for NanoString analysis using the nCounter Human Organ Transplant Panel.

Results: Morphologically, of the 53 samples analyzed (samples from 2011/12 and 2015), twenty-five patients showed no signs of rejection, twelve had borderline rejection,
four showed cellular rejection, seven had humoral rejection, and five presented with combined rejection. Preliminary analysis of gene expression by T-distributed Stochastic Neighbor Embedding (t-SNE), Random Forest and Principal Component Analysis (PCA) showed clear differences between samples with rejection (humoral and cellular) and without rejection. Reaction samples revealed high expression of chemokine ligands compared to rejection-free tissues. A common pattern of samples without rejection and borderline rejection was observed. Our results displayed good correlation with the former molecular microarray-based diagnosis from the INTERCOM/INTERCOMEX study.

**Conclusions:** Molecular diagnostic approach using the NanoString platform may supplement morphological diagnosis of renal grafts especially in unclear cases and thus enhance precision diagnostics with small tissue requirement. Morphological and molecular evaluation in the same biopsy core from FFPE tissue enables direct histological-molecular correlation. Additionally, this technology also improves our understanding of pathophysiology in renal and other transplants.

**PO2557**

**Donor Biopsy and Kidney Transplant Outcomes in Pediatric Recipients**

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**Background:** Deceased Donor DD kidney biopsies are routinely used in the context of clinical concerns about donor quality in adult kidney transplants. We sought to examine the use of DD kidney biopsies in pediatric transplants. We aim to evaluate prognostic utility of glomerulosclerosis GS level in predicting graft outcome.

**Methods:** Data was used from recipients who received kidney transplant between 1994 and 2018 documented in the Scientific Registry of Transplant Recipients database. Pediatric recipients were defined as recipients <18 years who received DD kidney transplant excluding multi-organ transplants. The recipients were further stratified according to degree of donor kidney GS into 0-5% and >5% categories. Demographic and outcome data were examined and graft survival was evaluated using STATA 16.

**Results:** 10,045 pediatric recipients received DDKT during this period. 644 had left and/or right DD kidney biopsies, 548 biopsies had 0-5% GS, 96 biopsies had >5% GS. Biopsies were mostly performed on kidneys harvested from higher risk donors. There was a significant difference in the number of biopsies performed across regions (region 5 lowest at 2.6% and region 9 highest at 17.5%). There was no significant difference among share characteristics or transplant center volume. Allograft survival was significantly worse for donor kidneys with GS-5% compared to 0-5% group and no biopsy group. There was no significant difference in the incidence of DGF, acute rejection, or chronic rejection.

**Conclusions:** Although the biopsied kidneys are mostly from higher risk donors, the majority of biopsies have GS level 0-5%. At this level of GS there is no difference in allograft survival compared to DD kidneys without biopsies. Thus utilizing kidneys with GS 0-5% can expand the DD kidney pool and should be strongly considered for use in pediatric population.

**PO2558**

**Predictors and Impact of Nephrocalcinosis in Renal Transplant Population: A Monocenter Retrospective Study**

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**Background:** Persistence of bone and mineral anomalies in post-transplant population has been suggested as contributing factors to nephrocalcinosis (NC) that could lead to graft dysfunction. However, adequate characterization of calcium deposits in biopsies from renal transplant patients are lacking. We thus aimed to determine: 1) the prevalence of NC in renal transplant patients, 2) the factors associated with NC and 3) the impact of NC on renal graft function.

**Methods:** This is a monocenter retrospective study using a protocolized renal biopsy from CHU de Quebec, l’Hôtel-Dieu de Quebec hospital from 2016-2018. All renal biopsies performed in 2016 at renal transplantation, at 6 and 24 months post-transplant were qualitatively and quantitatively analyzed for NC. Demographic, comorbidities and biochemistry parameters were collected from patients’ records. Appropriate statistical analyses (Pearson’s chi-squared, Wilcoxon-Mann-Whitney, Spearman’s correlation and logistic regression) were performed to assess factors associated with NC and its impact on graft function.

**Results:** We included 53 patients (mean age of 52±13 years, 55% of men, 94% with hypertension, 23% with peripheral arterial disease and 19% with prior parathyroidectomy). Forty-nine patients (92%) were on chronic dialysis treatment before transplant for a mean duration of 34±29 months. The presence of NC was observed in 14% at baseline, 37% at 6 months and 50% at 24 months. The severity of NC as assessed by the number of calcified foci in the tubulointerstitial compartment also tended to increase over time. Analyses showed that the presence of NC at 6 months was associated with male sex, presence of NC at baseline and high PTH levels (> 600 ng/L) at the time of transplant. Presence of NC at 24 months was also associated with prior NC and male sex. Interestingly, the presence of NC at 6 months was associated with use of phosphate supplements immediately after engraftment and with active vitamin D treatment at 6 months. Finally, NC at 24 months was correlated with the level of graft function as expected.

**Conclusions:** This study reveals that uncontrolled mineral and bone metabolism parameters before renal transplant are associated with development of NC in the post-transplant period that may contribute to deterioration of renal graft function.

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

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PO2560
Antiphospholipid Antibody Syndrome Causing Thrombotic Microangiopathy in the Immediate Post-Transplant Patient: A Case Report
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Introduction: Differential diagnosis of thrombotic microangiopathy on kidney biopsy specimen includes infection, hypertension, malignancy, or inherited complement disorders. In the the post-transplant period the differential also includes calcineurin inhibitor toxicity and rejection.

Case Description: A 29 year-old AA female with ESRD disease due to lupus nephritis and HTN. Her care was provided in another state until 2011- she had a stroke in the past which she reports was secondary to uncontrolled HTN. No h/o blood clot, never been pregnant. Native kidney biopsy in 2015 showed lupus: class V membranous GN, focal segmental and diffuse glomerular sclerosis with collapsing features, and focal acute thrombotic microangiopathy. In 2019, she underwent deceased donor kidney transplant. On post-op day 4, Sr Cr began to increase and biopsy demonstrated thrombotic microangiopathy. Chart review revealed increased aPTT prior to surgery. DsDNA was negative. Tacrolimus troughs were low, donor-specific antibodies were negative. She was treated empirically with high-dose steroids and plasma exchange. Workup revealed positive anti-cardiolipin IgG (46 GPL units/mL) and positive anti-beta-2 glycoprotein IgG (532 units/mL). She recalled being on warfarin following her CVA in 2010, for embolic stroke. She received a dose of Rituximab, has been maintained on tacrolimus and mycophenolic acid along with warfarin for her antiphospholipid syndrome (APLs) and has normal graft function

Discussion: This case highlights the importance of a complete serological workup to rule out APLs in the pre-transplant patient, even in the presence of alternate explanatory diagnoses. Patients with APLs should be treated with lifelong anticoagulation to prevent further embolic complications, including loss of transplanted organs.

PO2561
Impact of Out-of-Hospital Organ Donor Cardiac Arrest and Cardiopulmonary Resuscitation on Donor Kidney Histology and Function
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Background: The mortality rate of patients listed for kidney transplantation (KT) is 5 per 100-patient years. Due to an organ shortage crisis, expansion of KD pool (KDP) is critical (1). Kidney donors (KD) with out-of-hospital cardiac arrest (OHUS-CA) and cardiopulmonary resuscitation (CPR) have low acceptance rate due to presumed delayed graft function (DGF). Donor CA in controlled setting (in ICU) does not impact KF post engraftment (PE) (2) but impact of OHUS-CA is unknown. We propose that terminal serum creatinine (TSC) and Kidney histology (KH) immediately prior to kidney transplantation predict KF post KT. We did a nested cohort study to study the impact of OHUS-CA and CPR of KDs on KT and KH

Methods: Our transplant program received thirty-five kidney organ donors offers with a procurement biopsy from UNOS during July to December 2019. Retrospectively we reviewed demographics, pre-hospitalization resuscitation information, hemodynamic data and KH. Four patients were excluded; two had missing data; one patient had ischemic infarct and one patient had kidney tumor. The study cohort (N=31) divided into CA-OHUS (N1=16) and No Cardiac Arrest (No-CA, N2=15) groups. The change (delta) in serum creatinine (DSC) while under donor management (DM) compared in each group. Hypotension during donor management (H-DM) and acute tubular damage score (ATDS) from donor kidney biopsy compared within each group of the cohort.

Results: TSC and ATDS prior to KT were evaluated as surrogates for KF post engraftment and there was no difference between OHUS-CA and No-CA (standard) donors. Effect of ischemic preconditioning was noted in OHUS-CA group (Table). Longer the duration of CPR greater was the residual KF (Fig 1).

Conclusions: KF and KH in KD with OHUS-CA are similar to standard criteria donors hence should not be prejudiced. This will expand the KDP.

PO2562
Living Donor-Derived APOL-1-Associated Collapsing FSGS in a Kidney Transplant Recipient
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Introduction: Homozygous high risk APOL1 mutations in donors can drive disease in recipients. We present a living kidney recipient with de-novo collapsing FSGS. His donor was homozygous for high risk mutations.

Case Description: 47 YO AA male with CKD due to biopsy proven diabetic nephropathy s/p LUKT in May 2018. Got thymoglobulin (5 mg/kg) with tacrolimus, mycophenolate sodium and prednisone. High risk for CMV (D+ / R-). EBV IgG +. Donor was his 35 years old AA wife. We were not testing APOL-1 on AA donors at the time. At month 6: Cr 1.4 mg/dl, Ur Pr/Cr of 0.22 g/g. Valganciclovir stopped. Two weeks later, Ur Pr/Cr of 2.92 g/g. CMV PCR +276 copies / ml and EBV PCR +492 copies / ml. PCR for Parvo Virus B-19 as well as DSA negative. Given steroids, plasmapheresis (X3) and IV ganciclovir. Biopsy CN collapsing FSGS. IF negative, including CMV and C4d. Donor tested for and found to be homozygous for APOL1 G1 mutations confirming donor derived APOL1 gene associated collapsing FSGS, presenting as an acute diffuse podocytopathy. Trends in his renal function, CMV, EBV and proteinuria are tabulated in Figure 1. Treated with RAAS blockade, antivirals & immunosuppression. He cleared his CMV Viremia promptly. However, EBV viremia worsened. Eventually, in May 2019, received Rituximab with resolution of EBV viremia. He is 18 months out from transplantation predict KF post KT. We did a nested cohort study to study the impact of OHUS-CA and CPR of KDs on KT and KH

Discussion: APOL-1 mutations place recipients of these kidneys at risk for adverse outcomes. Few instances of APOL-1 mutation driven kidney disease in recipients from...
living donors are documented. This presentation supports the two-hit hypothesis - The high injury state due to CMV and EBV viremia precipitated APO-1 associated FSGS in this kidney with homozgyous high risk mutations. APOL-1 screening in AA donors, especially young donors, should be considered for risk stratification and counseling.

PO2563

Pediatric Donor Glomerulopathy in Pediatric En-Bloc Kidney Transplants


Background: Use of pediatric en-bloc kidneys (EBK) have equivalent outcomes to standard deceased donor kidneys and has helped expand the pool of donor kidneys. The size mismatch related hyperfiltration injury in pediatric EBK and pediatric single kidney allografts is associated with pediatric donor glomerulopathy whose effect on allograft outcomes is not well documented.

Methods: We retrospectively reviewed for cause biopsies of pediatric EBK from 1/2015 to 1/2020. Our center performed 37 transplants using pediatric EBK. Recipient weight criteria was ≤ 75 kg to minimize donor-recipient size mismatch. One recipient died with a functioning graft at 4 months; one graft failed due to fungal infection of the vascular anastomosis requiring nephrectomy at 1 month.

Results: Fourteen biopsies were performed in 10 patients between 1 to 24 months after transplantation. Indications for biopsy were: graft dysfunction (10; 3 with proteinuria), proteinuria alone (2), BK viremia with proteinuria (1), and de novo donor specific antibody (DSA) (1). Biopsies from 5 EBK recipients demonstrated pediatric donor glomerulopathy represented by the presence of glomerular abnormalities including subepithelial multilayering/remodeling of the basement membrane, segmental glomerulosclerosis, mesangial hypercellularity, mesangial sclerosis, podocyte hypertrophy, and/or segmental mild podocyte foot processes effacement. Ten biopsies also showed thin basement membranes (BM) on EM consistent with the age of the donor kidney. Other diagnostic findings among the entire biopsy cohort were acute cellular rejection (ACR), antibody mediated rejection (AMR), or mixed ACR and AMR (5), acute tubular necrosis (ATN) (3), and pyelonephritis (1). Biopsies with pediatric donor glomerulopathy were performed early after transplantation and were associated with proteinuria. Semiquantitative proteinuria in the 5 recipients at the time of biopsy was 1-3+; 1.2-9.5 g/day in 4. Follow up 4-39 months post-transplant (mean 17 months) in patients with pediatric donor glomerulopathy showed serum creatinine 0.55-2.07 mg/dL (mean 1.13) and urine protein 0.4 to 1.2 g/day (mean 0.73).

Conclusions: Overall, pediatric donor glomerulopathy seen early post transplant period did not appear to negatively affect long-term graft function; this outcome may be related to growth of these kidneys occurring early post transplant.

PO2564

Pre-Transplant Genetic Testing of Living Related Donor in a Case of Atypical Hemolytic Uremic Syndrome

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Introduction: Atypical HUS (aHUS) is a rare thrombotic microangiopathy caused by dysregulation of the alternative complement pathway either through mutations in regulatory genes or autoantibodies directed against regulatory proteins. Here we report a case of genetic testing pre-transplant in a patient who developed aHUS with variants in the CFH and PLG genes and her living related donor.

Case Description: A 27-year-old female presented to the hospital with diarrhea, abdominal pain, AKI, and microangiopathic hemolytic anemia requiring dialysis. She was initiated on eculizumab but progressed to ESRD. Renal biopsy showed TMA with focal crescents and severe interstitial fibrosis and tubular atrophy. Workup revealed aHUS with complement dysfunction—low C3 and C4, normal CD46 and Factors H, I, and B, and no autoantibodies to CFH. Genetic testing showed mutation on exon 9 (SCRT7) of CFH that has been shown to cause aHUS as well as another variant on exon 7 of PLG, which is present in 0.3% of European Americans and may be pathogenic but is of uncertain significance for her. Ten months later, she was evaluated for living related renal transplant from her brother. Since she had a mutation known to cause aHUS, genetic testing was done for her brother as part of donor evaluation. He was found to have the same mutation in CFH but not PLG, despite being asymptomatic with no hemolytic anemia, normal kidney function. The transplant was cancelled because of increased risk of disease in the future in the brother. Genetic counseling was provided to brother about his possible risk of aHUS.

Discussion: Mutations in CFH are associated with aHUS; however, it is thought that a trigger—e.g. infection or additional acquired genetic variant leads to progression to aHUS in carriers of complement gene mutations. Genetic testing is recommended for patients with aHUS to determine cause and inform long-term treatment. This patient had a combination of a variant in the complement pathway gene CFH and coagulation pathway gene PLG, while her brother, a candidate for living related donor, had the same variant in CFH. We recommend genetic testing for a living related donor if any mutation is found in the index case to minimize posttransplant recurrence or precipitation of aHUS in the donor.

PO2565

Trouble Brui-ing: A Case of Doppler Discovery

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Introduction: This case highlights the clinical presentation and management of an uncommon kidney transplant biopsy complication.

Case Description: A 19 year old male with ESKD, now status-post second deceased donor kidney transplant, presented to clinic with hypertension. Post transplant course included 3 prior normal surveillance kidney transplant biopsies. Graft function was stable (creatinine 1 mg/dL), and tacrolimus trough level was therapeutic. His blood pressure was 130/85. Exam showed a palpable thrill with audible bruit over the graft site. Ultrasound showed a sonolucent lesion in the lower pole of the transplant kidney, which was not present on prior imaging. Doppler revealed turbulent flow concerning for an arteriovenous malformation (AVM). Renal angiography confirmed the diagnosis, and he underwent endovascular embolization with coil [Image]. Graft function and blood pressure readings remain normal on most recent follow up.

Teaching Points: Ultrasound with Doppler is critical for the diagnosis. Endovascular embolization is an effective and minimally invasive management option for most patients.

PO2566

Renal Transplant Artery Stenosis and Kinking: An Unusual Association

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Introduction: Renal artery stenosis of the kidney graft associated with kinking is not a frequent finding. As a correctable cause of graft dysfunction it is important to diagnose it as soon as possible to avoid further graft damage.

Case Description: A 62-year-old woman with ESRD due to ADPKD had a deceased donor kidney transplant (KTx) in her right iliac fossa (1 vein/1 artery) anastomosed to external iliac vessels. Immunosuppression: basiliximab, tacrolimus, everolimus and steroids. Creatinine drop halted 2 weeks post-op. Blood pressure was normal, CMV load : undetectable. Tacrolimus level:7-9 ng/mL. A KTx US was done, showing high velocities within KTx renal artery close to the anastomosis, increasing near a kinking image adjacent to the hilum (image 1), not present on Doppler US 1 day post-op. A CT angiography confirmed renal artery stenosis at anastomosis level and kinking of the graft renal artery (image 2). Endovascular angioplasty of the stenotic area without stenting was performed, but unsuccessful. Open surgery vascular reconstruction was carried out a week after angioplasty: renal artery was shortened and reimplanted. Within a week, graft function improved and Doppler US was normal.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

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Discussion: Renal artery stenosis is a correctable cause of hypertension and graft dysfunction in KTx. Graft renal artery kinking is rare, even more in association with stenosis, worsening its prognosis as kinking renders angioplasty less effective. Complete Doppler US mapping of the graft’s arteries is essential to make an early diagnosis and nephrologists could do this examination promptly.

PO2567
Proliferative Glomerulonephritis Monoclonal Immunoglobulin Deposits (PGNMID) in a Kidney Allograft Successfully Treated with Rituximab
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Introduction: PGNMID is a rare distinct form of glomerulonephritis (GN) characterized by glomerular monoclonal immunoglobulin deposits. There is no definite treatment for this condition. We present a case of PGNMID in a recurrent renal transplant patient who responded well to rituximab.

Case Description: A 43-year-old male with ESRD secondary to MPGN s/p 3rd renal transplant complicated with failure of previous transplants due to rejections (on cyclosporine and everolimus) presented with worsening pain at the graft site and AKI. Creatinine 5.6 mg/dL (baseline 2.5 mg/dL), UPC 1.5 gm/dL, RBC, and RBC casts on microscopy. Detailed serological, immunological, and infectious workup was negative. Renal biopsy showed mesangial, subepithelial, and subendothelial proliferation with electron dense deposits of IgG1 and IgG3 with kappa predominance most consistent with PGNMID. Monoclonal workup was negative and bone marrow biopsy showed no clear evidence of hematologic malignancy. He received two doses of rituximab in addition to home immunosuppression. Renal function improved to baseline (creatinine 2.5, negative blood, UPC 0.5) and has been stable for past year.

Discussion: GN recurrence in kidney allografts is responsible for around 24% of kidney graft losses. Approximately 70% of PGNMID patients have no detectable monoclonal proteins in serum or urine. Multiple regimens have been used for the treatment of PGNMID after renal transplant, including RAAS blockers, steroids, rituximab, bortezomib and plasmapheresis. Few reported cases of PGNMID responded well to rituximab, and a large prospective multicenter controlled study is warranted to better understand this rare disease.
**Transplant Complications: Glomerular Disease and Genetics**

**PO2569**

**Case Study of Repository Corticotropin Injection (RCI) Prophylaxis for FSGS Recurrence in Kidney Transplant**

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**Introduction:** Idiopathic FSGS recurs post-transplant in one third of cases and is associated with a five-fold higher risk of graft loss.1

**Case Description:** In this single center pilot case study, 8 patients with biopsy-proven FSGS were treated with RCI prophylaxis 80 units subcutaneously twice a week for 6 months from day of kidney Tx, compared with a group of 6 patients who were treated with RCI later after the diagnosis of FSGS recurrence.

**Discussion:** All patients received rATG as induction and were on standard immunosuppression with FK, MMF, and prednisone. Patients in the control group were diagnosed with recurrent FSGS between 5-63 days post Tx. There were 3 patients in the study group that developed recurrent FSGS, 2 of them required plex. Patient 1 in the study group had DGF after a live donor kidney Tx from recurrent FSGS. Her protocol biopsy performed one year after transplant and still shows foot process effacement but no fibrosis or sclerosis in light microscopy. All but one patient in the control group have still functioning allografts. Conclusions: This is a small pilot study, but its findings suggest that use of RCI at time of kidney transplant surgery in patients with FSGS decreases the severity of the disease with less fibrosis in follow up biopsies despite the presence of foot process effacement. There may also be a decreased need for plex in the study group, however, further studies are needed to confirm this.

**PO2570**

**Does Therapeutic Plasma Exchange Improve Kidney Function in Renal Transplant-Associated Thrombotic Microangiopathy?**

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**Background:** Therapeutic plasma exchange (TPE) is performed in patients with renal transplant thrombotic microangiopathy (t-TMA) to improve the kidney function. The goal of our study is to evaluate the short-term efficacy of TPE in patients with renal t-TMA.

**Methods:** We retrospectively compared the outcome of TPE-treated vs. non-TPE-treated patients with biopsy-proven diagnosis of t-TMA. Histologic criteria for diagnosis of t-TMA included presence of thrombi in the artery/arteriole/glomeruli, mesangiolysis & double contours, and electron microscopic evidence endothelial cell injury including subendothelial rarefaction/accumulation of fluffy material and mesangial interposition. Both groups received concomitantly other modalities of treatment. Creatinine and creatinine clearance levels were determined at the time of biopsy (T0) and after 1, 3 and 6-months (T1, T3, T6 respectively).

**Results:** In 13 TPE-treated and 9 non-TPE-treated patients, the mean creatinine levels at 6 months decreased 32.5% and 45% respectively over baseline, while the creatinine clearance increased by 68% and 65% respectively, although not statistically significant (p>0.05) Graph1.

**Conclusions:** No significant differences were noted in creatinine or creatinine clearance levels within and between either groups at any time point. Our study suggest that no significant benefit in renal function is associated with performing TPE in patients with renal t-TMA. Larger studies are needed to confirm our data.
PO2571

Patient and Graft Outcomes of Kidney Transplant Recipients with Anti-Human Neutrophil Antigen Antibodies
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Background: Antibody mediated rejection (AMR) is a well-established cause of poor graft outcomes in kidney transplant recipients (KTR). While the most common targets are human leukocyte antigen (HLA) antibodies (abs), there are data implicating some non-HLA abs in the process of AMR. Human neutrophil antigens (HNA) are glycoproteins expressed on neutrophil surfaces. Anti-HNA abs have been associated with transfusion-related acute lung injury but their role in AMR in KTR is unclear. The aim of our study was to examine the outcomes of KTR with anti-HNA abs at our center.

Methods: We retrospectively reviewed the medical records of KTR with non-HLA abs between 1/2008-5/2020. Relevant clinical and graft outcome data were obtained. Descriptive statistics were expressed as absolute numbers (%) for categorical data and as medians with interquartile range (IQR) for skewed distribution.

Results: There were 6 KTR with non-HLA abs during the study period, all anti-HNA abs. Three patients (pts) were male (50%), 5 white (83%), and 4 had polycystic kidney disease (PKD) as primary disease (66%). Median age at KT was 46 (29.75-57). Pts’ characteristics, clinical course and outcomes are detailed in Table 1. Five pts developed biopsy-proven AMR at a median of 32 months (13.8-68.2) from KT. During follow-up (FU), 3 pts had graft loss, 1 of which was re-transplanted while 2 are re-listed but dialysis-dependent. Mean creatinine of the 4 pts with working allografts is 1.21mg/dL (1.14-1.27) at median FU of 68 months (52-105).

Conclusions: We observed varied clinical courses and graft outcomes in our pts, partly due to our small cohort. Although majority developed AMR, it was not necessarily associated to graft loss or shortened graft survival. Of note, PKD was the primary kidney disease in the majority of pts, similarly observed in one other case series. More studies are needed to determine the specific significance of anti-HNA abs in KTR.

Table 1. Patient and donor characteristics and allograft outcomes.

PO2572

Transplant Outcomes in Children with Lupus Nephritis
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Background: Children receiving dialysis for end stage kidney disease secondary to lupus nephritis (LN) have decreased survival and a lower likelihood of kidney transplantation compared to children with non-lupus glomerular diseases (NLGN). Whereas a previous North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) analysis reported equivalent patient and graft survival for LN patients when compared to matched controls, a comparison of recent transplant outcomes in children with LN and LN has not been conducted.

Methods: Retrospective analysis of the NAPRTCS registry data of subjects <21 years old who received a kidney transplant between 1987-2018. Outcomes for LN patients (n=191) were compared to NLGN patients (n=8675) during pre & post 2000 eras. Statistical analyses included Kaplan-Meier curves and multivariable logistic and Cox regression models.

Results: After adjusting for race, LN patients were less likely (p=0.001) to receive a preemptive transplant (OR=0.12). There was also a trend for LN patients being less likely to receive a living donor (LD) transplant (OR=0.8). When comparing pre- and post-2000 eras, time to 1st rejection and graft survival improved for both LN and NLGN groups, although the graft survival benefit in LN group was not sustained after 3.5 years of follow-up. Time to 1st rejection and graft survival for LN patients remained inferior to NLGN group during both eras (Figure 1 & 2).

Conclusions: LN patients are less likely to receive a preemptive, and possibly a LD transplant. Overall, outcomes for both LN and NLGN transplant patients improved after 2000, but the outcomes of the LN group were inferior to those of the NLGN group during both time periods.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

PO2573

Effect of Rituximab Dose on Induction Therapy in ABO-Incompatible Living Kidney Transplantation: A Network Meta-Analysis
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Background: Rituximab is an induction immunosuppressant essential for ABO-incompatible kidney transplantation, but studies on its dosing, which differs between countries and transplant centers, are lacking we retrospectively investigated this phenomenon.

Methods: We retrospectively investigated this phenomenon by including five groups: ABO compatible; placebo; and rituximab 200 mg, 200–500 mg, and 500 mg. Publications were retrieved using CENTRAL, MEDLINE, EMBASE, and Science Citation Index Expanded databases from 1970 to February 2020 and analyzed. Reviews, observational studies, and clinical trials with unclearly defined outcomes or omitted graft failure as an outcome were excluded. We performed direct and indirect network meta-analyses using Bayesian models and ranked different rituximab doses using generation mixed treatment comparison. The GRADE of network meta-analysis approach specified four levels of certainty for a given result: high, moderate, low, and very low. The outcomes were patient survival, graft failure, and infections including bacterial and viral.

Results: Twenty-one trials with 4,256 subjects were analyzed for glomerular filtration rates, graft loss, antibody-mediated rejection, T-cell mediated rejection, fungal infection (Candida), and patient survival rates, which did not differ among four groups. However, incidence of sepsis and cytomegalovirus infection (0.728 and 0.855, 95% confidence interval: 0.572–0.926 and 0.724–0.921, respectively) were significantly lower in rituximab 200-mg group than in other groups.

Conclusions: In conclusion, in ABO-incompatible kidney transplantation, low-dose rituximab is more efficacious than higher doses and reduces serious infection risks. Future studies of large-scale, long-term data and further discussions on using lower rituximab doses are necessary.

PO2574

Delayed Diagnosis of Renal Allograft Uroenteric Fistula in a Pediatric Transplant Patient
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Introduction: The diagnosis of uroenteric fistula can be challenging and is often delayed for several months after symptoms begin. Here, we describe a rare case of a pediatric patient post en bloc kidney transplant who developed a urinoma post biopsy with a ureteral fistula into the small bowel resulting in profound acidosis and deceptive watery diarrhea.
Case Description: The patient is an 8 year old girl with end stage kidney disease secondary to steroid resistant nephrotic syndrome and focal segmental glomerulosclerosis (FSGS). She underwent a right native nephrectomy and a deceased donor “en bloc” kidney transplant with two separate ureters. She had a renal allograft biopsy for suspected rejection. A few days after the biopsy, she began experiencing watery diarrhea and metabolic acidosis. A comprehensive screening for diarrhea produced inconclusive findings. She was maintained on parenteral nutrition with no oral intake to try to slow the diarrhea. However, the watery diarrhea increased while urine output decreased. Throughout this period, the patient maintained normal kidney function. The watery stool and bladder urine were analyzed for solutes, pH and creatinine. An MRI with contrast was performed which demonstrated fistulization of the distal transplanted ureters into the small bowel. She underwent corrective surgery which identified the fistulous tract which was resected and the ureters were re-implanted. The surgery went well without complications. The diarrhea resolved and she was discharged 2 weeks later with normal renal function.

Discussion: This is a perplexing case of the development of a uroenteric fistula in a pediatric transplant patient that went undiagnosed for almost 3 weeks due to the deceptive nature of the watery diarrhea which was actually urine. An important aspect of the uroenteric fistula is the severe acidosis that results when urine is diverted in to the intestinal tract. This occurs in some cases of bladder augmentations that use the intestine. Another important diagnostic tool is the solute excretion in the diarrhea. Despite the watery nature of the diarrhea, the stool was not hyperosmolar and did not contain reducing substances. This made osmotic diarrhea unlikely and a fistula more likely.

PO2575

Effect of Therapeutic Plasma Exchange on Glomerular Filtration Rate in Patients with Antibody-Mediated Rejection
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Background: AMR is the main risk factor for graft loss, especially after the first post-transplant year. Up to 80% of patients achieve response with immunosuppressive treatment and TPE, although the response is lower in patients with late AMR. The objective was to determine the effect of TPE in GFR at TPE and 3 months postTPE.

Methods: Retrospective study that included patients with a renal transplant of the CMN “November 20” in Mexico City, from 2016 to 2019, undergoing membrane TPE for AMR. Analysis was performed using student’s t or MannWhitneyU, repeated measures analysis, and Spearman or Pearson test. Significant p was less than 0.05.

Results: 25 patients with AMR who received TPE were evaluated. Age: 32± 11.6 years, 72% from living donor, 52% received Basiliximab. 87% received tacrolimus. 80% of AMR were late. Prevalence of HLA class II DSA (66%), specifically vs DQ and DR (57.2% and 28.8%). There was a significant difference between preTPE GFR and at the end of treatment (p=0.015, r=0.53), and no significant differences between preTPE GFR, with 1or3 months postTPE (r=0.58; p=0.36). When evaluating IFTA or histological score (g+ptc), no difference was detected in the GFR at 1or3 months post-TPE. When comparing the effect of the AMR temporality on the GFR, difference was found at 1and3 months (p=0.022; p=0.01) postTPE, with lower recovery of GFR in patients with early AMR. There was a moderate correlation between GFR at the time of diagnosis of rejection and GFR at 3 months postTPE (r=0.68, p=0.01). Fig. 1.

Conclusions: Significant difference was demonstrated between the preTPE GFR and immediate postTPE GFR. In our study patients with early AMR presented a poor response to treatment. The GFRupon admission correlated positively with theGFR detected at 3months post-TPE. This suggests a beneficial effect of TPE over GFRfall during the first 3months after diagnosis.

PO2576

Significant Variability in Results from Different Tacrolimus Assays Is a Potential Recipe for Toxicity and Kidney Allograft Rejection
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Background: Tacrolimus (tac) is an immunosuppressive medication used to prevent organ rejection and prolong graft survival after transplantation. It is the main pillar of any combination immunosuppression regimen. Due to its narrow therapeutic window, it requires timely administration, close monitoring with 12-24 hours trough levels and dose adjustments. Previously done studies have shown a discordance between different assays, with a positive bias for immunoassay (2.8 -9.2%) compared to LC/MS-MS assay; due to cross-reactivity with tac metabolites.

Methods: Results from 33 stable kidney transplant patients who had routine transplant labs drawn at Labcorp® were reviewed. Each of these patients had tac trough levels checked by both LC/MS-MS assay and QMS immunoassay(Thermo-Fischer). The comparison of two assays was done with Deming regression and a Bland-Altman analysis for bias done using XLSTAT®. Linear regression was done using SPSS v26.

Results: Deming regression analysis shows that there is a statistically significant difference between the two assays with $y=1.36x-0.26$. Bias(avg.) calculated by Bland-Altman plot was 2.35 ng/mL(Figure). Percentage difference in tacrolimus immunoassay and LC/MS-MS correlated with tacrolimus dose (p = 0.031).

Conclusions: A significant discordance of tac troughs (upto 85%) was found on our analysis; obtained by the two assays. This is clinically significant as tac has a narrow therapeutic window and adjustments of dose based on these assay results; can risk immunologic injury, DSA formation, rejection and nephrotoxicity at either ends of the spectrum. Standardization of assays in future, would be ideal. In the meantime, nephrologists should be adjusting trough goals based on the assay used, especially when different assays are in play.

Funding: Clinical Revenue Support
PO2577

Single-Dose Rituximab and Antithymocyte Globulin (ATG) in Hypersensitized Kidney Transplant Recipients

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Background: Hypersensitized kidney transplant recipients (calculated panel reactive antibody (cPRA) ≥ 98%), may represent a population at high risk of posttransplant immunologic events. Their optimal induction regimen so far remain uncertain. The goal of this study was to compare 1-year outcomes of patients receiving rituximab and ATG as induction, the majority of whom were hypersensitized, with highly sensitized recipients (cPRA ≥ 80%) who received ATG alone.

Methods: All patients ≥ 18 years received a cross-match compatible kidney transplant between December 2014 and May 2020. We excluded patients who underwent pretransplant desensitization, simultaneous multi-organ transplantation, or received O-HLA antigen mismatched organ. The exposure of interest was receipt of single dose rituximab (500mg) at induction. The 1-year outcomes were 1) patient and death censored graft survival, 2) glomerular filtration rate (GFR), 3) de novo DSA formation, 4) biopsy proven T-cell or antibody mediated rejection, 5) the composite of dDnDSA and rejection, 6) BK viremia, and 7) CMV viremia.

Results: 70 patients received rituximab and ATG (Ritux) and 39 received ATG alone (Control). The Ritux group were (numerically) younger, more sensitized, received kidneys with a longer cold ischemia time, and lower kidney donor profile index. ATG doses were similar. The majority were deceased donor transplants. 1-year patient and death censored graft survival, mean GFR, incidences of BK viremia and CMV viremia were similar for Ritux and Control. 2 patients with primary graft non-function (1 in each group) and 1 patient with early posttransplant death (in Ritux) were excluded from the remaining outcome analyses (Table 1).

Conclusions: The addition of rituximab to ATG as induction for hypersensitized patients appears to be safe and is associated with excellent 1-year outcomes in patients with high panel reactive antibodies (>80%)

Table 1

PO2578

Risk Factors and Outcomes of Acute and Refractory Antibody-Mediated Rejection

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Background: Major gaps remain in our understanding of antibody-mediated rejection (AMR) after kidney transplantation. We examined incidence, risk factors, response to treatment, and effects on outcomes of locally-managed AMR at 7 transplant programs in the Long-Term Deterioration of Kidney Allograft Function (DeKAF) prospective study cohort.

Methods: Consecutive kidney or kidney-pancreas transplant recipients were enrolled in the DeKAF study from October 2005 through April 11, 2015. To determine the effect of AMR on death censored graft failure (DCGF), we performed Cox proportional hazards analyses including AMR as a time-dependent covariate.

Results: Among 3313 kidney and kidney-pancreas recipients, there were 194 with a first AMR episode during a mean 4.8±1.86 years of follow-up for the entire cohort. Mean time to first AMR was 0.97±1.17 years post-transplant. After adjusting for other risk factors, patients with AMR had 10 times the risk of DCGF compared to patients with no AMR (aHR 10.1, 95% CI 6.5-15.7). Among the 50 (25.8%) patients whose AMR was refractory to treatment, defined as ≥2nd AMR diagnosis within 100 days or no improvement in cGFR by 42 days, the HR for DCGF was 7.5 (2.2-25.6, P=0.0013) in the 1st 180 days post biopsy; 3.8 (1.4-9.8, P=0.007) in the 1st year post biopsy, and 1.6 (0.9-3.0, P=0.11) at any time during follow-up compared to patients whose AMR responded to treatment.

Conclusions: Patients with AMR had substantially greater risk of DCGF compared to patients without AMR. While patients with refractory AMR were more likely to lose their graft compared to non-refractory cases in the first year following the AMR diagnosis, the likelihood of graft survival after that year was the same regardless of response to treatment.

Funding: Commercial Support - CSL Behring

PO2579

Allograft Loss and Patient Death Among Kidney Transplant Recipients: Is Therapy Nonadherence the Underlying Perpetrator?

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Background: To ascertain causes of allograft dysfunction, loss and death in a cohort of kidney transplant patients.

Methods: Retrospective cohort study, 943 patients with isolated kidney transplants between years 2013-17 were analyzed for the following transplant outcomes: 1. Death-censored allograft loss 2. Graft dysfunction 3. Death.

Results: 80 of 943 (9%) patients died while 63 (7%) lost their graft and 38 (4%) suffered allograft dysfunction. Death- Death was attributed to a combination of infection (29%), Cardiovascular (CV) disease (29%) and malignancy (12%), a significant proportion of patients who died from either CV disease (43%), infection (26%) or malignancy (20%) had prior biopsy proven T-Cell Mediated Rejection (TCMR) in 1st post-transplant year.

Graft Loss- In this cohort TCMR (39%) was the most widespread factor contributing to allograft loss. While Infection (17%) and surgical causes (14%) were the next common associations, donor related disease accounted for 2% of graft losses.

Graft Dysfunction- TCMR (42%) was strongly associated with allograft dysfunction in our patient cohort. The other factors associated with Allograft Dysfunction included a). Infection (21%) b). Donor Related causes (11%) and c). Other Causes (15%). Surprisingly ABMR was only noted in 11% of patients with allograft decline. Rejection and Non-Adherence- As TCMR was a common contributing factor to all the three hard outcomes in our study cohort, we examined the factors associated with TCMR. 40% of patients with TCMR were found to be non-adherent (defined by > 3 consecutive sub- therapeutic CNI levels, clinic no shows and poor adherence to regular lab draws). Importantly, patients who were non adherent were significantly younger (mean age 38 vs 55 yrs; p<0.0001) and a greater proportion of them were of African American (47% vs 22%;p<0.05) compared to those who were adherent to therapy.

Conclusions: While the causes of death, early allograft loss and dysfunction were diverse, TCMR was the most dominant contributor. Non-Adherence was strongly associated with TCMR and was more common in younger patients and those with African American ethnicity. Addressing non adherence in this cohort of patients early with novel interventions could be a key to optimizing patient outcomes in this high risk cohort.

PO2580

Identifying the Causes for Kidney Allograft Failure


Background: Since it has been proposed that several causes (C) can contribute to graft loss (GL), we analyzed transplant (Tx) recipients in our center and attributed a C to each persistent decline in renal function, finally leading to GL.

Methods: We retrospectively analyzed 1477 Tx, transplanted between 1997 and 2017 in a single center, of which 303 progressed to GL. An adjudication committee consisting of 3 physicians evaluated biopsies, laboratory data and medical history. Nonreversible decreases in renal function were attributed to primary and secondary C.

Results: Overall graft survival for all patients is 93.7% for 1 year, 80% for 5 years and 60.6% for 10 years. The most frequent C leading to GL were intercurrent medical events in 36.3%, followed by T-cell mediated rejection (TCMR) in 34% and antibody-mediated rejection (ABMR) in 30.7% (table1). For primary C, ABMR (21.5%) was the leading C, followed by medical events (21.1%) and TCMR (12.9%). As expected, we observed an increasing relevance of ABMR in late GL (figure 1). Over 50% of GL had >1 C.

Conclusions: Analyzing GL, we observed that >50% were multifactorial. Our results show a significant role of TCMR in GL. Additionally, we were able to attribute medical events to GL in 36.3% of Tx and to highlight the role of ABMR in late GL.
PO2581

Assessing Cumulative Immunosuppressive Drug Exposure: Metrics, Outcomes, and Implications for Kidney and Non-Kidney Transplant Patients

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Background: Immunosuppressive drugs are used in the long-term management of post-transplant patients to prevent rejection of transplanted organs. Lacking in prior qualitative systematic review on this topic, we aimed to characterize the metrics used to measure cumulative immunosuppressant exposure and their associated outcomes in kidney and non-kidney transplant patients.

Methods: We conducted a literature search using search terms related to immunosuppressants and cumulative exposure in Ovid MEDLINE, Ovid EMBASE, Cochrane CENTRAL, and Cochrane Database of Systematic Reviews. No date restrictions were applied. An additional search was performed on Google Scholar and references of studies included in the primary search were screened. Studies were limited to the English language with adult human transplant patient populations. Study risk of bias was assessed using the Quality in Prognostic Studies Tool where each domain was rated as low, medium, or high risk of bias.

Results: A total of 29 articles were included in our qualitative synthesis. Kidney transplant populations account for 12 (41%) of the studies in our analyses. Fifteen of the articles (51%) calculated the total dose of immunosuppression over the treatment period while 9 (31%) used long term area-under-the-curve (LT-AUC) of trough level concentrations to quantify cumulative immunosuppression exposure. Nine articles found certain cumulative exposure metrics to be predictive of adverse outcomes such as decreased kidney function, cancer recurrence, and bone fractures. Furthermore, an adequate mycophenolic acid LT-AUC was associated with a decreased risk of allograft rejection, while cumulative corticosteroid exposure was not associated with allograft rejection.

Conclusions: This review analyzed a comprehensive set of articles and metrics that predict long-term outcomes of immunosuppressants in transplant patients. The wide variety of metrics studied highlight the lack of agreement on the best measures of drug exposure in transplant patients. Although certain metrics may demonstrate an association with outcomes, future studies should investigate the predictive power and validation of these metrics.

PO2582

Fludrocortisone Corrects Tacrolimus-Associated Hyperkalemia in Renal Transplant Patients

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Background: Hyperkalemic metabolic acidosis is commonly observed following kidney transplantation. This is often due to calcineurin inhibitors which are known to cause type 4 renal tubular acidosis either due to hyporeninemic hypoaldosteronism or due to direct effect on aldosterone responsive potassium secretion in the distal nephron.

Methods: We report 5 post-renal transplant patients (5 males) on tacrolimus with hyperkalemia treated with daily doses of either 50 mcg (n=3) or 100 mcg (n=2) of fludrocortisone. We retrospectively collected data at 3 time points before and after fludrocortisone with serum concentrations of sodium, potassium, bicarbonate, creatinine and tacrolimus as well as eGFR and blood pressure (BP). We recorded emergency admissions and length of stay (LoS) for treatment related to hyperkalemia. Data are presented as mean +/-SD and analysed with a paired students t-test.

Results: Pre and post-fludrocortisone serum concentrations for potassium was 6.3 ± 0.3 mmol/L and 5.1 ± 0.3 mmol/L (p=0.002); venous bicarbonate 18.4 ± 1.8 mmol/L and 20.4 ± 2.0 mmol/L (p=0.108); sodium 135 ± 1.6 mmol/L and 135 ± 2.2 mmol/L (p=0.873); creatinine 184 ± 12.2 mmol/L and 155 ± 10.6 mmol/L (p=0.058); eGFR 39 ± 3.4 ml/min and 47 ± 4.2 ml/min (p=0.035); blood tacrolimus levels 9.8 ± 2.1 ng/mL and 11.2 ± 1.0 ng/mL; BP was 133/69 ± 12.9 mmHg and 129/70 ± 8.6 mmHg before and after fludrocortisone respectively. We were able to either reduce or stop sodium bicarbonate after starting fludrocortisone due to increase in serum bicarbonate levels. Prior to fludrocortisone there were 6 episodes of serum potassium greater than 6.5 mmol/L, of which 3 patients required admission for hyperkalemia management, with LoS 1-3 days. The majority occurred with tacrolimus levels in target range. Reduction in potassium levels to ‘safe levels’ were noted within 24-48 hours of starting fludrocortisone.

Conclusions: Treatment of hyperkalemic metabolic acidosis with fludrocortisone resulted in rapid normalization of serum potassium. There were no adverse effects on BP, serum sodium levels or clinical evidence of fluid retention. Instigation of fludrocortisone prevented emergency admissions for treatment of hyperkalemia and allowed the clinicians to run adequate tacrolimus levels. Fludrocortisone can be a cheap, safe and effective option for the treatment of hyperkalemia in renal transplant patients on tacrolimus.
**PO2583**

Changes in Serum Klotho in Kidney Transplant Recipients and Prognostic Marker for Allograft Function: A Systematic Review and Meta-Analysis

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**Background:** Klotho is a well-known anti-aging factor that regulates systemic phosphate metabolism. Mutation of klotho in mice can lead to phenotypes resembling human aging. Since klotho expression is highest in the kidney, patients with advanced chronic kidney disease have progressive decline in klotho levels. However, changes in serum klotho levels in kidney transplant (KTx) patients and its prognostic significance on allograft function remain unclear.

**Methods:** A literature search was conducted using MEDLINE, EMBASE and Cochrane Database from inception through October 2019 to identify studies evaluating 1) change in serum klotho levels after KTx, 2) klotho levels among KTx vs non-KTx patients, and 3) prognostic significance of klotho levels on allograft function after KTx.

**Results:** Study results were pooled and analyzed utilizing random-effects model.

**Conclusions:** There is a significant increase in serum klotho levels after KTx. There is potential role of klotho levels as prognostic marker for renal allograft function.

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**PO2584**

Braving the Storm: Cytokine Release Syndrome with Rabbit Antithymocyte Globulin Therapy after Kidney Transplant

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**Introduction:** Cytokine release syndrome (CRS) is an acute systemic inflammatory syndrome associated with chimeric antigen receptor (CAR)-T cell therapy or therapeutic antibodies. CRS can present with a variety of symptoms ranging from mild flu to severe life-threatening manifestations of shock, vascular leakage, DIC and multi-organ failure. We present a case of a CRS following rATG induction.

**Case Description:** A 29-year-old female with a history of T1 DM s/p kidney/pancreas transplantation 12 years experienced the rejection of transplanted kidney 1 year back. Her home immunosuppression included Tacrolimus, MMF and Prednisone. She underwent a kidney retransplant from a living donor. The induction immunosuppression consisted of rabbit anti-thymocyte globulin (ATG), methylprednisolone and MMF. Two hours after the rATG infusion (1.5mg/kg) on day 1 of transplant; she developed breathing difficulty, temp of 102.7, RR of 23, HR of 160 and fall in BP to 108/55 mmHg. Lab work showed a drop of Hb from 11.4 to 9, platelets from 187 to 126 and WBC from 17 to 9.8. CXR was unremarkable. ECHO showed normal cardiac function. LE Doppler was unremarkable.

**Discussion:** CRS is an inflammatory cascade that develops within minutes to hours after immunotherapy. The case emphasizes the successful rapid recognition and proper management of CRS in preventing the patient decapsulation. The massive cytokine release triggers an inflammatory response leading to capillary leakage, severe hypotension and respiratory failure. The management differs from usual shock as the aggressive blood pressure support is not enough. Fluids and inotropes were given. Steroids and pressors are the mainstay of therapy and should be administered early. The treatment is largely supportive with ventilation for respiratory failure and steroids for inflammation.

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**PO2585**

Proton Pump Inhibitor Prevalence and Documented Indication in a Small Kidney Transplant Program

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**Background:** Proton pump inhibitors (PPIs) are commonly prescribed post kidney transplantation, and their use was prevalent in 44.48% of recipients. Prolonged exposure to PPIs could be associated with renal and non-renal adverse outcomes, including hyperammonaemia and hip fracture (OR: 1.39, 95% CI: 1.04-1.84). The objective of this report is to evaluate the prevalence and the documented indication of PPI use in our kidney transplant program, while exploring the potential PPI withdrawal and GERD recurrence in a future Quality Improvement (QI) project.

**Methods:** This is a retrospective study to assess the prevalence and the documented indications of PPI use among all of kidney transplant recipients in our program by March 31st, 2020. The primary variables were the prevalence of PPI use and the percentage of patients with documented indication of PPI use in our Health Information System (HIS).

**Results:** Out of 202 kidney transplant recipients, 113 (55.9%) patients were on PPIs (Mean age 58 years, Male 68 (60.2%), mean post-transplant longevity 106 months, compared with 12 (5.9%) patients on H2 blockers. Thirty three (29.2%) patients who used to be on H2 blockers were switched to PPI in late 2019 due to contaminated and backordered ranitidine resulting in an adjusted prevalence of PPI use of 39.5% (Figure 1).

The indication of PPI use was documented in our HIS as gastro-esophageal reflux disease (GERD) in 53 (46.9%) patients, and as peptic ulcer disease (PUD) in 9 (8%) patients, while its indication was undocumented in 51 (45.1%) patients.

**Conclusions:** PPI use was prevalent among our kidney transplant recipients similar to other studies. Due to its association with multiple adverse outcomes, better documentation of its indication in the medical record is required. Consideration to withdraw PPI in our kidney transplant recipients and to reassess the risk of GERD recurrence will be assessed in a future QI project.

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**PO2586**

Unexpected Recurrence of Undiagnosed ANCA-Associated Vasculitis in a Kidney Transplant Recipient

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**Introduction:** ANCA Associated Vasculitis (AAV) is one of the leading causes of End-stage Kidney disease (ESKD). The relapses of AAV after kidney transplant are relatively rare. As per the literature, the positive ANCA status in not a contraindication for transplant and patients usually get transplant once in clinical remission. Here, we are describing a unique case of ESKD due to renal limited AAV which was diagnosed retrospectively after the development of the recurrence two months post-transplant.

**Case Description:** A 69 years old Caucasian female with ESKD presumed due to hypertension received a deceased donor kidney transplant in Oct 2019 after being on dialysis for 4 years. She received almtuzumab for induction followed by tacrolimus, mycophenolate mofetil, and prednisone for the maintenance immunosuppression. Her immediate post-transplant course was complicated by delayed graft function and her creatinine never went down below 2 mg/dl. Allograft biopsy was planned after 2 months due to persistent microscopic hematuria with progressive sub nephrotic range proteinuria. The immuno-histopathology and electron microscopy was suggestive of pauci-immune crescentic GN. Her serology workup was positive for ANA, ANCA with high titters of MPO. She lacked any other systemic involvement, and drugs induced ANCA was ruled out. She was treated with a pulse dose of methylprednisone and one dose of rituximab. Gradually her creatinine improved to 1.37 mg/dl with down trending MPO antibody titers within 6 weeks. The review of her chart retrospectively showed clinically asymptomatic ANCA positivity with high MPO titters 3.5 years back, supportive of recurrence of AAV more than De novo AAV post-transplant.

**Discussion:** Physician should always be vigilant about the recurrence of the primary disease after transplant, especially when patients have undiagnosed primary kidney disease like AAV, where early diagnosis and treatment in the early stage of the disease is important to optimize results of renal transplantation. A randomized prospective study is needed to answer the question whether the ANCA positivity at the time of transplant adversely affect the outcomes.
**PO2587**

**A Case of Porphyria Cutanea Tarda After Kidney Transplant**
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**Introduction:** Porphyria cutanea tarda (PCT) is the most common subtype of porphyria and can be associated with kidney failure due to reports of kidney transplantation curing the disease. We report the case of a patient who had previously undergone kidney transplantation and developed PCT after transplantation.

**Case Description:** A 40-year-old man with end stage renal disease due to unknown chronic glomerulonephritis status post kidney transplant 4.5 years ago was admitted with non-healing blisters on both hands. Patient initially presented one month earlier with similar symptoms and was diagnosed with bullous impetigo due to methicillin resistance staphylococcus aureus. At that time, he was treated with vancomycin followed by trimethoprim-sulfaethoxazole (TSM-SMX) for a total of 14 days. He was also noted to have cytomegalovirus viremia which was treated with valganciclovir. Patient reported ongoing development of lesions despite antibiotic treatment and presented for follow-up where he was noted to have an acute kidney injury and hyperkalemia. At presentation his medications included mycophenolate sodium, tacrolimus, prednisone, triamcinolone cream and mupirocin ointment. There was no family history of skin disease and he did not drink alcohol. He underwent skin biopsy which was consistent with porphyria or pseudoporphyria. Urine and plasma porphyrins were checked showing elevated uroporphyrin and also elevated heptacarboxyl, hexacarboxyl and pentacarboxyl porphyrins with normal coproporphyrin I and III consistent with PCT.

**Discussion:** PCT is the most common form of porphyria and is associated with hepatitis C, iron overload, estrogen administration and alcohol use. It has also been associated with hemodialysis often with resolution at the time of kidney transplantation. However, elevated iron stores are often present in kidney transplant patients and PCT can be misdiagnosed as bullous impetigo as it was in this case.

**PO2589**

**What Is the Safe Anti-A2 Titer for a Successful A2-Incompatible Kidney Transplantation?**
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**Background:** The new kidney allocation system implemented in December 2014 allowed for use of A2/AB donors to B recipients. However, there is no mandate by UNOS regarding what anti-A2 titers are acceptable. We aimed to investigate the safety of kidney transplant in patients with anti-A2 titers equal or less than 1/4.

**Methods:** We performed 41 A2-incompatible kidney transplants at our institution if pre transplant anti-A2 titers were equal or less than 1/16. All patients received anti-thymocyte globulin induction. Patients with donor-specific anti-hLA-antibodies (DSA) received pretransplant immunosuppressive therapy.

**Results:** Of the 41 recipients, 85% were male, 48% African-American, with a median age of 53 (20-73) years. There were 38 deceased donor renal transplants and 3 living related. Median donor age was 42 (16-65) and median KDPI was 52 (2-86). Twenty-one patients had PRA 0% and 8 had pre transplanted DSA. Pretransplant anti-A2 titers were 1/2 in 16, 1/4 in 9, 1/8 in 6, and 1/16 in 5 and too weak to titrate in 5 recipients. During a median follow-up of 33 months (6-57) patient and graft survival were 100% and 90.2% respectively. Twelve patients underwent a clinically indicated kidney biopsy at a median 28 days post transplant (6-190). There was one case of acute T cell mediated rejection type IIA, and one chronic antibody-mediated rejection which was due to non-compliance leading to graft loss. Interestingly C4d positivity was seen in 9 biopsies, of which 8 did not have any findings of antibody mediated rejection and no microvascular inflammation. Median serum creatinine level at last follow up was 1.3 mg/dL (0.6-3.2) and only 3 patients had spot urine protein/creatinine more than 1 g/day.

**Conclusions:** A2-incompatible transplantation appears to be safe in patients with anti-A2 titers equal or less than 1/16 with or without DSAs and excellent short-term kidney allograft outcomes. C4d positivity is frequent in allograft biopsies without acute rejection suggesting accommodation to the allograft.

**PO2590**

**Post-Transplant Outcomes for Highly Sensitized Kidney Transplant Recipients with Non-Highly Sensitized Recipients in the Era of the New Kidney Allocation System: A Single-Center Case-Control Comparison**
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**Background:** The new UNOS kidney allocation system (KAS) of December 2014, gives substantial priority points to highly sensitized (HS) adult kidney transplant recipients (KTR) with cPRA of 99% or higher. There is a concern of worse post-transplant outcomes in HS KTR compared to non-HS KTR. When comparing pre-KAS to post KAS, similar 3-year patient and graft survival has been reported in HS KTR. The comparative outcomes of HS KTR to non-HS KTR in the past KAS era are unknown.

**Methods:** We studied outcomes in HS adult kidney transplant recipients (KTR) and compared them to non-HS KTR in the post KAS era. We included all recipients of deceased donor kidney transplants at the University of Alabama at Birmingham, from December 2014 to March 2020. HS patients were defined as those with cPRA 99% or higher. The HS patients were matched 1:2 with non-HS patients on age, sex, and time of transplantation. A Kaplan Meier analysis was performed for patient survival and the combined endpoint of graft and patient survival.

**Results:** A total of 717 deceased donor kidney transplants were performed during the study period, of which 106 HS KTR were identified. There is concern of worse post-transplant outcomes in HS KTR compared to non-HS KTR. When comparing pre-KAS to post KAS, similar 3-year patient and graft survival has been reported in HS KTR. The comparative outcomes of HS KTR to non-HS KTR in the past KAS era are unknown.

**Conclusions:** We aimed to investigate the safety of kidney transplantation in patients with anti-A2 titers equal or less than 1/16. The HS patients were then compared with 228 matched non-HS deceased donor controls.

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.**
The matched controls had a median cPRA of 0% (IQR 0-29.5%). There was no difference in death (p=0.17) or combined endpoint of death or graft survival (p=0.35) in the two groups (figure 1).

Conclusions: HS patients have similar mortality and graft survival as compared with non-HS controls. The results of our study support continuing to give HS patients priority in organ allocation.

PO2591
Who Is at Risk for a Transplant Nephrectomy After Graft Loss?
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Background: Patients with failed kidney transplants who subsequently develop clinical symptoms such as fever, allograft pain and gross hematuria usually require a transplant nephrectomy to alleviate symptoms. Identifying patients at risk for a nephrectomy after graft loss may aid clinical decision-making and care at time of, and after graft loss.

Methods: We retrospectively reviewed all patients with death-censored graft loss (DCGL) from 1/2000 to 6/2018 at a single center. We collected baseline demographic and clinical characteristics at time of transplant, at time of, and after DCGL by manual chart abstraction. Data were analyzed using summary statistics. Predictors for nephrectomy were determined a priori. A Cox proportional hazards model was used to quantify the association of age, race, gender, body mass index (BMI) at time of graft loss, diabetes, acute rejection as cause of graft loss, and use of prednisone with the risk of nephrectomy.

Results: The study included 333 patients with DCGL of whom 75 (23%) underwent a transplant nephrectomy. Median (IQR) time from graft loss to nephrectomy was 135 (70, 267) days. Among 292 patients without missing data, baseline and transplant characteristics were as follows: age at transplantation 45 (36, 57), 59% male, 40% black, 20% diabetic, 53% with a deceased donor, 83% on calcineurin-based immunosuppression (CNI-IS), 71% on prednisone. Twenty four percent and 69% of patients lost their graft due to acute rejection and chronic allograft nephropathy, respectively. At the time of DCGL: BMI was 25.9 kg/m² (22.7, 31.4), SCR 7.5 mg/dl (5.6, 9.6), albumin 3.3 (3.0, 3.8), 86% on CNI-IS, 91% on prednisone. In the Cox model, black race was associated with more than twice greater risk of nephrectomy compared to non-blacks (HR 2.4, 95% CI 1.3-4.3, p<0.01) but this did not reach statistical significance.

Conclusions: Transplant nephrectomies are common after graft loss and black race is associated with increased risk. Closer monitoring of these patients after graft loss may aid clinical decision-making and care at time of, and after graft loss.

PO2593
Evaluation of Reproductive Care Provided to Adolescent Patients in Pediatric Nephrology Clinics
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Background: An increasing number of adolescents are living with end-stage renal disease (ESRD) or chronic kidney disease (CKD) in the US. Therefore, it is important that nephrologists can manage reproductive and women’s health issues in adolescents with CKD. In this study, we aimed to determine the confidence levels of nephrologists in the US in managing women’s health issues in adolescent females with CKD.

Methods: Using Qualtrics Online Survey Platform, a survey was distributed by email to members of the Pediatric Nephrology Research Consortium. The survey contained 19 questions pertaining to provider demographics, training, current practice, frequency of documenting and/or discussing women’s health issues, and level of confidence in managing women’s health issues in adolescent female patients.

Results: Seventy-five nephrologists participated, with a majority practicing in academic centers (88%). For most providers, adolescents comprised 25-74% of all patients. Ninety-eight percent denied formal training in women’s health or obstetric nephrology. History of pregnancy termination/loss, last menstrual period (LMP), contraceptive use, sexual activity, number of sexual partners, and history of sexually transmitted infections were infrequently documented. Most providers documented discussions about risks of teratogenicity with use of ACEi/ARBs or mycophenolate and risks of infertility and fertility-preserving options with use of cyclophosphamide. Most providers weren’t comfortable managing pregnant adolescents and referred them to adult nephrologists. Most were uncomfortable discussing fetal risks with pregnancy in CKD. While most were confident discussing barrier methods, they were much less confident discussing oral contraceptives and long-acting reversible contraceptives (LARC).s.

Conclusions: Sexual development and pregnancy appear not to be a focus of nephrologists caring for adolescent females with CKD. Providers also appeared to have a low level of confidence in discussing and managing fertility and pregnancy-related issues in adolescents. Nephrology training needs to incorporate focused women’s health content to improve healthcare delivery to adolescent girls.
PO2594
Reproductive Health in Kidney Transplant Recipients
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Background: Women with advanced chronic kidney disease develop menstrual irregularities and infertility that can improve after kidney transplant. However, some women do not have menstrual cycles return after transplant and pregnancy rates are lower than in the general population, which could be due to a combination of biologic and social factors.

Methods: We sent a survey on reproductive health to all women aged 18 to 44 at the time of transplant at all 3 Mayo Clinic sites between 1996 and 2014. We sent a second survey to all non-respondents from the first mailing and then called all remaining women to ask for their participation. We included questions on menstrual cycles, pregnancy, and menopause. Parity at the time of transplant was determined by chart review.

Results: There were 816 unique women, aged 18 to 44 at the time of transplant, in the period from 1996 to 2014. After excluding women who had passed away (n=91), and those with no current address or living outside the US (n=10), there were 715 eligible women and 190 responded (26.6% response rate). Respondents were more likely to be white and to have had a pregnancy post-transplant. Only 10% of women reported a pregnancy post-transplant, though 14.2% reported actively pursuing pregnancy at the time of the chart review. Nearly half (42.1%) of women said they were advised not to get pregnant, most often by a nephrologist. There were 61 pregnancies post-transplant, of which 80.1% were planned pregnancies. The majority of pregnancies resulted in livebirths (57%), and miscarriage occurred in 39% of pregnancies. Anemia occurred in 34.2% of women pre-transplant, and 23% of these women did not have cycles return after transplant. The median (interquartile range) age of menopause was 44.5 (36-49) years.

Conclusions: While only 14.2% of respondents reported actively pursuing pregnancy after transplant, nearly half said they were advised not to pursue pregnancy, often by their nephrologists, which could in part explain low pregnancy rates in the kidney transplant population. While anemia prior to transplant occurred in the minority of women, 23% of these women did not have menstrual cycles return post-transplant. Furthermore, the median age of menopause was much earlier than the general population. These findings suggest that kidney disease and/or transplantation itself may impact long-term gonadal function, which should be a target of future study.

Funding: Clinical Revenue Support

PO2595
Menstrual Irregularities and Subfertility in Women with Glomerular Disease

Background: Women with CKD are known to have high rates of irregular menses and subfertility (an extended period of unwanted non-conception). Those with glomerular disease may be at particularly high risk due to exposure to immunosuppression, such as cyclophosphamide, that may lower fertility.

Methods: A women's health survey was distributed to women ages 18-65 in the Glomerular Disease Collaborative Network, a longitudinal research registry in the southeastern United States. Descriptive statistics were employed to assess responses.

Results: The survey was completed by 192 women (response rate 16%) with median age 48 (34-57 interquartile range(IQR)) and BMI 28 (24-35 IQR). The most common diseases were IgA nephropathy/vasculitis (22%), Lupus nephritis (20%), ANCA vasculitis (18%) and FSGS (16%). At the time of the survey, 17% had a kidney transplant or required dialysis. Table 1 describes self-reported menstrual cycle length and permanent cessation of menses by age group. Of those over age 45, 41% reported permanent cessation of menses had occurred at a 44 years old. Cyclophosphamide use was reported by 63 of 192 (33%), and their fertility preservation methods included leuprolide (6%, 10%), and oocyte cryopreservation (1, < 2%). One in four women (50/192, 26%) reported a median (interquartile range) age of menopause was 44.5 (36-49) years.

Conclusions: Women with glomerular disease and/or vasculitis had high rates of irregular menstruation and early menopause which may contribute to subfertility. Our data is limited as we do not know GFR, nor the timing or amount of cyclophosphamide prescribed. Response bias from women with a positive history may have also played a role. Future efforts should elucidate reproductive endocrinology utilization and success in this population.

Funding: NIDDK Support

Menstrual Cycle Length and Cessation Of Menses By Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N</th>
<th>Median (IQR)</th>
<th>Menstrual(≤ \text{45 days})</th>
<th>Menstrual(&gt; 45 \text{days})</th>
<th>Cessation of menses(≤ \text{45 years})</th>
<th>Cessation of menses(&gt; 45 \text{years})</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-35</td>
<td>101</td>
<td>41 (32-51)</td>
<td>60 (50-70)</td>
<td>40 (30-50)</td>
<td>10 (8-12)</td>
<td>30 (20-40)</td>
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<tr>
<td>36-44</td>
<td>90</td>
<td>54 (48-63)</td>
<td>35 (25-50)</td>
<td>45 (40-55)</td>
<td>5 (4-6)</td>
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<td>68 (58-75)</td>
<td>12 (10-17)</td>
<td>12 (11-13)</td>
<td>6 (4-8)</td>
<td>14 (12-16)</td>
</tr>
</tbody>
</table>

Conclusions: While only 14.2% of respondents reported actively pursuing pregnancy after transplant, nearly half said they were advised not to pursue pregnancy, often by their nephrologists, which could in part explain low pregnancy rates in the kidney transplant population. While anemia prior to transplant occurred in the minority of women, 23% of these women did not have menstrual cycles return post-transplant. Furthermore, the median age of menopause was much earlier than the general population. These findings suggest that kidney disease and/or transplantation itself may impact long-term gonadal function, which should be a target of future study.

Funding: Clinical Revenue Support

PO2596
Buffy Coat Methylation Is Representative of Methylation Patterns in White Blood Cell Types in Normal Pregnancy
Ranim Ghanrawi,1 Natasa Milic,2 Sonja Suvakov,1 Wendy White,1 Vesna D. Garovic.1 Mayo Clinic Minnesota, Rochester, MN; 2Medicinski fakultet Univerzitet u Beogradu, Belgrad, Serbia.

Background: Epigenetic changes through DNA methylation are increasingly identified in renal diseases and hypertensive disorders. Our previous studies identified an altered methylation pattern in preeclampsia compared to normotensive pregnancies. Epigenetic studies typically use buffy coat- a heterogenous cell population- that varies throughout pregnancy and could potentially interfere with DNA methylation results. The objective of the current study was to assess to what extent the buffy coat methylation is representative of the distinct cell types that it contains namely polymorphonuclear leukocytes(PMN) and lymphocytes(LYM) in normal pregnant women.

Methods: We performed a pairwise comparison of the differential methylation in the buffy coat, the polymorphonuclear fraction and the lymphocytic fraction drawn from the same individual in normoretensive pregnant women (n=29) within the 24 hours prior to delivery. We analyzed 412481 cytosine-guanine (CpG) sites using an Illumina Human Methylation450 BeadChip.

Results: The three pairwise comparisons yielded a small number of probes that are differentially methylated. After multiple testing corrections, the smallest number of differentially methylated probes was found when comparing the buffy coat to the polymorphonuclear group (2.96%). Pathway analysis of the differentially methylated probes identified a matched process involved in leukocyte lineage. The differentially methylated CpG sites preferentially affected the open seas and shelf regions that have little effect on epigenetic regulation.

Conclusions: The buffy coat DNA methylation profile is representative of the PMN and LYM fractions on an Illumina Human Methylation450 BeadChip. The use of buffy coat is an acceptable approach for DNA sampling in DNA methylation studies and separation is only needed when studying lineage specific diseases.

Funding: Other NIH Support - NHI

PO2597
Pregnancy Outcomes in Women with AKI
Silvi Shah, Kathleen Harrison, Annette Christianson. University of Cincinnati, Cincinnati, OH.

Background: Acute kidney injury (AKI) during pregnancy is a public health problem and is associated with maternal and fetal morbidity and mortality. Literature concerning pregnancy outcomes in women with AKI is scarce.

Methods: We evaluated a retrospective single-center cohort of all women who delivered infants between 2012-2019 at our center (N=21,038) to assess the AKI rate and whether the history of AKI during pregnancy was associated with adverse maternal and fetal outcomes. Using multivariate logistic regression models, we determined factors associated with AKI during pregnancy and is associated with maternal and fetal morbidity and mortality. Literature concerning pregnancy outcomes in women with AKI is scarce.

Results: Overall, 109 deliveries were identified with AKI during pregnancy. AKI rate was 0.5%. The mean age of women was 28 years, 55% were black, and 36% were white. 25% had a history of diabetes and 24% had a history of hypertension. With regards to maternal outcomes, 46% had preeclampsia, 27% had gestational diabetes, 40% had gestational hypertension, and 57% had cesarean section deliveries. Maternal mortality was 4%. With regards to fetal outcomes, among women with AKI during pregnancy, 19% had preterm deliveries, the live birth rate was 85%, the stillbirth rate was 5%, and neonatal mortality was 5%. Diabetes and hypertension were associated with a higher adjusted likelihood of AKI during pregnancy (OR, 4.5; 95% CI, 2.87-7.50 and OR, 5.97; 95% CI, 1.63-9.80 respectively). In the adjusted model, AKI during pregnancy was associated with a 5.6-fold higher likelihood of preeclampsia (OR, 5.57; 95% CI, 3.70-8.39), 2.2-fold higher likelihood of cesarean section (OR, 2.21; 95% CI, 1.50-3.27), 2-fold higher

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PO2599
Pregnancy Following Kidney Transplantation: Experience of a Tertiary Renal Obstetric Service Between 1996 and 2020
Sarah Gleeson,1 Michelle Willicombe,1,2 Sevada Hassan,1 Daniel Christiadi,1 Philip Webster,1,2 Liz Lightstone.1,2 Imperial NHS Healthcare Trust, London, United Kingdom; 1Imperial College London Faculty of Medicine, London, United Kingdom.

Background: Compared with dialysis, fertility & pregnancy outcomes are more favourable following transplantation. However, pregnancies post transplant renal allocation challenging with a risk of adverse maternal & obstetric outcomes.

Methods: All transplanted patients attending the renal obstetric clinic were identified from an in-house database. Further data were collected from their health records.

Results: We identified 52 pregnancies in 39 women. The mean age at delivery was 33±3 years. 57% were white, 17% black & 21% Asian. The cause of ESKD was glomerulonephritis (46%), reflux (17%), unknown (other) (27%) & diabetes (10%). 3 patients (5%) miscarried & are not included in further analysis. The mean time from transplantation to pregnancy was 84±56 months. The mean follow up after delivery is 6±2.5 years. The mean gestational age at delivery was 39±2.8; at 6 months postpartum it was 39±2.5. The mean birth weight was 2400±588 grams. 24% were <10th percentile.

Conclusions: Pregnancy outcomes in patients with transplants are better compared with those on dialysis. Compared with complications still occur. The rate of preeclampsia (56%) is representative of the current literature & much higher than for women without transplants. Diagnosing preeclampsia in patients with pre-existing hypertension & proteinuria, as for many of our patients, remains challenging. In our experience, reflected here, there are relatively low rates of rejection & graft loss but high rates of obstetric complications. We believe these patients are ideally managed in a joint obstetric clinic.

PO2600
Prepartum 1,3-Butanediol Supplementation Does Not Prevent Onset of Superimposed Preeclampsia in the Dahl S Rat
Jeanne A. Ishimwe, Michael R. Garrett, Jennifer M. Sasser. University of Mississippi Medical Center, Jackson, MS.

Background: Chronic hypertension increases the risk of developing superimposed preeclampsia (PE). Previous reports showed that 1,3-Butanediol (BD) lowers blood pressure (BP) in male Dahl salt sensitive (S) rats and female S SHR(S) rats. The goal of this study was to test if attenuating hypertension before pregnancy through the placental period via BD prevents the onset of PE and improves kidney function.

Methods: Female Dahl S rats (a spontaneous model of superimposed PE, 11-16 weeks old) were divided into two groups; BD treated (20% via drinking water) and control (ad libitum water). Animals received BD for 7 weeks, baseline BP measurements (teleometry) were taken, and both groups were then mated. On gestation day (GD) 12, treatment was stopped because pilot studies showed that treatment reduced water intake during late pregnancy. Both groups were maintained on normal rodent chow (Teklad 7013, 0.3% Na; n=9/group). At GD18 (late pregnancy), urine artery resistance index (UARI) was measured via Doppler ultrasound, 24h urine was collected on GD19, and tissues were harvested on GD20. Statistical comparisons between groups were done by Student t-test and repeated measures ANOVA used for BP analysis.

Results: Mean arterial pressure was lower in the treated group at baseline (141.9±4.0 vs. 165.7±4.53 mmHg, p=0.0076), early (135.9±3.42 vs. 169.±4.55 mmHg, p=0.0003), mid (142.0±5.16 vs. 170.8±4.61, p=0.0048) but not late pregnancy (144.9±5.87 vs. 161.9±4.52 mmHg, p=0.1650). Treated dams had a lower UARI (0.71±0.02 vs. 0.81±0.02, p=0.0472) and a 5.7-fold higher likelihood of neonatal death (OR, 4.04; 95% CI, 1.60-10.20), and a 5.7-fold higher likelihood of preterm births (OR, 1.97; 95% CI, 1.22-3.16), 4-fold higher likelihood of stillbirths, and mortality. This finding increases our understanding and need for change in policies for the management of AKI during pregnancy.

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hypervolemic hyponatremia due to nephrotic syndrome. She was placed on fluid restriction. Repeat serum sodium and 24 h urine protein to creatinine ratio (UPCR) were 118 mEq/L and 4.4 g/g creatinine, respectively. Her obstetrician decided to perform emergency delivery. Prior to oxytocin induction, she received 3% saline, 0.9% saline, and IV furosemide. Three hours after delivery, serum sodium was 125 mEq/L and UPCR was 0.2 g/g creatinine. Fluid restriction continued for the first 24 hours after delivery and her serum sodium remained stable. Over the next 24 hours, her serum sodium corrected to 138 mEq/L with liberalization of the fluid restriction.

**Discussion:** Hyponatremia in pregnancy may be due to antidiuretic hormone (ADH)-dependent factors, such as “reset” osmostat, diffuse vasodilation, nausea, and pain. Administration of oxytocin, which is structurally similar to ADH, can also reduce serum sodium. In preeclampsia, hyponatremia may occur due to decreased effective circulating volume secondary to antiangiogenic factors or nephrotic syndrome, non-osmotic release of ADH with consequent water retention, or SIADH. Worsening hypertension with end organ damage are severe features of preeclampsia often requiring emergent delivery, but severe hyponatremia is often overlooked as a severe feature. This case illustrates that patients with preeclampsia may develop severe hyponatremia, which improves after delivery. Refined guidelines should consider severe hyponatremia and its management in preeclampsia.

**Figure 1:** Clinical data & Jones stain showing glomerular basement membrane duplication, characteristic of TMA.

**PO2604**

**Hypereosmin Gravidarum-Induced Acute Tubular Necrosis: A Case with More Than Fivefold Rise in Serum Lipase Level Above the Upper Limit of Normal**

Samira Z. Chandra, 1,3 Bruna Tavares Garcia, 2 Belinda Jim, 2 Bangladesh College of Physicians and Surgeons, Dhaka, Bangladesh; 3Jacobi Medical Center, Bronx, NY; 4Dhaka Medical College and Hospital, Dhaka, Bangladesh.

**Introduction:** Hypereosmin gravidarum (HG) occurs in 0.3 to 10 percent of pregnancies with only 0.8 percent requiring hospitalization. HG usually starts within 4th to 6th week of gestation, peaks around 9th week and fades away between 16th to 20th gestational weeks. In some cases, HG may last until the third trimester. Here we are reporting such a case which was associated with serious complication like acute renal failure. Co-incidentally the patient was also found to have serum lipase level 5 times above the upper limit of normal (ULN). Since HG exerts multisystemic manifestations, the unusual pattern of raised serum lipase is often due to associated renal impairment.

**Case Description:** A 25-year old primigravida at 16th week of gestation was admitted for severe dehydration and acute kidney injury (S. Creatinine 5.1 mg/dl). She was suffering from HG since the beginning of her pregnancy. A month prior to this admission, the patient was hospitalized on multiple occasions for extreme nausea and blood-tinted vomiting. Her initial labs were suggestive of high anion gap metabolic acidosis (anion gap 31.9mmol/L). Urine electrolytes (Na+<20mEq/day, K + 29mEq/day, Cl - <20mEq/L) confirmed renal failure. Co-incidentally the patient was also found to have serum lipase level 5 times above the upper limit of normal (ULN). Since HG exerts multisystemic manifestations, the unusual pattern of raised serum lipase is often due to associated renal impairment.

**Discussion:** Patients presenting with nephrotic syndrome and hyponatremia ≥ 20 weeks gestation pose a diagnostic dilemma. Renal biopsy is necessary to distinguish PEC from GN but pathological diagnosis of TMA can lead to persistent diagnostic uncertainty. Measurement of circulating angiogenic factors can be useful, with sFLT-1:PlGF ratio > 38 supporting a diagnosis of PEC. Further validation and widespread availability of such testing is needed to assist in management of early pregnancy complications.

**Figure 1:** Clinical data & Jones stain showing glomerular basement membrane duplication, characteristic of TMA.

**PO2603**

**Proteinuria in Early Pregnancy: Role of sFLT-1:PlGF Ratio**

Nay Seif, Carla L. Ellis, Shikha Wadhwani. Northwestern University Feinberg School of Medicine, Chicago, IL.

**Introduction:** A 32-year-old nulliparous woman at 20.5 weeks gestation by in vitro fertilization was admitted for hypertension (HTN), proteinuria, and acute kidney injury. Exam was notable only for trace leg edema. Given nephrotic syndrome early in pregnancy and unremarkable hemolysis work-up (Figure 1A), there was concern for acute glomerulonephritis (GN). Renal biopsy showed signs of thrombotic microangiopathy (TMA) (Figure 1B) without evidence of immune-complex mediated GN. As Atypical hemolytic uremic syndrome (aHUS) and Preeclampsia (PEC) were both on the differential, serum was tested for sFLT-1 and PlGF. Based on emerging evidence of alternative complement pathway activation in PEC, Eculizumab use was discussed but not pursued due to uncertain fetal viability, even with pregnancy prolongation. Ultimately, patient chose to terminate the pregnancy and subsequent pathology review revealed maternal vascular malperfusion and early intrauterine fetal demise. Levels of sFLT-1 (95.228 pg/ml), PlGF (139.3 pg/ml), and sFLt-1: PlGF ratio (683.6) were all consistent with severe PEC (Figure 1C). At 2-month follow-up, proteinuria had resolved and HTN was controlled with Nifedipine.

**Discussion:** Patients presenting with preeclampsia and hyponatremia may develop severe hyponatremia, which improves after delivery. Refined guidelines should consider severe hyponatremia and its management in preeclampsia.

**Figure 1:** Clinical data & Jones stain showing glomerular basement membrane duplication, characteristic of TMA.

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PO2605
Outcomes of Delivery Hospitalizations Among Pregnant Women with Kidney Transplant in the United States
Api Chewcharat,1,2 Andrea G. Kattah,1 Charat Thongprayoon,1 Wisit Cheungpasitporn,2 Boonpripop Boonpheng,4 Maria Lourdes Gonzalez Suarez,1 Jasmina Craici,1 Vesna D. Gavovic,1 1Mayo Clinic, Rochester, MN; 2Mount Auburn Hospital, Cambridge, MA; 3University of Mississippi Medical Center, Jackson, MS; 4University of California Los Angeles, Los Angeles, CA.

Background: Outcomes of delivery hospitalizations, including acute kidney injury, obstetric and fetal events among pregnant women with kidney transplants (KT) compared to those with no known kidney disease and chronic kidney disease (CKD) stage 3-5 are unclear.

Methods: Hospitalizations for delivery were identified using the enhanced delivery identification method in the National Inpatient Sample dataset from the years 2009 to 2014. Diagnoses of CKD stage 3-5, KT along with obstetric events, delivery methods, and fetal events were identified using ICD-9-CM diagnosis and procedure codes. Logistic regression accounting for the survey weights and matched regression were conducted to investigate the risk of maternal and fetal complications in women with KT as compared to women with no kidney-related diagnosis and compared to women with CKD stage 3-5.

Results: A total of 5,408,215 hospitalizations resulting in delivery were identified, including 405 women with CKD stage 3-5, 295 women with functioning KT, and 5,405,499 women with no kidney diagnosis. Pregnant KT recipients were at higher odds of pregnancy-induced hypertension (OR = 3.11, 95% CI [2.26, 4.28]), preeclampsia/eclampsia/HELLP syndrome (OR = 3.42, 95% CI [2.54, 4.60]), preterm delivery (OR = 2.46, 95% CI [1.75, 3.45]), fetal growth restriction (OR = 1.74, 95% CI [1.01, 3.00]), and acute kidney injury (OR = 10.46, 95% CI [5.33, 20.56]) as compared to women with no kidney-related diagnosis. There were no significant differences in rates of gestational diabetes and cesarean section. Pregnant women with KT had 1.30-time longer length of stay and 1.28-time higher cost of hospitalization. However, pregnant women with KT had 1.30-time longer length of stay and 1.28-time higher cost of hospitalization. However, pregnant women with CKD stage 3-5 were at higher odds of AKI, preeclampsia/eclampsia/HELLP syndrome and fetal death, and had longer hospital stay and cost of hospitalization compared to pregnant women with KT.

Conclusions: Pregnant women with KT were more likely to experience adverse events during delivery when compared to women with no known kidney disease. However, pregnant women with advanced CKD were more likely to experience serious complications than KT recipients. Women with advanced CKD who wish to conceive might consider conception after transplantation for better pregnancy-related outcomes.

PO2606
Successful Pregnancy in a Patient with Congenital Renal Dysplasia After Initiation of Dialysis
Jennifer C. Tang,1,2 Annika K. Khine,1,2 University of Southern California Keck School of Medicine, Los Angeles, CA; 2Los Angeles County University of Southern California Medical Center, Los Angeles, CA.

Introduction: Chronic kidney disease (CKD) is a well-known risk factor for adverse maternal and fetal outcomes including preeclampsia and fetal growth restriction. For those on dialysis, increasing the frequency and duration of dialysis has shown to optimize outcomes. However, it remains unclear if and when pregnant patients with CKD should start dialysis to improve outcomes. We present a patient with congenital renal dysplasia who successfully gave birth after starting dialysis.

Case Description: A forty-one-year-old female with an intrauterine pregnancy of 25 weeks and a history of two miscarriages, preeclampsia, and congenital renal dysplasia presented to nephrology clinic. Patient was unaware of her kidney dysfunction and had residual renal function with a creatinine of 3.76 and urine pr/cr ratio of 1.18. A fetal ultrasound revealed a fetal weight in the 12th percentile, head circumference in the 2nd percentile, and biparietal diameter (BPD) in the 33rd percentile. Therefore, the patient had no signs of renal recovery, her immunosuppression was discontinued. The patient returned to the hospital with hypoxic respiratory failure due to parainfluenza virus linear deposits on immunofluorescence, confirming the diagnosis. In addition to daily hemodialysis, the patient underwent plasmapheresis and immunosuppression with pulse dose steroids followed by a steroid taper as well as azathioprine and tacrolimus. The treatment of choice in anti-GBM disease is plasmapheresis to remove circulating antibodies and immunosuppression to reduce antibody production. However, pregnancy presents a unique challenge in choosing immunosuppressive agents as both maternal and fetal effects need to be considered. The involvement of high risk obstetricians as well as neonatologists in the care of these patients is imperative to ensure the best possible outcomes.

Discussion: Initiation of dialysis resulted in significant interval fetal growth and this patient’s first viable infant. Further research is warranted to assess if starting dialysis earlier in pregnant patients with CKD may improve fetal outcomes.

Fetal ultrasound prior to dialysis with a femur length in the 6th percentile and an estimated fetal weight of 635 grams in the 12th percentile.

PO2607
The Ethics of Caring for Pregnant Patients with CKD: A Scoping Review
Elizabeth M. Hendren, Michelle A. Hladunewich, Ariel Lefkowitz. University of Toronto, Toronto, ON, Canada.

Background: Physicians must consider many ethical principles when managing patients with chronic disease before and during pregnancy. An ethical framework could guide joint decision making between physicians and their patients, but does not currently exist.

Methods: We performed a scoping literature review to explore the ethical considerations associated with pregnancy in patients with chronic disease. We searched for articles published between 1975 and 2019 using the terms “Ethics” and “High risk Pregnancy/Pregnancy” along with 29 chronic disease-specific MeSH terms (e.g. scleroderma, diabetes, cystic fibrosis).

Results: We identified 968 articles and excluded 947 based on their title or abstract. 12 full text articles were included in the final scoping review representing discussions, case reports, and literature reviews on the ethics of high-risk pregnancy in 8 chronic diseases. The extracted data were examined and integrated into analyses of clinical cases in order to develop recommendations for ethically caring for this patient population.

Conclusions: Physicians have an ethical duty to their patients to facilitate autonomous decision-making and informed consent. Secondarily, they have a duty to protect the fetus and to use resources judiciously as long as it does not negatively impact the care they provide to their patient.

PO2608
Anti-Glomerular Basement Membrane Disease in Pregnancy
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Introduction: Anti-glomerular basement membrane (anti-GBM) disease is a rare cause of renal failure due to the production of IgG antibodies against type IV collagen. Its occurrence during pregnancy is even less common and can lead to poor maternal and fetal outcomes.

Case Description: A 23-year-old female with history of depression presented at 15 weeks 3 days gestation with weakness, nausea and vomiting for one week and anuria for 24 hours. Labs were significant for a creatinine of 19.8 mg/dL, BUN 113 mg/dL and potassium 7.1 mmol/L. Labs six months prior were normal. Nephrology was consulted and the patient was transferred to the intensive care unit for urgent hemodialysis. Further serologic investigation revealed elevated anti-GBM antibodies. A kidney biopsy was performed which demonstrated 100% cellular crescents on light microscopy and linear deposits on immunofluorescence, confirming the diagnosis. In addition to daily hemodialysis, the patient underwent plasmapheresis and immunosuppression with pulse dose steroids followed by a steroid taper as well as azathioprine and tacrolimus. The patient returned to the hospital with hypoxic respiratory failure due to parainfluenza virus further complicated by pre-term premature rupture of membranes at 24 weeks 4 days. As the patient had no signs of renal recovery, her immunosuppression was discontinued. The patient remained inpatient receiving daily hemodialysis until 28 weeks 0 days when the patient developed uncontrollable hypertension requiring an emergent cesarean section. The patient gave birth to a live male weighing 1.1 kg. Her post-partum course was uncomplicated, though the patient remains dialysis dependent.

Discussion: The treatment of choice in anti-GBM disease is plasmapheresis to remove circulating antibodies and immunosuppression to reduce antibody production. However, pregnancy presents a unique challenge in choosing immunosuppressive agents as both maternal and fetal effects need to be considered. The involvement of high risk obstetricians as well as neonatologists in the care of these patients is imperative to ensure the best possible outcomes.

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PO2609

Identification of Renal Disease in Women with Hypertensive Pregnancies

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Amelia M. Holloway,1 Kate Bramham,1,2 Katherine R. Clark.1,2 King’s College
Hospital NHS Foundation Trust, London, United Kingdom; 2King’s College
London School of Lifecourse Sciences, London, United Kingdom.

Background: Hypertension in pregnancy can be associated with renal injury, which
may be masked by gestational change. Additionally, pregnancy affords an opportunity
to diagnose asymptomatic renal disease. Postpartum assessment enables detection of
on going renal abnormalities. We aimed to determine prevalence of renal disease in
postpartum women with chronic hypertension, pregnancy induced hypertension or
preeclampsia in a previous or current pregnancy.

Methods: Women with singleton pregnancies seen in a specialist clinic for hypertension with estimated GFR (CKD-EPI) below 90mL/min/1.73m² and/or proteinuria at six-weeks postpartum were offered specialist renal midwifery clinic follow-up.

Results: 143/341 women offered follow-up attended renal clinic (Median IQR 246.25) days after delivery. 82 (57.3%) women had proteinuria and/or low eGFR.

Conclusions: Over half of women with proteinuria and/or reduced eGFR at six weeks postpartum had sustained evidence of renal disease regardless of hypertensive diagnosis. Postpartum assessment may afford an opportunity to detect renal disease.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Chronic Hypertension (%)</th>
<th>PIH in current pregnancy (%)</th>
<th>PIH in previous pregnancy (%)</th>
<th>History of Preeclampsia (%)</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>38 (28.32)</td>
<td>68 (31.49)</td>
<td>4 (1.08)</td>
<td>48 (35.71)</td>
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<tr>
<td>B</td>
<td>28 (20.85)</td>
<td>52 (23.22)</td>
<td>3 (0.70)</td>
<td>36 (26.36)</td>
</tr>
</tbody>
</table>

BP: Blood Pressure PE:Pre-eclampsia; PIH: Pregnancy induced hypertension; PCR: Protein Creatinine Ratio; ACR: Albumin Creatinine Ratio

PO2610

Senescence Markers in Women with Preeclampsia Pregnancies

Sonja Suvakov,1 Ranine Ghamrawi,1 Haiato Tu,1 Wendy White,1 Natasa Milic,1 Joseph P. Grande,1 Vesna D. Garovic.1 Mayo Clinic Minnesota, Rochester, MN; 1The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China.

Background: Preeclampsia, a hypertensive disorder of pregnancy, is characterized by increased angiogenesis and inflammation. Data indicate that preeclampsia is mechanistically related to cellular senescence, an irreversible cell-arrest mechanism which has been increasingly associated with accelerated aging. The aim of this study was to determine if senescence plays a role in the pathophysiology of preeclampsia. To that end, we compared SASP components in blood and fat tissue sections between preeclamptic and normotensive pregnancies, as well as p21 and p16 expression in the fat and kidney tissue samples.

Methods: Blood samples from preeclamptic and normotensive patients at the time of delivery were used to study circulating senescence-associated secretory phenotype (SASP) components. Plasma SASP components were tested using Luminex 200 system. Fat tissue explants (3-5 g) were obtained during the surgery from pregnant women who were clinically indicated for C-section. Kidney sections originated from the autopsy material of patients who died from preeclampsia. Upon protein isolation from fat tissue, SASP components were measured. Fat and kidney tissue sections were immunostained for p16 and p21. Preeclamptic and normotensive participants were matched for age and BMI.

Results: Significant increase of senescence markers were found in blood of preeclamptic pregnancies for NGF (1.30±0.82 vs. 0.77±0.19, p=0.032), MCP1 (316.9±163.95 vs. 207.53±84.78, p=0.047), TNFα (2.79±1.08 vs. 2.06±0.64, p=0.043) and Pai1 (58.0±18.85 vs. 38.1±20.86, p=0.023). Similarly, significant increase in senescence markers was found in preeclamptic pregnancies for MCP1 and TNFα. Expression of p16 was significantly increased in fat tissue, whereas the difference in p21 expression between preeclamptic and normotensive patients was not observed. Expression of p16 in preeclamptic renal sections was significantly higher (p=0.02) than in sections from normotensive pregnancies. The p21 expression did not differ between preeclamptic and normotensive kidney sections.

Conclusions: Women with preeclampsia have higher senescent burden compared to normotensive pregnant women at the time of delivery. Senolytic agents that target senescence may offer the opportunity for mechanism-based therapies.

Funding: NIDDK Support, Other NIH Support - NIH grant

PO2611

Sexual Dimorphism and Hard Outcomes in AKI: Is Female Sex Protective? The Jury Is Still Out

Maria Isabel Acosta-Ochoa, Armando Coca, Jimmy R. Sanchez Gil, Alicia Mendiluce. Hospital Clinico Universitario de Valladolid, Valladolid, Spain.

Background: Many studies focus on sex dimorphism and its influence on hard outcomes when suffering an AKI episode. Some report that women, while others report that men are protected against adverse clinical events. In a real world cohort of individuals suffering from AKI, we compared hard outcomes between sexes with a novel approach: paired-matched study.

Methods: Retrospective paired-matched study of in-patients with AKI diagnosis; cases were matched based on sex, age and Charlson’s Index. We used KDIGO-2012 criteria to define AKI, analyzed clinical variables, and compared the hard outcomes: length of hospital stay, need for acute HD, HD dependence at discharge, and in-hospital mortality.

Results: We included 383-paired matches. Male individuals suffered from peripheral arterial disease and COPD, and were hospitalized in surgical wards more frequently than women. We found no statistically significant difference between groups regarding to the prevalence of common comorbidities and admission to ICU (Table 1A). The distribution in global KDIGO-AKI Stages was similar, but when analyzing every sub-criterion of the classification we found that women fulfilled the serum creatinine (SCr) increment ≥1.5-1.9x more frequently, and men fulfilled reaching a SCr >4 mg/dl more commonly. We found no statistically significant differences in hospital stay, need for acute HD, HD dependence at discharge, and in-hospital mortality (Table 1 B).

Conclusions: To our knowledge, a paired-matched design regarding to this topic has not been previously published. Although experimental studies find differences in clinical outcomes between sexes when suffering an AKI episode, in this real world study, we did not observe a clear distinction in the incidence of adverse outcomes between sexes. We conclude that sex (either female or male) may not be protective against AKI’s hard outcomes.
PO2612
Effects of Veverimer on Serum Bicarbonate and Physical Function in Women with CKD: A Subgroup Analysis from a Randomized Controlled Trial
Vandana S. Mathur,1 Donald E. Wesson,2 Neeli Kandarpa,3 Yurii Stavis,4 Dawn Parsell,5 Elizabeth Li6, Gerrit Kraener,7 David A. Bushinsky,7 Mathur Consulting, Woodside, CA; 8Baylor Scott & White Health and Wellness Center, Dallas, TX; 9University of Manitoba, Winnipeg, MB, Canada; 10Tricida, Inc., South San Francisco, CA; 11Pharmacia LLC, Fremont, CA; 12University of Rochester Medical Center, Rochester, NY.

Background: More women than men have CKD. However, women have been underrepresented in clinical trials. Veverimer is an orally administered, non-absorbed polymer that treats metabolic acidosis by binding and removing HCl from the GI tract. In Phase 3 randomized, double-blind, placebo-controlled trials, veverimer significantly increased serum bicarbonate and improved physical function in acidic patients with CKD (Wesson et al. Lancet, 2019). Here we analyzed efficacy and safety among the women in these studies of up to one year.

Methods: Physical function was assessed using the Kidney Disease and Quality of Life Physical Function Domain (KDQOL-PFD) which quantifies limitations on daily activities and by performance on the repeated chair stand (RCS) test.

Results: Of the 217 pts randomized, 83 (32%) were women, of whom 81% were post-menopausal (≥55 yrs). Select comorbidities included hypertension (95%), diabetes (64%), and congestive heart failure (30%). At Baseline, mean eGFR in women was 28.4 mL/min/1.73m2 and mean serum bicarbonate was 17.3 mEq/L. More women receiving veverimer met the primary study endpoint, had a significant increase in serum bicarbonate and improved both KDQOL-PFD scores and RCS time (Table) compared with placebo. The effects of veverimer exceeded the minimal clinically important difference for both KDQOL-PFD (+3 to +5 points) and RCS (+1.7 seconds). Rates of serious, non-serious and GI adverse events were similar in both groups; none required treatment discontinuation.

Conclusions: Given their lower bone and muscle mass, women with CKD may be particularly vulnerable to the adverse effects of metabolic acidosis. We found that in women with CKD and metabolic acidosis, treatment with veverimer significantly improved how women felt and functioned. The safety of veverimer was similar to placebo.

Funding: Commercial Support - Tricida, Inc.

- P-values are vs. placebo; An ANCOVA rank-based method was used for physical function endpoints
- *Based on evaluable patients enrolled in controlled extension study (placebo, n=31; veverimer, n=46)

PO2613
 Dietary Intake Syndrome, Risk of Kidney Stone, and Survival in the Women’s Health Initiative (WHI)
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Background: The effect of dietary magnesium intake (DMI) on the risk of stone is controversial, and its effect on survival among kidney stone formers is unknown.

Methods: We examined participants enrolled in WHI, a prospective, longitudinal, multicenter study investigating the health of postmenopausal women, and used Cox regression analyses to determine the independent effects of DMI on the risk of incident kidney stone and survival amongst the stone formers.

Results: 145,942 participants were identified free of kidney stone history at baseline. 83% were Caucasian, mean age was 63. Among them, 60,24 (4%) developed incident kidney stone during 1,601,750 person-years of follow up. The mean daily DMI was 318 mg, with 26% in tertile 1 (241 mg), 41% in tertile 2 (241-348 mg) and 33% in tertile 3 (>348 mg). The incidence of kidney stone disease was 3.1, 3.3, and 3.9 per 1000 person-year in high, moderate and low DMI groups, respectively. The corresponding multivariable-adjusted hazard ratios were 0.82 (95% CI: 0.71-0.94) for high vs low DMI when dietary oxalate intake (DOI) is high, and 1.01 (95% CI: 0.81-1.26) for high vs low DMI when DOI is low. Among incident stone formers, 82% were Caucasian, 23% were above age 70. Mean daily DMI was 304 mg, 32% in tertile 1, 38% in tertile 2, and 30% in tertile 3. Subsequently, 1346 (22%) died. Older age, histories of hypertension, diabetes and heart disease, low serum vitamin D, cigarette smoking, and hormone replacement association significantly with mortality, p<0.05. However, DMI had no impact on mortality after adjusting for demographics and potential confounding factors, hazard ratio (HR) 0.91, 95% CI 0.73-1.14, p=0.4 when compared high DMI vs low DMI groups, HR 0.90, 95% CI 0.73-1.11, p<0.3 when compared medium DMI vs low DMI groups.

PUB001
Consequences of Improper Interpretation of ANCA
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Introduction: Antineutrophil cytoplasmic antibodies (ANCA) is important in suspected vasculitis. False positive or atypical ANCA (A-ANCA) can lead to erroneous interpretation of immunofluorescence (IF) causing disastrous consequences. We present a patient who was initially reported as Perinuclear-ANCA (P-ANCA) positive and was therefore treated with steroids rendering him adrenal insufficient (AI).

Case Description: A 79-year-old man with history of CKD, A Fib, protein C deficiency, prostate cancer and ANCA positivity that was treated with steroids, presented to the ER with dizziness, bradycardia and hypotension. He was weak, fatigued, and unarousable. In the ER, he was started on vasopressors and methylprednisolone. His creatinine rose from 2.6 to 3.1 mg/dl. RPGN was suspected and kidney biopsy was performed that showed typical immune complexes related to ANCA vasculitis in clumps. His AM cortisol level was 3 ug/dl (10-20). Because of hypotension, polycyria and natriuresis, hydrocortisone and fludrocortisone were started. His serum K level decreased and fludrocortisone was stopped. After next few days, he became normotensive and his mentation improved with increasing dose of hydrocortisone. Hypokalemia slowly resolved with potassium supplements.

Discussion: ANCA are a group of antibodies that bind to antigens of neutrophils, causing systemic vascular inflammation. These autoantibodies can be found in the serum of patients with systemic, small vessel vasculitis and is a biomarker for ANCA-associated vasculitis. A positive staining of ANCA can be classified as: Cytoplasmic, Perinuclear, and Atypical, based on the pattern of IF. In cases with C-ANCA, the staining is diffuse throughout the cytoplasm and the cause of staining is due to antibodies directed against Proteinase 3 (PR3). In cases with P-ANCA, the staining is around the nucleus and it is due to antibodies directed against myeloperoxidase (MPO). A-ANCA can be found in conditions other than vasculitis and does not require immunosuppressive steroids for treatment. A-ANCA can be reported erroneously as P-ANCA or C-ANCA and patients can receive aggressive treatment with high dose steroids. Therefore, we suggest to confirm the ANCA results with MPO or PR3 before initiating aggressive therapy for vasculitis to avoid disastrous consequences.
Publication-Only

PUB003

Metabolic Encephalopathy due to AKI in a Patient with Recent Infusion of Intravenous Immunoglobulin (IVIg)
Sheikh Raza Shalzad, Kelly H. Beers. Albany Medical Center, Albany, NY.

Introduction: IVIg induced AKI is extremely rare (1% of cases). We present a case of AKI requiring hemodialysis secondary to recent IVIg administration.

Case Description: A 61-year-old woman presented with acute onset altered mental status (AMS) for 2 days. Her past medical history included CKD G3, HTN, COPD, PVD, and CAD. A week prior, she received 3 doses of sucrose-containing IVIg for chronic inflammatory demyelinating polyneuropathy. Shortly thereafter, the patient developed a facial rash, poor oral intake, low urine output, and AMS. Labs showed BUN 71 mg/dL, SCr 10.62 mg/dL, baseline Scr 2.6 mg/dL. ABG showed pH 7.07, pCO2 30 mmHg and HCO3 8 mmol/L. Toxicology screen was negative, CPK and lactic acid were normal. No NSAIDs use was reported. She required only 1 session of hemodialysis with the recovery of renal function and mental status. AIM due to IVIg and/or IVIg induced osmotic nephrotoxicity may be the culprit for her presentation.

Discussion: IVIg can produce adverse reactions thought to be caused by activation of the complement cascade by the aggregation of IgG. To avoid this, a variety of stabilizing agents, including sucrose, are used. Sucrose is absorbed into proximal convoluted tubular cells and is followed by water due to the changed osmotic pressure. This results in cytoplasmic vacuolization and degeneration of the proximal cells. CKD, HTN, DM, advanced age, dehydration, hyperviscosity, use of sucrose stabilizers, high dose IVIg therapy (400–2000 mg/kg), high rate of IVIg administration, or treatment with other nephrotoxic medications increase the risk of AKI. About 30% of cases require dialysis. The mortality rate is 10%. Adverse renal outcomes usually occur within 10 days of initiation of IVIg, and the duration of renal failure lasts between 3 and 45 days. Most cases resolve spontaneously. Early recovery of renal function can be achieved by diahylic removal of excess sucrose from the circulation. To make a diagnosis, access to renal function data for a ten-year period is necessary to be established with the administration of IVIg. A clinical diagnosis is made after ruling out other causes and is confirmed with a renal biopsy. Measures to prevent AKI include using sucrose-free IVIg or amino-acid-stabilized formulations, adequate hydration, avoiding other nephrotoxins and diuretics, reductions in dose, concentration (<5%), and/or rate of administration (<3mg sucrose/kg/min) of IVIg.

PUB004

A Patient with a Record High Blood Urea Nitrogen Value Surviving Without Dialysis
Hay Me Me, Urvashi Hooda, Aditi A. Sen, Amol Mittal, Michael Connery. Westchester Medical Center, Valhalla, NY.

Introduction: The blood urea nitrogen (BUN) has limited value as an index of glomerular filtration rate to access kidney function. It can be increased not only in the setting of acute or chronic renal failure but also in hypovolemic state, gastrointestinal tract bleeding, high catabolic states, and by certain medications. Dialysis is the effective treatment for uremia. However, there is no consensus on when to initiate the dialysis for high BUN in acute kidney injury.

Case Description: A 64-year female with history of hypertension, hyperthyroidism, hyperlipidemia, alcohol use disorder, chronic kidney disease (CKD) with baseline creatinine of 1.5 mg/dl was admitted for head trauma after fall. Patient had poor intake and was nott adequately hydrated. She was found to be confused by family. No history of analgesic or herbal supplements usage was present. Laboratory results were significant for BUN of 298 mg/dl, Creatinine (Cr) of 13.5 mg/dl, serum potassium of 5.4 mEq/L, phosphate of 6.1 mEq/L and severe hyperlipidemia, alcohol use disorder, chronic kidney disease (CKD) with baseline creatinine of 1.5 mg/dl. Initial management was to aggressively resuscitated with intravenous fluid including bicarbonate and her cognitive function improved without dialysis. The blood urea nitrogen (BUN) of 42 mg/dl was found to be normal bilateral kidney sizes. Patient was aggressively resuscitated with intravenous fluid including bicarbonate and her cognitive function improved without dialysis. Her BUN eventually decreased to 30 mg/dl and Cr to 1.26 mg/dl.

Discussion: The blood urea nitrogen (BUN) of 42 mg/dl was found to be normal bilateral kidney sizes. Patient was aggressively resuscitated with intravenous fluid including bicarbonate and her cognitive function improved without dialysis. Her BUN eventually decreased to 30 mg/dl and Cr to 1.26 mg/dl. Labs showed BUN 71 mg/dl, SCr 10.62 mg/dl, baseline Scr 2.6 mg/dL. ABG showed pH 7.07, pCO2 30 mmHg and HCO3 8 mmol/L. Toxicology screen was negative, CPK and lactic acid were normal. No NSAIDs use was reported. She required only 1 session of hemodialysis with the recovery of renal function and mental status. AIM due to IVIg and/or IVIg induced osmotic nephrotoxicity may be the culprit for her presentation.

Discussion: From the literature, this is the highest reported BUN in acute on chronic renal failure patient who improved without dialysis.

PUB005

Spontaneous Page Phenomenon in a Pelvic Kidney
Yahya R. Ahmad, William L. Wilson, Megan M. Robinson, Taha Ayach. University of Kentucky, Lexington, KY.

Introduction: Page kidney or Page phenomenon refers to compression of the renal parenchyma by subcapsular hematoma. Here we report the first case of spontaneous Page phenomenon in a native pelvic kidney.

Case Description: A 64-year-old male with a diagnosis of diabetes mellitus, essential hypertension, chronic kidney disease stage 3b, stage 3 obesity with a body mass index of 53, congenital right-sided pelvic kidney, presented to the emergency room with acute onset, severe, right lower quadrant abdominal pain. Patient denied having any recent trauma and had no urinary or gastrointestinal complaints. He was not on any antiplatelet or anticoagulation medications. CT angiogram of the abdomen and pelvis was performed which demonstrated a subcapsular hematoma around the right pelvic kidney. He had AKI with a peak creatinine of 4.2 mg/dl from a baseline of 2.2 mg/dl. He remained non-oliguric, with gradual improvement of his renal functions and never required renal replacement therapy or any intervention for Page kidney. He presented with markedly elevated blood pressure of 190/110 mmHg and his hospital course was significant for sustained elevated blood pressure requiring addition of four new anti-hypertensive medications by discharge. Subsequent imaging showed marked decrease in the subcapsular hematoma in a week.

Discussion: Page phenomenon is a rare but potentially fatal condition that can result from trauma, tumor, vasculitis, renal cyst rupture, or procedures like kidney biopsy. External compression of renal parenchyma can result in interstitial schema, tubulointerstitial nephritis and compression of intrarenal vessels thus activation of renin angiotensin system (RAS), resulting in AKI and hypertension associated with Page kidney. Persistently elevated blood pressure unresponsive to medical therapy or gradually enlarging hematoma with worsening renal functions might require percutaneous drainage, caspofungin or even nephrectomy. Optimal medical management of Page kidney includes medications targeting the RAS pathway.
Case Description: A 78-year-old male with coronary artery disease, hypertension, hyperlipidemia, and atrial fibrillation was admitted for an invasive pulmonary disease was diagnosed as hepatocellular carcinoma by transesophageal angiography of celiac and superior mesenteric arteries. He was admitted to the hospital for an operation of hepatocellular carcinoma. Serum creatinine level gradually increased from 1.71 to 5.87 mg/dL with eosinophilia (4404/μL) and high C-reactive protein (CRP) level (4.86 mg/dL). He started hemodialysis ten weeks after angiography and had been suffering from nausea. Endoscopy showed multiple gastric ulcers. Treatment with proton pump inhibitor started, but did not improve. Cyanosis was present in his bilateral toes and skin biopsy showed cholesterol crystal clefs. He was diagnosed with cholesterol embolism and treated with intravenous prednisolone (PSL) 20 mg/day, resulting in decrease of eosinophil, CRP levels and improvement of gastric ulcers. However, he was unable to withdraw from dialysis and developed disseminated cutaneous herpes zoster. Finally, he died of sepsis. Autopsy showed severe erosion of atherosclerotic plaques at the level of celiac artery. Cholesterol clefs were present in the vessels of kidney, stomach, intestines, liver, spleen, pancreas, diaphragm, adrenal glands and testes. The distribution of cholesterol crystal embolism was consistent with the site of angiography performed from celiac and superior mesenteric arteries.

Discussion: Cholesterol crystal embolism is caused by not only percutaneous coronary interventions and vascular surgery, but also by primary and secondary hyperlipidemia. We need to consider cholesterol crystal embolism when acute kidney injury and refractory gastric ulcers after transmembral angiography. Although PSL is administered for cholesterol crystal embolism, tapering strategies is important for patients on dialysis.

PUB008

Hyperkalemia in Community-Acquired AKI: Associated Factors and Clinical Consequences

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Background: Hyperkalemia (hyperK) frequently occurs in the context of acute kidney injury (AKI). However, little about the factors associated with hyperK and its clinical consequences in patients with community-acquired acute kidney injury (CA-AKI). The aim of present study was to analyze it.

Methods: The present study is based on a cohort of patients with CA-AKI admitted to the nephrology service from January 1st to February 15th, 2015. Hyperkalemia was defined as potassium levels above 5.1 meq / L. Results: A total of 308 patients were included. The mean age was 73.22 ± 13.95 years. 58.4% were men. Charlson comorbidity index (CCI) was 7.16 ± 3.66 and the length of stay was 12.25 ± 11.69 days. In view of the Etiology of AKI, 69.5% prenual AKI and 30.5% non-prerenal ones. 212 patients had previous chronic kidney disease (CKD) (68.8%). Hemodialysis (HD) was required in 54 patients (17.15%). 38 patients (12.3%) died during hospital stay. HyperK occurred in 173 cases (56.2%). Mean potassium was 5.45 ± 1.41 meq/L. There was a significant correlation between potassium and pH as well as between K and CCCI. There was an association between hyperK and intake of potassium-sparing diuretics (p < 0.001); ACEI/ARB (p = 0.003) and beta blocker (p < 0.001). Using a multiple linear regression model the equation that predicted serum potassium was: K = 36.44 – (4.4 x pH) + 0.98 (if intake of potassium-sparing diuretics = 0) + 0.10 x CCCI. Potassium level did not influence the length stay. Patients with HyperK required HD in a higher proportion (23.7 vs. 9.6%; p < 0.01) and also had higher mortality during hospital stay (15.6 vs. 8.1%; p = 0.048). After a follow-up of 2 years from hospital discharge, Kaplan-Meier survival curve analysis produced a significant difference (Log Rank (Mantel-Cox): p < 0.001) between patients with hyperK and patients that did not present it.

Conclusions: HyperK occurred in just over half of our patients. The potassium level was associated with high pH, and the intake of potassium-sparing diuretics. HyperK patients required HD and died in a greater proportion during hospital stay. Mortality after discharge was higher in patients who presented hyperK. Appropriate measures must be taken to correct hyperK early in patients with CA-AKI.

PUB009

A Case of Anti-Tubular Basement Membrane Antibody-Associated AKI

Masanori Terao, Takatsuji Ishi, Akira Kurosawa, Takasuke Shichino, Hironori Hasegawa.

Introduction: We report here a case of idiopathic anti-tubular basement membrane (TBM) antibody-related acute interstitial nephritis (AIN).

Case Description: Our patient was a 44 years man and had no history of renal disease. He was pointed out renal dysfunction of serum Cr 1.50 mg/dL in the health checkup 2 months prior to admission. The patient was admitted to our hospital because of worsening of renal function of Cr 2.89 mg/dL. Because renal dysfunction progressed (Cr 10.36 mg/dL), hemodialysis was started on the 8th hospital day. Urine abnormalities such as proteinuria or hematuria was not apparent, however, he showed remarkable elevation of urine NAG and β2-microglobin excretion, bilateral kidney enlargement, and renal accumulation was shown by Scintigraphy. Based on those findings, AIN was suspected and dialysis was continued for 22 days. The patient had undergone nephrectomy and microscopic examination revealed inflammatory cell infiltration in the tubulo-interstitium, and immunostaining showed linear deposition of IgG and C3 in the tubular basement membrane. Similar findings were observed in the tissue sections of other patient with no tubular disorder by the treatment of 10 mg/kg of PSL (PSL) 40 mg/day (0.8x kg/day) was started from the 13th day and methyl PSL 500 mg/day for 3 days was added on the 21st day. Renal dysfunction and inflammatory reaction disappeared after the treatment could not be maintained, however, proteinuria continued because of sudden psychosis. Cyclophosphamide 375-500 mg/day and multiple plasma exchange was added thereafter, however, finally he was shifted to the maintenance dialysis.

Discussion: Cases of TBM antibody-related AIN are very rare, and most of the reports are those induced by drugs and those developed after kidney transplantation, and few cases are considered to be idiopathic. Antigen of TBM antibody are thought to be a non-collagen protein that interacts with type-4 collagen, laminin and integrin, which is present in the proximal tubular basement membrane, but the mechanisms and clinical course that cause AINs are unknown. Accumulation of cases including this case is considered necessary.

PUB10

A Triple Threat: Baclofen Toxicity and Posterior Reversible Encephalopathy Syndrome in the Setting of AKI

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Introduction: This is a case of apparent baclofen toxicity and posterior reversible encephalopathy syndrome (PRES). Both conditions are seen in patients with kidney dysfunction but direct association between the two conditions has otherwise been defined. The case highlights areas of special consideration in the evaluation and management of mental status changes in patients with acute kidney injury (AKI). No other reported cases of the combined diagnoses were found on literature review.

Case Description: A 71-year-old female admitted with sepsis due to ESBL E. coli bacteremia and pyelonephritis became unresponsive on her 7th day of hospitalization. This was accompanied by abnormal renal function and hypertension. Her creatinine was 1.5mg/dL (baseline 1.5 mg/dL). AKI was attributed to prerenal physiology and sepsis-associated ATN. Mental status changes were attributed to baclofen neurotoxicity. She then developed evidence of partial complex seizures and subsequent imaging revealed findings of PRES. Levetiracetam, antihypertensives, and continued antibiotic therapy were provided. Systolic blood pressure increased to 180 mmHg with a MAP of 115 during the hospitalization. After several days, the patient recovered completely. Creatinine stabilized at 2.0 mg/dL. Discussion: Medications are a leading cause of acute mental status changes, especially in patients with impaired kidney function. Our case highlights the risks of baclofen toxicity in improving but impaired kidney function. The clinical-radiopathologic diagnosis of PRES may have been missed without imaging. The varying presentations of this condition are a reminder the importance of an expanded differential diagnosis and the need for a better understanding of the pathology. There is no reported association between PRES and baclofen. The role of AKI in the development of PRES is not entirely understood; however, the hypertension-hyperperfusion theory remains a leading consideration in our patient. Management decisions in our patient included forgoing dialysis, blood pressure control, and the use of anti-seizure medications.

PUB011

Renal Zygomycosis: A Rare Presentation in an Immunocompetent Patient

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Introduction: Zygomycosis is a broad term which refers to the infections caused by zygomycetes, fungi belonging to the order Zygomycetes. It is an azoic-opportunistic opportunistic infection which can usually present in four different ways including, pulmonary, gastrointestinal, renal and disseminated disease. Like other opportunistic infections it has predilection for immunocompromised patients however very rarely, it has been reported in immunocompetent patients.

Case Description: Here we report a case of an immunocompetent patient who was affected by renal zygomycosis and presented as a picture mimicking rapidly progressive glomerulonephritis (RPGN). The patient presented with hematuria, proteinuria and high creatinine and was suspected as a case of RPGN initially. CT scan abdomen showed bilateral smoothly tapered distal ends of the renal arteries with non-perfused enlarged kidneys. These findings were consistent with the diagnosis of Zygomycosis which has angi-invasive nature. Bilateral nephrectomy was done and diagnosis was confirmed on histopathology report. Post operatively, the patient was extubated from ventilator, recovered from shock and improved a lot. He was doing fine on maintenance hemodialysis until two weeks later he developed septic shock due to Acinetobacter Baumannii which could have triggered the re-activation of disseminated zygomycosis due to metabolic catastrophe.

Discussion: Isolated renal zygomycosis is very rare, although few cases have been described in literature. In our case, patient was referred to us as glomerulonephritis as his clinical picture initially resembled rapidly progressive glomerulonephritis. We were not able to highlight that isolated renal zygomycosis have can have presentation mimicking glomerulonephritis, so young nephrologists should rule out infections like zygomycosis before embarking on the diagnosis of Acute glomerulonephritis as misdiagnosis can be catastrophic.
Light Chain Cast Nephropathy in an African-American Woman with Waldenström Macroglobulinemia

Mohamedanwar M. Ghandour, Hillel Sternlicht. Wayne State University School of Medicine, Detroit, MI.

Introduction: Waldenström’s macroglobulinemia (WM) is a rare cancer of the lymphatic system due to excess IgM monoclonal protein with a rare renal involvement. Renal involvement is rare with an incidence of 3 cases per million people per year. We describe a case of MW presenting with acute renal failure.

Case Description: A 63-year-old female who admitted to our hospital for influenza B complicated by acute renal failure during the hospital stay, with creatinine up to 6 mg/dL, despite adequate hydration. Electrophoresis revealed a monoclonal component in the gamma region, which classified as an IgM k. A kidney biopsy was performed, showing light cast chains suggested the possibility of myeloma kidney. Furthermore, bone marrow histology was performed, revealing lymphoplasmacytic lymphoma. The patient was treated with bortezomib, dexamethasone, and cyclophosphamide, with complete recovery of renal function.

Discussion: Overall, renal manifestations are not commonly seen in Waldenström’s macroglobulinemia. Approximately one-third of patients are asymptomatic at the time of diagnosis. Like our patient who did not have renal symptoms and acute kidney injury discovered serendipitously. Moreover, reported rates of full renal recovery following adequate treatment are almost more than 50 percent. Patients with reversibly renal failure had longer median survival compared with patients who did not restore renal function.

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PUB015
Misleading Serologies in Thrombotic Microangiopathy due to Malignant Hypertension
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Introduction: Nephrologists use autoimmune panels to screen for glomerular disease. Some of these markers cause false positives in other systemic diseases which leads to misdiagnosis. We report a rare case of false positive MPO-ANCA and ANA in patient with thrombotic microangiopathy (TMA) due malignant hypertension.

Case Description: A 65 year old African American patient with a history of hypertension, breast cancer s/p right mastectomy, and CKD with baseline creatinine of 1 was admitted hypertensive urgency with pressures of 239/123. She had Acute Kidney Injury with creatinine of 6.6 and her work-up revealed new pericardial effusion, thrombocytopenia (platelets of 90), and anemia (hemoglobin of 9). Autoimmune panel was positive for ANA (1:520, speckled) and positive RNP (>8). The presumptive diagnosis was mixed connective tissue disease. Pericarditis was negative for malignancy and infections. She began dialysis but her renal function never improved. She was discharged dialysis dependent. The patient refused outpatient dialysis and her medications. She was re-admitted few weeks later with uremia and hypertensive urgency with pressures of 299/104. A repeat evaluation showed a newly positive MPO-ANCA (13.4), ANA (1.640, speckled), and a low C3 (72.8). The concern for vasculitis, a kidney biopsy was performed. Her biopsy was significant for global glomerulosclerosis, periglomerular ischemia, and severe interstitial fibrosis with tubular atrophy. There was extensive arteriolar onion skin intimal fibroplasia with red blood cell fragments. Based on her clinical history, patient had TMA secondary to hypertension. Her biopsy lacked findings of vasculitis due to an absence of necrotizing crescentic glomerulonephritis and negative immunofluorescent stains. The patient was maintained on hemodialysis and hypertension medications.

Discussion: Diseases associated with TMA can have false positive autoimmune markers and they require early recognition. There are cases that show Thrombotic Thrombocytopenic Purpura can produce MPO-ANCA and anti-DNA markers. The markers were correlated to intensity of the disease because the patients with active disease had higher titers. These markers are created secondary to immune dysfunction during TMA. This case also emphasizes the importance of kidney biopsy in order to distinguish between active vasculitis and non-vasculitic diseases.

PUB016
AKI, Diplopia, and Altered Psyche: One Rare Case of Extrapulmonary Sarcoidosis
Hillary DeRose-Calderg. Western Reserve Health Education, Youngstown, OH.

Introduction: Sarcoidosis is a multi-organ system disease primarily affecting the lungs. Pathological diagnosis requires the presence of non-caseating granulomas. Sarcoidosis is a genetic associated autoimmune disease more prevalent in African Americans. Renal sarcoidosis manifests in about 5-20% of patients with hypercalcemia, hypercalciuria, and nephrolithiasis on normal screening. Renal parenchymal involvement is typically granulomatous tubulo-interstitial nephritis. Neuro-sarcoidosis also occurs in about 1/3 of patients, affecting primarily the cranial nerves. CNS involvement can present with visual and occasionally behavioral changes. Ocular sarcoid presentations include uveitis and retinal lesions.

Case Description: 63-year-old white male with a history of rheumatoid arthritis, pulmonary nodules, glaucoma, presented with one year of blurry vision and weird psyche. He was referred to nephrology after an ophthalmologist found intermittent diplopia, transient optic disc swelling and intraretinal hemorrhage. Abnormal labs from 5/2019 with 11/2018 in parenthesis: Scr 2.73 (1.51 mg/dL), BUN 27 (22), Egrf naa 28 (49/min), Ser Calcium 8.6 (9.2 mg/dL) ACE 73 U/L, Alc 5.4. Given the worsening CKD IV; the following were drawn: ANA-IFA: positive, speckled p1 1.640, UA bld 10, fn gran cast; 0-5, crs gran cst 0.5, ur prot rad 24. Renal biopsy demonstrated nonscaseating granulomatous interstitial nephritis, numerous noncaseating granulomas with giant cells. He was referred to Cleveland Clinic Sarcol Clinic and started on 40mg prednisone for renal sarcoid. CXR with prior noddles, no hilar or parenchymal changes. CC Ophthalmology clinic’s fundal exam revealed peripheral hyopigmented lesions possibly consistent with ocular sarcoid. Vision had resolved. At 1 month, steroids were tapered with plans to start Azathioprine. The patient’s Ser improved on tapering steroids.

Discussion: Less than one in ten patients present solely with extrapulmonary sarcoidosis. This case demonstrates a rare presentation of neuro-ocular and renal sarcoidosis in the absence of lung findings. Sarcoidosis ought to be considered in AKI or new chronic kidney disease, particularly if a patient presents with other atypical findings such as retinal or optic nerve changes representing a syndrome of multi-organ involvement. Multiple system involvement is a predictor of progression to ESRD. Glucocorticoids are first-line therapy. Most cases respond to steroids.

PUB017
Dynamics of Tissue Injury mRNA Expression to Bilateral Renal Ischemia-Reperfusion Injury
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Background: Acute kidney injury (AKI) secondary to acute renal ischemia is associated with high mortality and morbidity with few effective treatments. The bilateral renal ischemia reperfusion injury (BRI) model is commonly employed in rodent studies of AKI. While disease progression is well characterized at the organism level, the dynamics of the molecular responses are less well understood. To improve the translational potential of compounds, the current study sought to temporally and mechanistically define the tissue mRNA expression profiles following discrete durations of IRI.

Methods: Rats underwent sham or warm, bilateral renal ischemia (30’ or 40’) surgery using PBI’s proprietary vascular clamps. Subsets of rats were sacrificed at 8 timepoints following reperfusion (0-48hr), with blood and kidneys harvested at each timepoint for subsequent analyses. Plasma and kidney mRNA were analyzed via clinical chemistry. The expression of 100 mRNA transcripts surveying genes across apoptosis, kidney injury, and inflammation/fibrosis pathways were measured by Quantigene.

Results: Plasma creatinine, the classical index of renal dysfunction in AKI was ischemia- and reperfusion time-dependently increased upon inception of reperfusion. Concomitantly, kidney injury and inflammation genes were upregulated early (<4hr) and remained elevated compared to shams throughout study duration. Upregulation of pro-apoptotic genes occurred as early as 4hr post-reperfusion, indicating the initiation of programmed cell death. Low-proteinic genes were upregulated 24-48hr post-reperfusion indicating onset of remodeling. The information content provided by each mRNA expression profile and clinical parameter was determined using a novel statistical framework to identify measures best able to distinguish disease state over 48hr of reperfusion.

Conclusions: This study demonstrated the temporal dynamics of response to renal IRI in rats. The early injury phase (~<4hr) was defined by mild, but significantly increased plasma creatinine indicating promptly reduced renal function along with upregulated injury response genes. Induction of pro-apoptotic and pro-fibrotic genes occurred during the late phase, in line with BRI-induced exacerbated renal failure. Our novel statistical framework identified “high information” genes/parameters that can serve as reliable, mechanistic indicators of AKI in future studies.

Funding: Commercial Support - Silver Creek Pharmaceuticals

PUB018
Antioxidant Ameliorates Pulmonary Renal Injury in an Experimental Model of COVID-19 Organ Failure
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Background: Since the outbreak and rapid global spread of COVID-19 multi-organ involvement has largely influenced prognosis and severe AKI has been an ominous clinical predictor with high mortality. The hyperinflammatory response of the body, associated with oxidative stress is a key player in mechanism of multiple organ failure.

Methods: In an experimental model of multiple organ failure of Covid 19 similar to human disease with single injection of Toxoid (TOX) rats were treated with antioxidant curbedol started daily 1wk pre-TOX-injection and continued for 1 wk post-TOX-injection. At 1-week post injection in both TOX+ Antioxidant and TOX groups lungs dry/wet weight ratios were measured to assess edema and lungs and kidneys from both group were analyzed for antioxidant enzyme activities including superoxide dismutase, glutathione peroxidase, catalase and oxidative stress. After sacrificing the animals, kidney and lung function were measured.

Results: Antioxidant treatment attenuated TOX induced lung and kidney injury and there was histopathological evidence of its beneficial effects. This was associated with decreased oxidative stress and increased activities of SOD and GSHPx in the lung and kidney.

Conclusions: In this experimental model that mimics human Covid 19 multiorgan failure, antioxidant improved survival, lung and kidney injury and also oxidative stress in the kidney. This suggest the beneficial effects of antioxidant as a kidney–lung protective strategy in patients with COVID-19.

PUB019
SRP14 Regulated Renal Tubular Apoptosis Induced by Ischemia-Reperfusion Injury via Interaction with RPS7
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Background: AKI could easily progress to CKD with increased incidence and mortality. Due to the complex pathogenesis, there is a lack of effective early warning to intervene in AKI.

Methods: We performed LFO proteomic analysis in HK, renal tubular epithelial cells after H/L molecule labeling and find SRP14 as a novel target to prevent AKI upon apoptosis in renal tubular epithelial cells. This study will further study the role and mechanism of SRP14 in regulating MDM2-p53 pathway in apoptosis of renal tubular epithelial cells in AKI. Then analyze the clinical correlation of SRP14 in AKI and explore the possibility of SRP14 as a potential therapeutic target for AKI.
Results: We identified that SRP14 could be involved in apoptosis of renal tubular epithelial cells due to oxidative stress. The inhibitors of SRP14 at or above 10 μM, could inhibit the cell proliferation through RPS7 in renal tubular epithelial cells to regulate apoptosis of renal tubular epithelial cells induced by IRI. The AUC value of SRP14 (AUC_{area} = 0.774) was close to serum creatinine (AUC = 0.796), suggesting the potential prognostic value of serum SRP14.

Conclusions: This study found that SRP14 regulated renal tubular apoptosis induced by ischemia reperfusion injury via interaction with RPS7 involving MDM2-p53 loop. This finding could provide some novel targets and ideas for AKI control in the future.

**PUB020**

A Case of Masked AKI

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Introduction: Despite wide recognition of pitfalls, changes in serum creatinine (Cr) and/or a decline in urine output (UO) remain the mainstay of AKI diagnosis. We report a patient whose extremely low Cr and preserved UO demonstrate the problem in reliance on these parameters.

Case Description: 57 F was admitted for respiratory failure due to COVID-19. Her management included tocilizumab, mechanical ventilation, vasopressors, ECMO, and antibiotics. On entry she weighed 54kg and Cr was 0.5 mg/dL. After 3 days, Cr nadir at 0.1 then gradually rose to 0.6 where it remained (day 15). Net fluid balance was 20L. By Cr, her eGFR was 110 ml/min/1.73m² but by cystatin C (CysC) it was 56. A biopsy confirmed microvasculitis.

Discussion: AKIN defines AKI by an absolute rise in Cr of 0.3mg/dl within 48 hrs, a relative increase in UO within 1 - 1.5x baseline in UO to <0.5x baseline/mL/kg/hr for at least 6 hrs. Cr is a flawed AKI biomarker due to uncertainty of the baseline, variability in rate of generation, and elimination by secretion and filtration. Cr generation falls rapidly with critical illness. The impact of volume expansion resulting in hyperfiltration or hemodilution are underrecognized. Antibiotics, diuretics, glucose, ketones and bilirubin may interfere with measurement. UO too is flawed since oliguria may occur in the absence of AKI due to antidiuretic hormone or conversely, UO may be maintained despite AKI due to osmotic diuresis, failure of tubular function or diuretic use. The choice of baseline Cr influences our patient’s diagnosis. If 0.5 is chosen, she fails to meet AKIN criteria, but based on nadir Cr, she has severe stage III AKI. AKI can also be demonstrated by adjusting Cr for volume expansion: measured Cr x (initial total body water [TBW] + cumulative fluid gain) / initial TBW = 1.4 in our patient. Our patient received tube feeds, suffered hyperglycemia resulting in high osmolar load driving an osmotic diuresis. Also, periodic furosemide was given to mitigate her positive fluid balance. Below normal Cr is generally seen in myopathies, cirrhosis or with drug interference, but hyperfiltration can occur with volume expansion contributing to low Cr. In this case, we believe a baseline small muscle mass, critical illness sarcopenia, and marked volume expansion conspired to mask significant AKI in our patient. Documentation of AKI by measuring CysC led to adjustments in drug dosing.

**PUB021**

Online Medical Education Significantly Improves Nephrologists’ Knowledge and Confidence for Intravenous (IV) Iron Use in Patients with Iron-Deficiency Anemia (IDA) in CKD

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Background: Purpose: To determine if online medical education for nephrologists (Neph) could improve their evidence-based knowledge and confidence to use IV iron to treat IDA in non-dialysis (ND) and dialysis dependent CKD patients

Methods: Participants completed a 30-item questionnaire plus confidence assessment before and after watching a 30-minute online video series of 4 expert interviews with slides. A matched pair design was used pre-/post-assessment, with scores compared to assess changes in the proportion of correct responses. A chi-square test assessed statistical significance at the P <.05 level. Launch 01/29/20; data through 04/13/20. Total Neph learners (n=572), 15% in dialysis.

Results: At baseline, 20% of Neph (n=114) answered all 3 questions correctly, increasing to 61% (P < .001) post-assessment. An average of 61% of all responses, correct pre-assessment increasing to 83% post-assessment, were correct after viewing the slides. A matched pair design was used pre-/post-assessment, with scores compared to assess changes in the proportion of correct responses. A chi-square test assessed statistical significance at the P <.05 level. Launch 01/29/20; data through 04/13/20. Total Neph learners (n=572), 15% in dialysis.

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Conclusions: The error distribution of the predictions is such that they 1) may be clinically meaningful as part of an effort to better control PTH, while potentially reducing excessive up-titration of etelcalcetide (and thus cost) and 2) may serve as a benchmark for future modeling efforts. Limitations include: a relatively small data set which precluded the use of other models (e.g., recurrent neural networks) and the dialysis program’s strict criteria for receiving etelcalcetide which led to a study population with significantly higher PTH values than may be encountered in the general dialysis population.

Funding: Private Foundation Support

**PUB023**

A Rare Case of Staghorn Calculi Complicated by Bilateral Xanthogranulomatous Pyelonephritis

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Introduction: Staghorn calculi are usually unilateral and typically occur in women. Chronic obstruction and infection of staghorn calculi can cause xanthogranulomatous pyelonephritis (XGP), a rare destructive granulomatous process of renal parenchyma. We describe a case of bilateral staghorn calculi in a man complicated with XGP and worsening renal function.

Case Description: A 64-year-old man with bilateral staghorn calculi and chronic kidney disease (CKD) stage 4 was admitted for fatigue and worsening renal function. He tested positive for COVID-19 by nucleic acid-based test. Serum creatinine increased from 3.5 (2 months ago) to 6.2 mg/dL. Renal ultrasound showed dilated left calyces and large shadowing calculi without hydronephrosis. History was notable for persistently alkaline urine (pH 6.5), 100% carbonate apatite (dahllite) on stone analysis, and urinary tract infection with Proteus mirabilis. CT imaging revealed bilateral staghorn calculi with “bear paw” signs (left > right), a typical appearance of XGP [Figure]. Compared to a CT scan completed 10 months ago, the left kidney was enlarged with greater low-attenuating spaces indicating worsened XGP; the right kidney decreased in size with less stone burden corresponding to the right percutaneous nephrolithotomy performed 7 months prior. AKI was thought to be related to COVID-19, and surgical intervention was deemed unnecessary. Bilateral XGP likely increased his risk of AKI and hampered renal recovery, and he was subsequently initiated on hemodialysis.

Discussion: In this rare case of staghorn calculi progressed to bilateral XGP, we observed the detrimental effects of staghorn calculi on the kidneys. More research on staghorn calculi is needed to improve the high morbidity and mortality associated with this disease.
Factors Associated with Serum Concentrations of 25-Hydroxyvitamin D (25D) and 1,25-Dihydroxyvitamin D (1,25D) in Stable Hemodialysis Patients

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**Background:** Serum 1,25D, an active form synthesized from 25D, is present in CKD patients (Ishimura, Kidney Int 1999; Wolf, Kidney Int 2007). However, factors associated with 1,25D and 25D are not well known. The aim of the present study is to examine the relationship between 1,25D, 25D and clinical parameters in hemodialysis patients.

**Methods:** Serum 1,25D and 25D were measured by a RIA2-Ab method and an ECLIA method, respectively, in 108 stable maintenance hemodialysis patients (72±10 years, 64 males, hemodialysis duration: 6.9±7.5 years, 45 diabetics) from December 2019 to February 2020, i.e., in the winter.

**Results:** Serum 1,25D were 14.6±8.0 pg/mL, demonstrating that 77 patients showed values less than reference ranges of healthy subjects (30-60 pg/mL). Serum 25D were 12.0±4.8 ng/mL, demonstrating that 101 patients showed vitamin D deficiency of <20 ng/mL. There was no significant correlation between serum 1,25D and 25D in maintenance hemodialysis patients in the present study, although 1,25D and 25D had been reported to show significant, positive correlations both in pre-dialysis CKD patients (Ishimura, Kidney Int 1999) and in incident dialysis patients (Wolf, Kidney Int 2007). There were no significant correlations between 25D and clinical parameters. However, there were significant, negative correlations between 1,25D and intact PTH (r = 0.344, p < 0.001) and between 1,25D and ALP (r = 0.309, p < 0.02), although no significant correlations were seen between 25D and other parameters, such as Ca and P. In multiple regression analyses, 1,25D was significantly, independently associated with intact PTH and with ALP after adjustments of several clinical parameters (R² = 0.345, p < 0.001; R² = 0.256, p < 0.001, respectively).

**Conclusions:** In maintenance hemodialysis patients, all patients showed hypovitaminosis D, in terms of serum 25D. 1,25D, even in low serum levels, correlated significantly and negatively with intact PTH and ALP. These results indicated that even low levels of serum active vitamin D, 1,25D, affect the status of CKD-MBD. The results may further indicate that the metabolism of vitamin D should be considered in the pathogenesis and treatment of CKD-MBD.

A Case of Parathyroid Hyperplasia with Single Explosive Growth

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**Introduction:** Exploration of parathyroid hyperplasia with single explosive growth

**Case Description:** A 46-YO Asian man with ESRD has been undergoing regular hemodialysis for 20 years due to glomerulonephritis. The patient has had bone pain and joint pain for 10 years. In 2018, the measurement of his serum iPTH was elevated and the value was over 1000pg/ml (no data about serum calcium and phosphate levels), and he didn’t have regular treatment. Serum calcium, phosphate and alkaliphosphatase were 2.46mmol/L, 2.4mmol/L and 380U/L, respectively, and serum iPTH was 2205pg/ml in this admission examination. The ultrasonography showed two hyperplastic parathyroid glands. They are 13*5mm on the right lower side of thyroid gland and 43*18mm on the left lower side. Parathyroid nuclide scanning showed three hyperplastic parathyroid glands. That is located in bilateral hypothyroidism and left upper sternum, consider parathyroid development, Total parathyroidectomy was successfully carried out with the general anesthesia in May 15, 2020. Four parathyroids were excised, which were 0.6*0.5cm in the upper left, 4.9*3.0cm in the lower left, 0.8*0.5cm in the upper right, and 1.5*1.0cm in the lower right (the maximum diameter and length). Pathological diagnosis showed that there was parathyroid nodular hyperplasia in the upper left, lower left, upper right and lower right. PTH values a week after surgery was less than 1.2pg/ml, serum calcium 2.13mmol/L, phosphate was 0.85mmol/L. Patient bone pain disappeared. Patient has been discharged and will be close followed up.

**Discussion:** Total parathyroidectomy is effective in uremic patients with secondary hyperparathyroidism which has explosive hyperplasia with parathyroid glands.
Conclusions: Our results show that in subjects with end-stage kidney disease a meal with high phosphorus content has only a negligible effect on plasma phosphate compared to a meal with low phosphorus content. Thus, large increases in plasma phosphate cannot be accounted for by a high intake of phosphorus in the hours prior to blood sampling.

Funding: Private Foundation Support

PUB027

A Rare Case of Severe Tertiary Hyperparathyroidism in a Patient with ESRD

Introduction: Refractory tertiary hyperparathyroidism is defined as severe, persistent & progressive elevation of PTH which cannot be lowered by medical management & associated hypercalcemia, hyperphosphatemia, bone/joint pain and/or fracture, extra skeletal calcification, calcification & pruritis.

Case Description: A 43-year-old undocumented Hispanic male with PMH of uncontrolled DM, HTN, ESRD (HDX 3/week) & persistent tertiary hyperparathyroidism (on Cinacalcet) presented with multiple bone fractures, bilateral leg weakness, soft tissue calcification & severe renal osteodystrophy. Significant lab findings included PTH 3518pg/mL, phosph 6.7mg/dL, Ca 10.9mg/dL & ak phosph 804 IU/L were all above goal. X-ray of lower ext. revealed diffuse osteopenia with chronic fracture in distal fibula, midfoot, distal tibia & dislocation of talonavicular joint as well as extensive atherosclerotic vascular calcification & multiple punctate soft tissue calcification. CT spine reported demineralized appearance of vertebral bodies & sacram, wide erosion of sacroiliac joints bilaterally & calcified atherosclerotic disease of abdominal aorta & bilateral interstitial arteries. Patient was diagnosed as refractory tertiary hyperparathyroidism & treated with doxercalciferol, phosphate binders & advised for parathyroidectomy on multiple previous encounters but was unable to do due to health care access issue.

Discussion: Parathyroidecmy which has mortality benefit is indicated in the setting of severe & sustained PTH value above 800-1000 pg/mL, refractory to medical treatment & associated to others indicators like hypercalcemia, refractory hyperphosphatemia, bone pain/fractures & our case has majority of the above mentioned indications. Various & associated to others indicators like hypercalcemia, refractory hyperphosphatemia, bone pain/fractures & our case has majority of the above mentioned indications. Various factors including immigration, insurance issues and post-operative intensive care requirements complicated the potential for parathyroidecmy in this patient. Although with advancement of medical field, the symptoms of severe hyperparathyroidism are rarely observed but the manifestations are real if not treated on time as per guideline recommendations.

Figures showing pathological fractures & muscular atrophy

PUB028

Progression of CKD Stage G3a Among African Americans
Yelvzaveta Pryavzanvuy, Ishu Puri, Jie Ouyang, Ernie Yap. SUNY Downstate Health Sciences University, Brooklyn, NY.

Background: Chronic kidney disease (CKD) stage 3 represents the most of all CKD patients. Stage G3 is divided into G3a (GFR 45–59 ml/min/1.73m²) and G3b (30–44 ml/min/1.73 m²) based on findings that showed differential kidney outcomes. Stage G3a has several unresolved paradigms. Firstly, it does not always imply kidney damage. It is recommended that cystatin C be used to confirm in people without manifestation of kidney damage to avoid over-diagnosis. Secondly, it primarily comprises of the elderly, and most will not progress to advanced CKD before succumbing to other causes of death. Thirdly, in people with manifestations of kidney damage, stage G3a becomes an important predictor of disease progression. The influence of ethnicity on eGFR in delineating these aberrancies in CKD G3a is unclear. In this study, we sought to analyze the progression of CKD G3a patients in a predominantly African American cohort.

Methods: We performed retrospective chart reviews of patients at our CKD clinic. GFR was estimated based on the MDRD formula. Continuous variables are presented as mean±SD. Comparison of continuous variables were performed using one-way ANOVA. Univariate and age and body mass index (BMI)-adjustment analyses was performed by Cox proportional hazards model. IBM SPSS v. 25 was used.

Results: 319 patients were analyzed. Median follow-up was 79.7 months (IQR: 93.1-259). 29% of patients had at least 2 years follow-up. In these patients, the mean annual GFR declines were 4.4±3.8, 2.3±2.1, 1.6±2.7 and 1±4±2.2 ml/min/1.73 m² for stages G2, G3a, G3b and G4 respectively (p<0.001). Univariate Cox proportional hazard analysis showed that CKD G3a, Gb and G4 had relative risks (RR) of progression to G5 of 1.0 (95% CI: 0.5-2.2, p=0.98), 3.6 (1.6-9.0, 0.003) and 19.4 (8.7-43.0; <0.005) respectively. When adjusted for age and BMI, risks of progression to G5 were: RR=1.3 (10.6-3.0; 0.5), 5.8 (2.3-14.7; <0.005) and 29.6 (12.1-72.2; <0.005) for CKD G3a, G3b and G4 respectively.

Conclusions: In our cohort of predominant African Americans, CKD G3a does not predict disease progression.

PUB029

Is Routine Screening with Serum and Urine Protein Electrophoresis in Evaluation of CKD Justified?
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Background: Current guidelines for the evaluation of chronic kidney disease (CKD) in Canada do not include routine screening with serum and urine protein electrophoresis (SPEP and UPEP). Previous studies suggest that M-spike is more common in CKD compared to the general population (1,2). This study aims to examine the use and cost of screening SPEP and UPEP in the evaluation of CKD pts.

Methods: This is a retrospective study of 149 sequential incident pts referred to a teaching General Nephrology clinic for evaluation of CKD between Jan and Nov, 2018. The SPEP and UPEP testing frequency, and proportion with M-spike were obtained by chart review, along with the routinely performed clinical, blood and urines tests, imaging, as well as reports of any Hematology consultation, renal and bone marrow biopsies performed.

Results: Screening SPEP and UPEP tests were done in 104 (70 %) pts, mean age 72.2 yrs, 42 (40 %) female, 52 (50 %) DM, and Caucasian majority. M-spike was present in 11 pts (10.6 %, 96 % C1 5.4 – 18.8 %), 2 IgG-k, 5 IgG-l, 1 IgA-k, 2 L C-k, and 1 L C-λ. Eight had Hematology consultation, 6 had bone marrow biopsy, and 3 had renal biopsy. Diagnoses were 7 MGUS, 2 myeloma (MM), 1 amyloidoid (AL) and 1 both MM + AL. There were no differences in clinical, demographic, CBC, serum calcium, urine albumin to creatinine ratio, urinalysis, or renal imaging among pts with and without M-spike but sample size did not allow multivariate analysis.

Conclusions: In this study, the prevalence of M-spike in CKD is higher than has been reported in the literature in the general population (5.4 - 18.8 % vs. 3 - 4 %). The cost for testing and interpretation fees for SPEP and UPEP are CDN $25.53 and $32.99 respectively, with detection cost per M-spike of $1.53; 2.52 per MGUS and $1.52 per myeloma or amyloid. These costs are consistent with previous studies controlled for inflation (1,2). Routine screening with SPEP and UPEP in the evaluation of CKD may be useful and cost-effective. Larger prospective studies are needed to identify subgroups with higher likelihood of M-spike to target testing. 1. AHwisch et al. J Am Soc Nephrol 2003 14:295A. 2. Chew et al. Am J Kidney Dis. 1999 Jul;34(1):135-9.

PUB030

Is Yakima County a CKDu Hot Spot? A Case Series of CKD in Latino Agriculture Workers
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Introduction: The first case series of chronic kidney disease of unknown etiology (CKDu) was described in 2002 in sugar cane cutters in El Salvador. This unique diagnosis is involved in agriculture. The majority of labor-intensive agriculture jobs are performed by Latino workers, drawing attention to Yakima as an unexpected hotspot for CKDu.

Background: Heat in Yakima, Washington, an agricultural community in the Pacific Northwest, has had the highest average temperature increase in the Pacific Northwest at 3°F over environments. Yakima, Washington, an agricultural community in the Pacific Northwest, has had the highest average temperature increase in the Pacific Northwest at 3°F over the past 30 years. Average summer temperatures for July and August are 88°F and 89°F, respectively. Yakima County is 49.5% Latino and 27.5% (29,331) of the total population is involved in agriculture. The majority of labor-intensive agriculture jobs are performed by Latino workers, drawing attention to Yakima as an unexpected hotspot for CKDu.

Case Description: We describe three Latino agricultural workers seen by a nephrologist in an MHD clinic in a local free clinic in the span of 8 months. The ages ranged from 58-68 and all worked ten years or more for local farms. Each patient had at least Stage 3 CKD (<60 ml/min/m²), hypertension, hyperuricemia, without proteinuria or albuminuria; there was no history of diabetes mellitus. Renal ultrasounds were unremarkable. Treatment was focused on controlling hypertension and hyperuricemia, however little disease modifying interventions are available.

Discussion: These cases, collected over a relatively short period of time, demonstrate that CKDu is more common than previously thought amongst agricultural workers in Yakima, Washington.
northern regions. At 46.6021° N latitude, Yakima is closer to the North Pole than other areas where CKDs have been documented. With increasing global temperatures, agricultural workers are on the frontline of climate-related health issues. Further study is necessary to develop awareness, earlier risk factor detection, and effective interventions for these essential and vulnerable members of our communities.

**PUB031**

The Correlation Among Management of the Comorbidities and Progression of Renal Dysfunction or Adverse Events for CKD Patients

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**Background:** It is well established that several factors including anemia, hypertension, hyperuricemia, metabolic acidosis, and CKD-MBD are associated with progression of CKD or adverse events of these patients. However, the significant factors which associated with progression of CKD or adverse events under the condition of appropriate control which according to guidelines have not been cleared.

**Methods:** The study was an observational study in a single center for a period of 3 years. In 88 patients with various stages of CKD (not on dialysis) who were treated by nephrologists, Hb, ferritin, iron and albumin and high sensitive C reactive protein (hsCRP), β2microglobulin (MG), HCO3 - and intact-parathyroid hormone (iPTH), in addition to urinary sodium, potassium, calcium, phosphorus protein, and β2MG levels, were measured. All patients were treated according to the clinical practice guideline for CKD. A time-dependent Cox hazard model was applied to evaluate the association between clinical parameters and adverse events.

**Results:** In multiple regression analysis, baseline of lower Hb (β=0.497, P=0.001) and vitamin D 125 (β=0.258, P=0.001) and high int-PTH (β=0.34, P=0.001), urinary phosphorus (β=0.328, P=0.001), urinary β2MG (β=0.225, P=0.031) and urinary protein (β=0.280, P=0.002) levels were selected as significant predictors of decline of estimated glomerular filtration rate (eGFR) or 1/creatinine(τς) at the end of the study. In the Cox hazard model, low calcium (HR: 0.37, P=0.026), high phosphate (HR:5.90, P=0.001), low 125 vitamin D (HR: 0.94, P=0.013), high int-PTH (HR:1.02, P=0.001) level, use of a phosphate binder (HR: 4.95, P=0.012), and use of vitamin D analogs (HR:3.75, P=0.014) are selected as risks for adverse event including initiation of dialysis.

**Conclusions:** In this study, we found that among several factors, anemia and CKD-MBD related factors (phosphate, calcium, vitamin D, int-PTH) were selected as significant predictors for renal dysfunction. Furthermore, although phosphate binder or vitamin D analogs were administered appropriately, CKD-MBD factors were associated with progression initiation or adverse events of these patients. From these results, we presumed that the early intervention or strict control for CKD-MBD factors might attenuate the risk for adverse events of CKD patients.

**PUB032**

Association of Anion Gap with the Risk of CKD Progression

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**Background:** Increased anion gap is a marker of acid retention most reflected in patients with CKD. This study’s objective is to assess whether a higher anion gap is a risk factor for CKD progression.

**Methods:** This retrospective cohort study assessed 4311 participants with CKD stage 2 to 4, who enrolled in a chronic renal insufficiency cohort study. Three types of anion gap were used as exposures, traditional anion gap (AG1), Albumin corrected anion gap(AG2), full anion gap(AG3). Multivariable adjusted Cox proportional hazard models were built using the lowest tertile as the reference of all three anion gaps for the composite outcome (50% decline in eGFR or ESRD) and ESRD. Models were adjusted for relevant covariates and baseline eGFR.

**Results:** This study included 4311 participants [mean (SD) age, 60.48(10.21) years; 1788 (43.28)% female]. During 2667.46 person years of follow up, 805 participants reached ESRD and 1138 participants reached a composite outcome of a 50% decline in GFR or ESRD. In a multivariable adjusted model each SD increase in AG1, AG2 and AG3 were independently associated with 10%, 10% and 12% increased risk for CKD progression: hazard ratio (HR) 1.10 ; 95% CI (1.01-1.21), HR 1.10 ; 95% CI (1.02-1.20), HR 1.12 ,95% CI (1.03-1.21), however each SD increase in AG2 and AG3 was independently associated with a 11% increased risk for ESRD [HR 1.11; 95% CI (1.02-1.21), HR 1.11; 95% CI (1.02-1.22)]. In multivariable adjusted models compared to tertile 1 (<10) those in tertile 3 (>12) had a 33% and 41% higher risk for CKD progression [HR 1.33;95% CI (1.09-1.62), HR 1.41,95% CI (1.16-1.71)] and 32% and 60% higher risk for ESRD [HR 1.32; 95% CI (1.06-1.64), HR 1.60,95% %CI (1.28-2.01)].

**Conclusions:** Higher albumin corrected and full anion gap may be a risk factor for CKD progression and ESRD.

**PUB033**

Childhood Risk Factors for Adulthul CKD

**Michal Stern Zimmer, Asaf Vivante. Sheba medical center, Ramat Gan, Israel.

**Background:** Chronic Kidney Disease (CKD) is a demographic health challenge, affecting ~ as much as 8 to 18% of the world population. Identifying childhood risk factors for future CKD may help clinicians make early diagnoses facilitating complication monitoring and initiation of preventive interventions for CKD and its accompanying comorbidities. We aim to describe these childhood risk factors that may predict development of overt kidney disease later in life.

**Methods:** PubMed publications (January 2009 - January 2019) were searched for publications by using terms and synonyms for chronic kidney disease (CKD) and specific childhood kidney related risk factors. We also manually searched the reference lists of key articles, reviews and meta-analyses.

**Results:** There are a multitude of childhood risk factors associated with future onset and progression of CKD. These risk factors can be grouped into five categories: genetic factors (e.g. monogenic or risk alleles), perinatal factors (e.g. low birth weight and prematurity), childhood kidney diseases (e.g. congenital anomalies, pyelonephritis, glomerular diseases and acute kidney injury), childhood onset of chronic conditions (e.g. cancer, diabetes, hypertension, dyslipidemia and obesity) and different lifestyle factors (e.g. physical activity and diet).

**Conclusions:** The available published information suggests that the lifelong risk for CKD can be attributed to multiple factors which appear already during childhood. However, results are conflicting on the effects of childhood physical activity, diet and dyslipidemia on future renal function. On the other hand, there is consistent evidence to support close monitoring for high risk populations.
PUB034

Therapeutic Interventions to Assess Outcomes and Disparities in Chronic Kidney Disease Among Veterans (TRI-CKD)

Keichi Sumida,1 Ankur A. Dashputre,1 Praveen Kumar Potukuchi,1 Fridjof Thomas,1 Jun Ling Lu,1 Miklos Z. Molnar,1 Cachet Wenziger,1 Elani Streja,1 Kamyar Kalantar-Zadeh,2 Csaba P. Kovesity3 The University of Tennessee Health Science Center, Memphis, TN; 2University of California Irvine, Irvine, CA.

Background: There continues to be a large unmet need in the management of CKD, due in part to a lack of effective intervention strategies to prevent CKD progression or decrease morbidity/mortality in patients with CKD. There is also a lack of race-specific application of clinical interventions, despite evidence suggesting racial differences in response to various therapies. High quality, large observational studies are essential to provide preliminary results in support of future clinical trials, and to offer suggestive, widely applicable evidence to inform clinical practice in this population when clinical trials are not feasible.

Methods: We established a cohort of 3,565,367 individuals with stable eGFR >60 mL/min/1.73m² during October 1, 2004-September 30, 2006, using an algorithm based on repeated serum creatinine measurements. Data about patients’ demographics, socioeconomic characteristics, comorbid conditions, administered medications, labs, vital signs, vital status, incident CKD and ESRD outcomes were obtained from various VA databases, from Centers for Medicare & Medicaid Services, and from USRDS.

Results: The mean (SD) age of the cohort is 59 (14) years; 93% are male; 16% are African-American; and 24% are diabetic. The mean baseline eGFR is 84 mL/min/1.73m². Individuals are followed longitudinally for up to 13 years. Overall, the crude rates of all-cause death and ESRD are 51 and 0.63 per 1000-patient-years (Figure).

Conclusions: We established a large nationwide cohort of US veterans with normal eGFR. Studies from this cohort will generate a wealth of information to examine therapeutic interventions used to treat various conditions associated with poor outcomes in patients with all levels of kidney function, potentially providing significant clinical, social, and policy implications for the care of US veterans and also for patients with kidney diseases in general.

Funding: Veterans Affairs Support

PUB035

Treatment Response in Patients with Uncontrolled Gout Co-Treated with Pegloticase and Leflunomide

Karmir R. Marsi,1 Kevin W. Winterling,2 Brian LaMoreaux,2 1Ben Secours Rheumatology Center, Richmond, VA; 2Horizon Therapeutics, Lake Forest, IL.

Background: Many patients with CKD develop gout with a prevalence ≤36% in later stage disease. Though oral urate-lowering therapies are used in CKD patients, some may not respond to or cannot tolerate them. Uncontrolled (refractory) gout can be treated with pegloticase (PEGylated uricase enzyme), however, anti-drug antibodies (ADAs) can cause loss of therapeutic efficacy. Compared with pegloticase alone, recent case series show markedly higher response rates with methotrexate/pegloticase co-therapy (42% vs. 80-100%). However, certain considerations with methotrexate use including significant side effects and hepatotoxicity may not be as restricting with leflunomide. This study examined the effects of co-therapy in patients with all levels of kidney function, potentially providing significant clinical, social, and policy implications for the care of US veterans and also for patients with kidney diseases in general.

Funding: Veterans Affairs Support

PUB036

A Double-Blind, Randomized, Placebo-Controlled with an Open-Label Rollover Extension Phase 2/3 Clinical Trial to Evaluate Safety and Efficacy of US-APR2020 in Subjects with CKD Stage IV

Narataram Ranganathan1, Usha N. Vyas,1 Pari Ranganathan,1 Anthony Irvin,1 Alan D. Weinberg,2 1Kibow Biotech, Newtown Square, PA; 2Mount Sinai Health System, New York, NY.

Background: CKD patients experience poor quality of life due to high levels of uric acid toxins in the blood. Renalyte™, a Pro/Prebiotic dietary supplement has been used in the market since 2010. It is proven to reduce several uric acid toxins in 3 pilot clinical trials with no adverse outcomes. The product is now awaiting FDA-IND approval for a drug trial. This will be a large scale 12-month RCT to validate US-APR2020 as a Live Bio-Therapeutic drug product (LBP) under CBER guidelines.

Methods: (A) 6-month randomized placebo-controlled parallel design in an outpatient setting followed by (B) 6 month Open-Label Rollover Extension which will enroll all patients from study A.

Results: Study end points: As compared to placebo; Primary: 1. Less than 10% adverse event in the study population. 2. Arrest the decline of gFR as per NKF-USFDA guidelines. Secondary: 1: Improvement in any of the basic blood uric acid metabolic markers. 2: Improvement in any of the disease-related markers (K/Na, serum albumin, hs-CRP, BUN, creatinine).

Conclusions: This is the first-ever clinical trial proposed using Pre/probiotics US-APR2020 as a Live Bio-Therapeutic drug product (LBP) for CKD IV patients. Being noninvasive the intervention avoids any possible infection. The addition of US-APR2020 with standard care of therapy may possess excellent potential towards CKD applications worldwide. Formal IND process under CBER/US FDA in progress. Seriously interested clinical PI’s please contact: rangan@kibowbiotech.com

PUB037

Effects of Tolvaptan on Long-Term Prognosis in CKD Patients

Kazuhito Fukushima, Yuko Shibata, Shinya Kaname. Kyorin University School of Medicine, department of Nephrology and Rheumatology Kyorin Daigaku, Mitaka, Japan.

Background: Tolvaptan is a novel diuretic agent used for the treatment of intractable edema and SIAHH in Japan, as well as polycystic kidney disease. Purpose: To determine whether tolvaptan prevent worsening renal function or prolongs the time to dialysis induction in pre-dialysis CKD patients.

Methods: A retrospective observational study (case-control study). Eligible patients were CKD patients treated with tolvaptan more than 30 days at our hospital between 2012 and 2018. The control patients were selected from CKD patients without the use of tolvaptan at our hospital that matched base line characteristics using the generated propensity score. The endpoints were a decrease in eGFR of more than 30%, introduction of dialysis, and death. The logistic regression analysis was performed on the indicator of the presence or absence of tolvaptan. Survival analysis was analyzed by the Kaplan-Meier method and tested with log rank, generalized Wilcoxon, and Barone-Ware. The software for the statistics was IBM® SPSS® Statistics ver. 24.

Results: A total of 106 patients received tolvaptan during the study period, including 52 who met the study criteria. The median age was 65 years, the mean duration of treatment was 533 days, and the dose was 8.16 mg/day. Of these, there were 15 cases of diabetes and 6 cases of nephrosis. The normal patient group matched to these cases was selected from 63209 cases. Tolvaptan was administered after hospitalization, with an 82.1% increase in urine output and a weight of -4.2% at discharge. The tolvaptan combination group had a significant prolongation of days to endpoint: control group (746.0 ± 9.013) vs Tolvaptan group (1076.3 ± 95.71, p = 0.0001, CI 749-1012).

Conclusions: Tolvaptan is expected to improve prognosis because of its ability to improve edema even in advanced CKD cases. Tolvaptan has been shown to improve edema in advanced CKD as well as inhibit the deterioration of renal function with long-term use.
Serum Calcium Changes and Renal Function: A Dual Path Track
Julia Lauria, Tiago E. Costa, Giovanni G. Nascimento Santos, Rosa M. Moyes, Rosilene M. Elias. Universidade de Sao Paulo Hospital das Clinicas, Sao Paulo, Brazil.

Background: Although hypercalcemia is associated with an impairment of renal function, the literature is scarce in demonstrating this relationship in clinical practice. We hypothesized that fluctuations in serum total calcium (tCa) may impact renal function in patients with chronic kidney disease (CKD).

Methods: This is a retrospective study which enrolled 148 patients with at least 2 clinical appointments with concomitant tCa and estimated glomerular filtration rate (eGFR) measurement in the period between January-2017 and December-2019. We collected demographic, clinical, and biochemical data. Up to 3 consecutive measurements were analyzed.

Results: Patients were mostly Caucasian women, aging 66 ± 15 years. Mean eGFR was 45.1 ml/min/1.73m². Hyperparathyroidism (parathyroid hormone > 65 pg/ml) was associated with a 2.8-fold increased risk for hypercalcemia (p=0.030). There was a non-linear relationship between change in tCa and change in eGFR, so that when tCa increased above the normal limit, there was a reduction in eGFR. Patients with hyperparathyroidism seem to present a significant lower risk of impairment in eGFR in the consecutive measurements when compared to other causes of hypercalcemia.

Conclusions: The development of hypercalcemia in patients with CKD is associated with a deterioration of renal function. Therefore, the strict control of serum calcium is advised in these patients.

The Tri-POCUS Approach for Assessment of Volume Status in Critically Ill Patients with COVID-19
Abhilash Koratala,1 Claudio Ronco,2 Olanrewaju A. Olayoe,1 Amir Kazory,1
1University of Florida, Gainesville, FL; 2Universita degli Studi di Padova, Padova, Italy; 3Medical College of Wisconsin, Milwaukee, WI.

Background: The volume status of patients with coronavirus disease 2019 (COVID-19) is dynamic and can range from severe hypovolemia (on initial presentation) to overt hypervolemia (after fluid resuscitation) due to its distinct clinical features such as cytokine storm. While lung point-of-care ultrasound (POCUS) is established as an invaluable bedside tool in assessment of volume status of the critically-ill, its use in this setting is limited by expanding lung infiltrates and a tendency for acute respiratory distress syndrome (ARDS).

Methods: We developed a combinational bedside ultrasound program to overcome the limitations of the individual methods of POCUS and provide a more precise evaluation of the volume status of critically ill patients with COVID-19. The Tri-POCUS approach represents concurrent bedside assessment of the lungs, heart (focused cardiac ultrasound [FoCUS]), and the venous system (blood flow pattern in the hepatic, portal and intra-renal veins) (Figure 1).

Results: In patients with COVID-19, distinguishing ARDS from cardiogenic pulmonary edema by lung POCUS alone is challenging due to several overlapping features. FoCUS allows for both static measures of preload as well as dynamic assessment (e.g. volume responsiveness to passive leg raise maneuver). Evaluation of blood flow pattern in the hepatic, portal and intra-renal veins not only can gauge fluid status but it also allows for direct assessment of the congestive state in end organs hence monitoring response to therapy.

Conclusions: The Tri-POCUS program is an extension of our previously published work focused on renal POCUS curriculum. The components of this combinational approach have been selected based on their ability to cover the limitations of each individual method and provide a synergistic effect, especially in clinical settings such as COVID-19 where there is a tendency for rapidly changing volume status confounded by distracting features (e.g. expanding lung lesions).

New-Onset Nephrotic Syndrome in a Child Associated with COVID-19 Infection
Siddharth A. Shah. University of Louisville, Louisville, KY.

Introduction: The COVID-19 outbreak has turned into worldwide public health emergency. The renal histo-pathological features of acute tubular necrosis or thrombotic microangiopathy are reported in adults previously with severe COVID-19 infections. In children, the renal manifestations associated with COVID-19 infection are not widely reported. Here, we describe a case report of a child with new onset nephrotic syndrome associated with COVID-19 infection.

Case Description: 8-year-old boy with no previous significant medical history presented with bilateral eye and facial swelling soon after his parents were diagnosed with COVID-19 infection. He had diarrhea but no fever or shortness of breath. One week after onset of swelling, the boy was also tested positive for COVID-19 infection. Based on clinical findings of significant proteinuria (Urine protein and creatinine ratio of 11.4), hyperalbuminemia (serum albumin of 2 g/dL) and hypercholesterolemia (Total Cholesterol of 384 mg/dL), he was diagnosed having nephrotic syndrome. He responded well to standard-dose prednisone treatment for nephrotic syndrome. In one week of starting prednisone treatment, he went into clinical remission. Lymphopenia continued to be present for 2 weeks after onset of symptoms. There were no complications related to clot formation or secondary infections with this presentation.

Discussion: This is the first case report to our knowledge of pediatric patient presenting with new-onset nephrotic syndrome associated with COVID-19 infection. Although, the burden of disease from COVID-19 is less severe in children, they can present with immune system related kidney disease like nephrotic syndrome. The patient responded well to standard-dose prednisone treatment used typically for new onset nephrotic syndrome.

Recurrent Arteriovenous Graft Thrombosis in COVID-19
Namratra Singhania,1 Saurabh Bansal,2 Girish Singhania.1 1CHI Saint Vincent Health System, Little Rock, AR; 2Mount Carmel East, Columbus, OH; 1University of Illinois at Peoria, Peoria, IL.

Introduction: COVID-19 has been associated with increased risk of hypercoagulability. We report a case of COVID-19-associated coagulopathy leading to recurrent arteriovenous (AV) graft thrombosis in an end-stage renal dialysis (ESRD) patient.

Case Description: 84 yo African American female with ESRD on dialysis via lower extremity AV graft, diabetes and atrial fibrillation on warfarin who was diagnosed with COVID-19 came back again 1 week later and was admitted due to hypoxemia. COVID-19 PCR was again positive. INR was 1.4, D-dimer 3.28 mcg/mL, platelet count 114K/mm², mildly prolonged PT, aPTT. She had elevated venous pressures during dialysis. Doppler suggested AV graft thrombosis. Heparin drip was started. Angiography and intravascular ultrasound (IVUS) showed thrombosed AV graft. (Figure 1a,1b) Thrombectomy was successful (Figure 1c,1d) with uneventful hemodialysis afterwards. She was discharged. Next day, she came back again with diarrhea. Coronavirus PCR was still positive. INR was 1.9. She again had high venous pressures. Doppler found recurrent thrombosis. Heparin drip was started. Vascular surgery placed dialysis catheter and held thrombectomy till her coronavirus PCR turns negative.

Discussion: Incidence of venous thromboembolism (VTE) can be as high as 58% in patients with COVID-19. All categories of ‘Virchow’s triad’ are involved, endothelial injury (increased cytokines and complements), stasis (immobilization) and hypercoagulable state (changes in prothrombotic factors). Risk factors are males, obesity, heart disease, hypertension, diabetes and ESRD. High D-dimer, mildly prolonged PT, aPTT and thrombocytopenia are common. Full-dose anticoagulation is recommended for documented VTE.
PUB042

Manage of a Peritoneal Dialysis Unit During the COVID-19 Pandemic

Background: Peritoneal Dialysis (PD) patients are special, as they are mainly independent in a “life-support technique” but susceptible to various potential complications related. This pandemic brought new challenges and PD Units had to be reorganized considering their specific population, human and material resources. We aimed to understand the impact of our restructuration and discuss some lessons learned.

Methods: We retrospectively reviewed the activity and intercurrences at our Unit during the COVID-19 state of emergency declared by our Government, from 19th March to 2nd May (6 weeks), and compared it to the correspondent past two years (table 1). In a normal period, most of our patients are evaluated in a monthly basis. Simple descriptive and Student’s paired T-test analysis were performed.

Results: We managed 34 patients in the correspondent period of 2018, 36 in 2019 and 38 in 2020. Clinical appointments in this 2020 period were realized by phone. Necessary dislocations to the Unit in 2020 included peritonitis, exit-site infections and catheter malfunctioning. No dropouts occurred. There were no positive cases of COVID-19. Student’s paired T-test analysis between 2020 and 2019, plus 2020 and 2018, showed no statistically significant differences in every evaluated phenomenon (except for non-presenter appointments; this discrepancy is justified by the Unit’s dynamic, without clinical implications).

Conclusions: Despite the restructuring, we were able to provide more teleassistance and the mean of complications/hospital admissions weren’t statistically worse. Some activities were postponed, but its true impact isn’t yet clear. Will suboptimal care bring long-term complications? Nonetheless, PD technique stands out for favorably, mainly if all the necessary support from medical and nurse staff is guarantee.

Activity and intercurrences at our PD Unit.

<table>
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<th>2018 (n=34)</th>
<th>MEAN ± SD</th>
<th>2019 (n=36)</th>
<th>MEAN ± SD</th>
<th>2020 (n=38)</th>
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<td>14.7 ± 7.7</td>
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<td>NON-PRESENT, APPOINTMENTS</td>
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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

Figure 1. (A) GO enrichment analysis on biological process, (B) cell component, (C) molecular function of COVID-19-induced renal injuries; (D) Venn diagram for the co-shared target genes of COVID-19, CKD and AKI; (E) Underlying significant target genes of a active compounds.
Complete Recovery from COVID-19 Infection in an ESRD Patient

Introduction: We report a hemodialysis case having both influenza and COVID-19 who presented without respiratory symptoms and recovered fully with treatment by Interleukin-6 (IL-6) inhibitor.

Case Description: 68-year-old Caucasian woman with history of hypertension, diabetes mellitus, obesity, sleep apnea, atrial fibrillation, and ESRD on hemodialysis came to hospital with fever of 102°F. Her symptoms were mental status changes, and decreased energy levels. There was no travel history and no contact with COVID positive or suspected COVID patients. On arrival to ER she had temperature of 99.4°F, bp 117/63, HR 102, RR 18, oxygen saturation of 99% on 2litters of oxygen. Examination revealed normal breathing sounds, no wheezing, and functional left forearm arteriovenous fistula. Rest of the exam was with in normal limits. Laboratory results showed sodium 138, potassium 5.7, chloride 96, bicarbonate 24, blood urea nitrogen 71, creatinine 13.5, C-reactive protein 15.06, ferritin 2532, She was positive for both influenza and SARS COV-2 PCR. Blood and urine cultures showed no growth. Imaging showed prominent interstitial vascular prominence; underlying pneumonia could not be excluded. Patient was admitted to hospitalization. He was discharged on TIW hemodialysis.

Discussion: Our case is unique of having both influenza and COVID-19 infection and improved. More studies are warranted to evaluate clinical benefit of the above therapies.
developed myalgia. There was no family history of myopathies, or binge alcohol intake beforehand. On physical examination, patient was hypertensive, euvoletic, and afebrile, with normal oxygenation. Chest x-ray showed suble increased interstitial reticulon in the perihilar regions and COVID-19 rapid test returned positive. Laboratory data showed very high creatine kinase (CK) (208,456 U/L). Uralysis showed trace proteinuria, large blood but only few red blood cells and confirmed myoglobinuria. However, his creatinine was normal (0.8 mg/dL), as well as serum calcium (8.4 mg/dL), phosphate (3.9 mg/dL), and uric acid (5.2 mg/dL) levels. Patient was admitted for treatment of assumed severe rhabdomyolysis. COVID-19 was treated conservatively with oxygen supplementation. Atorvastatin and diltiazem were held, and normal saline and isotonic sodium bicarbonate fluids were administered. CK continued to rise with a peak of 499,020 U/L on day 3, but decreased steadily to 58,745 U/L on day 7. Renal function remained stable all the time during the treatment (serum Cr 0.68 – 0.82 mg/dL), with maintained urine output and well-preserved electrolytes and uric acid levels throughout.

Discussion: There are increasing number of reports of COVID-19-associated rhabdomyolysis, but risk factors and characteristics are fairly known. The clinical and laboratory manifestations are suggestive of COVID-19 associated rhabdomyolysis rather than statin-induced. We are not aware of any other reports documenting such extreme CK values – with a proper rise and fall of CK – without impacting renal function. As far as we know, this is the first case of COVID-19 associated rhabdomyolysis with peak CK of 499,020 U/L, without AKI and concurrent electrolyte abnormalities. The relationship to COVID-19 vs. individual genetic susceptibility remains to be explored.

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Underline represents presenting author.

PUB048
CKD Patients on Hemodialysis (HD) with COVID-19 Infection: Characteristics and Outcome

Background: The COVID-19 pandemic has special significance for Chronic Kidney Disease patients on HD. Clinical characteristics and outcome from low resource settings are not well known.

Methods: From March 15 2020 until May 20, 2020, quality managers reviewed all patients with confirmed COVID-19 infections in 200 HD centres among MHD patients. For patients with COVID-19 infections: age, gender, geographical zone, type of Insurance, continuity of care was noted, HD characteristics and outcome were reviewed. Comparison of median was done with Mann Whitney-Wilcoxon 2 sample test and proportion with Fisher exact test. All patients were transferred to public hospital for regulatory compliance limiting follow up of HD sessions.

Results: 39 out of 18402 patients developed COVID-19 infection. M: F: 28: 11, Age: 54.62 ± 14.92 years. Geographically: East zone:3(7%), North:12(31%), South:5(12%), West:19(50%). Payers: self pay:19(49%), government insurance:15 (38%) and private insurance:5(13%). 5(13%). 32(82%) hypertensives, 23(59%)diabetics. Outcome: 8(20%) expired, 49(13%) were on ventilatory support.

Discussion: Comparison of survivors and non-survivors in maintenance HD patients with COVID-19 infection shows that despite survivor’s lower age, there is increased mortality in COVID-19 patients on HD which is comparable to reports in normal population and is associated with need for intensive care, steroid use and ventilatory support.

Comparison of survivors and non-survivors in maintenance HD patients with COVID-19 infection

PUB049
Starvation-Induced Metabolic Acidosis in a COVID-19-Infected Pregnant Patient
Muhammad R. Mustafaj, Stony Brook University, Stony Brook, NY.

Introduction: Suffolk County in NY was hardest hit with COVID 19. We present a case of a pregnant female with COVID 19 infection and high anion gap acidosis.

Case Description: 34 yo female, 33 weeks twin pregnancy, a/w fever, SOB and polyuria. Her oral intake was poor. She was positive for COVID 19. Her T - 100 F, O2 sat 99% with O2 by NC at 2 L. She had bibasilar crackles. Both babies were moving. CXR showed multifocal pneumonia. Nephrology was consulted for metabolic acidosis. A diagnosis of starvation ketosis of pregnancy was made due to anion gap acidosis, high serum beta-hydroxybutyrate and ketonuria. Dextrose 5% with sodium bicarbonate was given. She had C section, remained intubated for 24 hours, recovered well and was discharged on hospital day 7.

Discussion: Almost 15% of pregnant patients develop server COVID 19. Pregnant patients with COVID infection are a higher risk group.

PUB050
Slow Low-Efficiency Dialysis (SLED) Implementation During the COVID-19 Pandemic Surge
Richard L. Barnett, Kenar D. Jhaiveri, Bessy Suyin Flores Chang, Azzour D. Hazzan, Shamir Hasan, Steven Fishbane, Mark A. Finger, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

Background: The high rate of ARF in COVID-19 hospitalized patients increased the demand for critical care renal replacement therapy 2-3 fold at Northwell Heath (NW). At the 2 largest hospitals, Long Island Jewish (LIJ) and North Shore University Hospital Hospital (NSUH), bedside HD was provided by HD RNs and continuous renal replacement therapy (CRRT) by critical care (CC) RNs. RN workload in these hypercatabolic patients soared as HD treatments more than doubled and CRRT increased from 9 to 30, Shortages of CRRT fluid and filter sets ensued. SLED, a technique utilizing standard HD dialsate and filters, combined with a collaborative approach between CC and HD RNs was considered.

Methods: In late March, a cohort CC bedside HD program, was initiated. Based on this success, a leadership panel of CC/HD RN and Renal CC MDs created a SLED project plan. Details were reviewed with stakeholders on Friday prior to the Tuesday “Go-Live.” 3 patients previously treated with HD or CRRT via a Shiley catheter were selected as a pilot for three 6-8 hour sessions, Fresenius 2008T, Revaclear 300 filters with dialysate flow rate 300 3cm/min and blood flow rate 200-300 cm/min were ordered. HD RN initiated treatments and available throughout, while clinical stability was monitored by CC RN.

Results: NSUH pilot involved 5 patients over 3 sessions. Suboptimal cohorting required remote tablet monitoring and frequent presence of several HD RNs. One patient was terminated in one session due to persistent hypotension. Clearances and UF goals were achieved. A week later the LIJ pilot used the design and advantage of NSUH experience with a 3 bed “SLED Room” model. The same 3 patients participated in all 3 sessions supervised by a single HD RN with no discontinuation. CC RN satisfaction with SLED was ranked “high” at both sites and by LIJ HD RNs but “Spread SLED” rated only “fair” by NSUH HD RNs. Pilots were extended 10 days. During this period SLED was initiated at 2 other NH sites. Future SLED programs will be focused on NH hospitals lacking CRRT.

Conclusions: SLED is an efficient alternative to CC HD and CRRT. The challenges of effective cohorting in a pandemic surge relegate its role to a piece of a comprehensive renal critical care program. It may be particularly valuable for hospitals lacking CRRT options.
Kidney Transplantation in the United States During the Coronavirus Disease 2019 Pandemic: An Interrupted Time Series Analysis

Ekmal Tantisattamo,1,2 Natnicha Leelaviwat,3 Sakdita Saowapa,3 Natchaya Polpichai,3 Busara Songtani,3 Possawat Vuthikraivit,3 Chawit Lopimipsih.1,2 Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California, Irvine School of Medicine, Orange, CA; 3Multi-Organ Transplant Center, Section of Nephrology, Department of Internal Medicine, William Beaumont Hospital, Oakland University William Beaumont School of Medicine, Royal Oak, MI; 4Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; 5Faculty of Medicine Songklanagarin Hospital, Prince of Songkla University, Songkla, Thailand; 6Phramongkutklao College of Medicine, Mahidol University, Bangkok, Thailand.

Background: The number of kidney transplant (KT) in the United States (US) has decreased during COVID-19 pandemic; however, the magnitude of this impact is unclear.

Methods: A period from January 5 to April 18, 2020 was divided into pre- and post-COVID-19 periods by assigning March 1, 2020 as the first day of the post-COVID-19 outbreak in the US. The number of waitlist candidates (WLC) and new KT every 7 days were obtained from OPTN/SRTR. An interrupted time series analysis was performed to examine an incidence rate ratio (IRR) between pre- and post-COVID-19 period by using multiple Poisson regression.

Results: Compared to pre-COVID-19 period, the average number of new KT during post-COVID-19 period decreased (479±33 vs 318±119 cases/week, mean differencesSEM 161±44, 95%CI 67, 255). The number of WLC was relatively stable (mean±SD 65,937±959 cases/week); whereas, it decreased during post-COVID-19 period (61,759±2203 cases/week). Mean incidence rates (IR) of new KT during pre- and post-COVID-19 periods were 727±58 and 511±76 cases/IR/week, respectively (Figure1). The IR of new KT during post-COVID-19 period was 29% lower than those during pre-COVID-19 period (IRR 0.71, 95%CI 0.96, 0.96). After adjusted by age group, transplant areas, and time-study period interaction term, the IR of new KT was 3% increase for every one more week during pre-COVID-19 period (IRR 1.03); whereas, there were 12% decrease for every one more week after March 1, 2020 (IRR 0.88). Compared to pre-COVID-19 period, the IR of new KT during post-COVID-19 period was 9% lower for every additional week for each corresponding period (IRR 0.91).

Conclusions: COVID-19 outbreak in the US since March 2020 is an independent factor of a significant decline in the number of new KT. Further information regarding ability of control COVID-19 may direct KT.

Spectrum of AKI in Patients with COVID-19 Infection


Introduction: With the gradual unfolding of the full spectrum of COVID-19 manifestations, Acute Kidney Injury (AKI) is emerging as a frequent association & a predictor of disease severity & mortality. We present 3 cases of AKI in COVID19 patients & illustrate the clinical course, management & outcome.

Case Description: The first case was a 50-yr old male with DM, HTN, & obesity, admitted with pneumonia, dyspnea & diarrhea, developed hypotension, arrhythmia, & required intubation on day 31 of admission. The next case was a hypertensive, obese 57-year-old female, admitted with pneumonia, worsening dyspnea & respiratory failure without hypotension, was intubated on day 30 of admission. Both of the cases developed AKI with oliguria & progressed to anuria 24 hrs post-intubation. Case 3 was a 72-year old female with hypertoidism admitted with pneumonia, dyspnea, diarrhea, & AKI, was intubated on day 12. All cases had bilateral pneumonia on chest radiograph & significantly raised inflammatory markers (CRP, LDH, Procalcitonin, Ferritin, ALT/AST, d-Dimer, & INR). Peak S. Creat. was 4.1, 6.6, & 3.07 for cases 1, 2, & 3 respectively. Urinalysis for all cases revealed proteinuria, hematuria, pyuria, 4+ budding yeast & signs of UTI for cases 1 & 2. Ultrasound revealed structurally normal kidneys for all cases. Case 1 & 2 were diagnosed as stage III AKI & Case 3 with stage II AKI. All cases received some form of antibiotics, hydroxychloroquine, & heparin for COVID19 and CVVHD for renal support the later iHHD for case 2. Gimerelumemephris specific workup could not be done due to the patient’s clinical status. Among the cases, case 2 made full recovery & discharged, case 1 was stable but hospitalized, case 3 expired on day 14 of hospitalization due to multiorgan failure.

Conclusion: Our cases highlight the inherent variability in causation & clinical course for AKI in COVID19. Interestingly, all 3 cases had the full spectrum of kidney involvement from proteinuria, hematuria to AKI. Although difficult to discern in the absence of biopsy, some potential causes of AKI in these patients include ischemia (renal ischemia, hypotension), hypotension, cytokine storm syndrome (case 3), or direct COVID19 induced acute tubular injury. Increased vigilance is required to recognize probable causes for AKI and to develop adequate management protocols to limit AKI-related morbidity or mortality.

COVID-19 Induction of a Wasting Syndrome in Hemodialysis Outpatients


Background: The SARS CoV-2 pandemic has disproportionately affected vulnerable patient populations including kidney transplant recipients (KTR).

Our transplant centre covers a large multi-ethnic urban population with high rates of co-morbidity and social deprivation, and provides follow-up care for approximately 1500 kidney transplant recipients. In line with national guidance, COVID-19 testing was largely restricted to those patients presenting to secondary care. While COVID-19 was confirmed or suspected, anti-proliferative drugs were stopped, maintenance corticosteroids increased, and calcineurin inhibitor was stopped in patients requiring admission. We performed a retrospective analysis of clinical presentations and outcomes in kidney transplant recipients with confirmed COVID-19 between 20 March and 10 May 2020.

Results: 25 patients (approximately 1.6%) had confirmed COVID-19. 11 (44%) were female and 14 (56%) male. The median age was 61 years (range 33 – 84 years). 11 (44%) were White - British, 12 (48%) Asian and 2 (8%) Afro-Caribbean. Median time post- transplant was 84 months (range 6 – 360), and more recently transplanted patients were not at increased risk. Respiratory symptoms were the predominant presenting complaint in 19 patients (76%) followed by GI symptoms in 4 (16%). Acute kidney injury (stages 1-3) occurred in 15 patients (60%) with 7 patients (28% of whole population 46% of patients with AKI) requiring renal replacement therapy. 6 patients (40%) recovered renal function at a median follow up period of 12 days (range 1 – 52). 4 (16%) were admitted to ITU for ventilation. 10 patients (40%) died (although one death was not related to COVID-19). Among the patients who died, median age was 65 years and 6 (60%) were male with ethnicity proportionate to the study population.

Conclusions: The strategy of performing COVID-19 testing only in patients requiring secondary care likely i) underestimates the incidence and ii) overestimates the disease severity. However, our data show that COVID-19 confers significant morbidity and mortality in kidney transplant recipients despite prompt reduction of immunosuppression. These data will inform a revised consent process for those patients awaiting kidney transplantation. Follow up studies are required to assess longer term outcomes, and potential complications in KTRs who have recovered from COVID-19.

COVID-19 Induces a Wasting Syndrome in Hemodialysis Outpatients: Outcomes in Rochester, New York

Rebecca D. Monk,1 Kristian Vitu,2 Samantha J. Mauser,3 Jaime L. Oneil,2 1University of Rochester Medical Center, Rochester, NY; 2University of Rochester, Rochester, NY; 3Fresenius Medical Care North America, Waltham, MA.

Background: COVID-19 (COV) has infected 2852 residents of Monroe County with a death toll of 218 to date. Hemodialysis (HD) patients (pts) are at high risk for developing COV due to multiple comorbidities. Many patients also reside in Skilled Nursing Facilities (SNF) which have high infection rates. One single Fresenius Medical Care (FMC) dialysis facility in the Rochester, NY area with no Tues/Thurs/Sat (TTS) nursing Facilities (SNF) which have high infection rates. One single Fresenius Medical Care (FMC) dialysis facility in the Rochester, NY area with no Tues/Thurs/Sat (TTS) shifts became the designated unit to provide maintenance HD for all COV positive (+) pts in care until they had 2 negative COV tests. This is a quality improvement review of our patients.

Methods: The study included all 18 pts thus far who received at least one HD treatment in our COV + unit. Demographics and labs – 2 months prior to their first COV test and during the first month in our COV unit were analyzed and compared with data from the 33 COV negative (-) Mon/Wed/Fri (MWF) patients in the same facility. Paired and unpaired T tests were used to determine the statistical significance of observed differences in weight (wt) and labs pre and post COV+ and between COV+ and - pts.

Results: Of our 18 pts, 50% were African American and 50% Caucasian American. Mean age 67, BMI 29.2. 50% resided in SNF prior to COV. All had ESRD. 3 initiated HD within 2 months of first COVID test. Paired and unpaired T tests were used to determine the statistical significance of observed differences in weight (wt) and labs pre and post COV+ and between COV+ and - pts.

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Conclusions: While respiratory symptoms of COV are often stressed we noted few symptoms in other populations and the illness was severe in ~10% of pts that had COV.

AKI in Hospitalized Patients with COVID-19: A Mexican Population

Victor H. Gomez Johnson,1 Gina C. Gonzalez-Calderon,1 Antonio Camiro Zúñiga,1 José A. García Gordillo,2 Adolfo Díaz Cabral,1 Alfredo Fonseca Chávez,2 Julio C. Arriaga,1 Jose S. Lopez Gil,1 Javier Zúñiga-Vargas,1 Juan Pablo Herrera Felix.1 1Centro Medico ABC, Mexico City, Mexico; 2Instituto Nacional de Cardiología Ignacio Chavez, Mexico, Mexico.

Background: Although severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection is primarily a respiratory disease, other organs are also affected. Several pathological studies confirm that SARS-CoV-2 invades kidney tissue causing endothelial damage, glomerular and vascular changes, extensive acute tubular injury and podocyte viral infection. AKI in COVID-19 appears to be frequent, with an AKI incidence of up to 46%, and a 20% requirement for renal replacement therapy (RRT). Patients with AKI show a trend towards worse outcomes and increased mortality. Information on Latin-American population is scarce.

Methods: We created a cohort to describe the incidence, risk factors, and outcomes associated with AKI in hospitalized patients with COVID-19 in Mexico City, excluding patients with a known chronic kidney disease. AKI was defined and classified according to KDIGO guidelines.

Results: We included 127 patients. 11 patients (8.66%) met the criteria for severe COVID-19, and were more likely to have to have AKI (81.82% vs. 54.31%, p=0.078). Of the 72 (56.69%) patients that had AKI, 48% were diagnosed at the time of admission. Patients with AKI were more likely to be men (61.7% vs. 42.4%, p=0.043) and older (55.68 years vs. 48.89 years, p= 0.018). With regards disease severity, 72% of them had a grade 1 AKI. 7 patients (9.72%) had grade 3 AKI, 4 of which needed renal replacement therapy. Overall length of stay was longer in patients with AKI (12 days vs. 7 days, p=0.003). A nonsignificant trend towards stay in critical care units was observed. 3 out of 127 patients died, all 3 had AKI.

Conclusions: Amongst our studied population, AKI was associated with a longer length of stay and with a trend towards a more use of critical care services. The lack of association of AKI with mortality could be due to the low overall in-hospital mortality of COVID-19 patients (2.40%).

AKI Lingering in a Patient with Novel Coronavirus

Marc Saad, Brandon Kirschner, Reuben K. Ellis. Mercer University, Macon, GA.

Introduction: Renal manifestations of the novel Coronavirus infection has been reported during the actual pandemic. While the renal injury was more pronounced in critically ill patients, the levels of AKI, proteinuria and hematocrit predicted the severity of the infection. We are reporting a severe case of AKI and proteinuria with SARS-CoV-2 infection out of proportion of its clinical manifestation.

Case Description: This is a 55 year old African American male patient with PMH of hypertension, aortic valve replacement on Warfarin anticoagulation and CKDIII-b with baseline eGFR of 50 ml/min/1.73m2 (creatinine of 1.5 mg/dL) and recent diagnosis of COVID-19 related gastroenteritis 10 days prior to presentation, was admitted with general malaise and decreased intake. He had no cardiac nor respiratory symptoms. He was afebrile and physical examination was non remarkable. His labs were significant for BUN level of 129 mg/dL and creatinine of 22.0 mg/dL. His blood glucose was 88 mg/dL. Urinalysis showed glucose 100 mg/dL, 0-3 RBCs, 10-3 WBC with a protein/creatinine ratio of 12.8 g/g. His renal ultrasound showed increased cortical echogenicity with edema. His serological workup was unrevealing with negative hepatitis B and C testing, low ASO levels, negative ANA, Anti-PR3, Anti-MPO and Anti-GBM antibodies. He had normal C3, C4 and negative serum immunofluorescent with free kappa/lamba ratio of 1.7. His Alb was 1.7g/dL with triglycerides levels of 184 mg/dL. A kidney biopsy was deferred for its high complication and underwent a kidney biopsy for its high complication.

Results: He continues to asymptomatic and is being monitored outpatient for his kidney recovery.

Discussion: Variable histopathological lesions (FSGS, collapsing glomerulopathy, podocytopathy and tubular interstitial disease) has been described in the renal manifestations of the novel coronavirus. While its physiopathological mechanisms remain unclear, the severity of proteinuria and renal injury observed in this clinically asymptomatic patient highlight an unusual infection-driven mechanism.

Patients with COVID-19 and Kidney Disease: Who Fared Best?

Micaela Antionios, David Jackson, Sadananda V. Aithal, Michael T. Shiel, Huw Davies. Swansea Bay University Health Board, Swansea, United Kingdom.

Background: COVID-19 poses the greatest global challenge in modern day healthcare. Chronic Kidney Disease (CKD) patients are classed as ‘high risk’ in terms of the morbidity and mortality associated with COVID-19. We present data from a large centre encompassing a 24-bed inpatient renal ward, 2 in-centre haemodialysis (HD) units and a large ITU. We aim to compare and contrast clinical outcomes for COVID-19 patients with renal disease.

Methods: Observational analysis was performed on 61 patients (mean age 65y), all positive for COVID-19. Patients were stratified according to their renal status at the point of contracting the virus (table 1).

Results: Acute Kidney Injury (AKI) (n=24; mean age 67y) – 23 of 24 patients were intubated and ventilated in ITU. 18 died. 4 remain on haemofiltration (1 patient transplanted for Extracorporeal Membrane Oxygination). Only 1 patient required ventilatory support and survived with resolution of the AKI. 1 patient requiring invasive ventilation survived with recovery of renal function. Chronic HD (n=28; mean age 60y) – 20 prevalent adult HD patients tested positive for COVID-19. 10 recovered and one died. 10 died. Kidney Transplant Recipients (KTR) (n=4; mean age 59y) – 3 were managed as outpatients and have recovered with functioning grafts. 1 died.

Peritoneal Dialysis (PD) (n=2; mean age 68y) – 1 was managed as an outpatient and has made a good respiratory recovery. 1 patient died. CKD (without renal replacement therapeutic modality) (n=1; mean age 78y) – 1 patient with pre-existing CKD (stages 3-5) contracted COVID-19. 5 made a recovery with no progression to RRT. 2 died without RRT. 2 received acute HD and subsequently died. 1 remains on acute HD and 1 has progressed to chronic HD.

Conclusions: AKI patients had the poorest outcomes in terms of need for ventilatory support and mortality. 50% of chronic HD patients with COVID-19 died. Despite immunosuppressants, only 4 KTTRs (total cohort of 352) contracted COVID-19. The introduction of virtual transplant clinics, minimisation of face-to-face contact and off label drug regimens may have influenced this. These data aim to reinforce the international collaborative against this global pandemic.
COVID-19 Financial Ramifications on the Pediatric Nephrology Workforce

Darcy K. Weidemann,1,2 Allison C. Redpath,4 Isa Ashoor.1 Children’s Mercy Hospitals and Clinics, Kansas City, MO; 3University of Missouri Kansas City, Kansas City, MO; 4LSU Health New Orleans, New Orleans, LA; 1University of Wisconsin System, Madison, WI.

Background: The adverse impact of the COVID-19 pandemic on state and federal budgets, coupled with widespread lockdown measures, and reduced non-COVID-19 clinical volume has forced healthcare and academic organizations to adapt to declining revenues. We examined the financial ramifications of the pandemic on the pediatric nephrology workforce.

Methods: Online survey distributed to active members of the American Society of Pediatric Nephrology (n=987) over 2 weeks in May 2020.

Results: Response rate was 16% (n=144). Most respondents (34%) were 35-44 years old, followed by 45-54 years old (24%). Most were White (65%) followed by Asians (24%). Respondents resided in the South (31%) followed by the Northeast (29%) and Midwest (22%). Most were faculty (92%) in early career stage (Assistant Professor, 31%), affiliated with a free-standing children’s hospital (55%) or a children’s hospital within an adult hospital (36%), working full time (79%) with an average of 60% effort dedicated to clinical activities. Most acknowledged feeling worried about the long-term financial ramifications of COVID-19 on their employer (88%) and their own financial future (75%).

Figure 1 summarizes the financial repercussions reported. The majority (47%) were unclear whether they will be expected increased clinical duties once stay-at-home orders are lifted, however, 44% reported new childcare or eldercare responsibilities.

Conclusions: Overwhelming concern regarding employee and employer financial security exists among practicing pediatric nephrologists in the context of the COVID-19 pandemic. Uncertainty, institutional hiring freezes, compensation reduction, and increased duties in one’s personal life all pose additional threats to a specialty with an already looming workforce shortage. Comprehensive strategies to prevent attrition and burnout are required to sustain the pediatric nephrology workforce during recovery from the COVID-19 pandemic.

Not All Coronavirus Patients Are Dying from Broncho-Pneumonia:
Most Might Be Dying from Cerebro-Neurologic-Vascular Diseases and Cardiovascular Complications

Yahya Sagiliker,1,2 Hassan S. Sagiliker,2,5 Piril Sagiliker Ozkaynak,4 Nuray Paylar.2 Sagiliker Nephrology and Hypertension Unit Çukurova Universitesi Tip Fakultesi, Adana, Turkey; 2Sagliker Nephrology and Hypertension Unit, Adana, Turkey; 3Karliova State Hospital, Bingol, Turkey; 4Karaisali Community Health Center, Adana, Turkey.

Introduction: Acute bronchopneumonia is not sufficient to explain deaths. Lungs, brain-nerves - heart- cardiovascular system might be playing for key roles. Three are playing together. In last days, lungs and brain and heart suddenly are stopping.

Case Description: Key places are neurological conjunction systems between brain, lungs and cardiovascular systems. All organs are being regulated by last two systems. All mentioned activities are being regulated in those systems. All decisions and functions of human are giving there.

Discussion: A neurologist and a cardiologist must be involved in treatment in late stages. This is vital. 1-Pulmonologists are following lungs. 2-Pulmonary-toracal surgeons should think two sided bronchial tubes from outside. 3-Cardiologist must follow EKG continuously. Echocardiography must be performed every day. They must know well inside of hearth and must question which drugs are taking. 4-Neurologists must perform MRG for brain, back lower brain and should make EEG, every day. AFFECTION-REACTION-EFFECTING-INFORMING BACK rules must be controlled. They must detect neurotransmission system is from top to bottom as I have written above like so called zig-zag-zig system or reverse neurotransmission system is occurring as zig-zag-zig system to destroy body. If it is so this strange system can be called from now on as SAGLIKER’S REVERSE NEUROLOGICAL WORKING SYSTEM.”.

COVID-19 and the Adverse Impact on Pediatric Nephrology Workforce

Weidemann,1,2 Redpath,4 Ashoor.1 Children’s Mercy Hospitals and Clinics, Kansas City, MO; 3University of Missouri Kansas City, Kansas City, MO; 4LSU Health New Orleans, New Orleans, LA; 1University of Wisconsin System, Madison, WI.

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Conclusions: Overwhelming concern regarding employee and employer financial security exists among practicing pediatric nephrologists in the context of the COVID-19 pandemic. Uncertainty, institutional hiring freezes, compensation reduction, and increased duties in one’s personal life all pose additional threats to a specialty with an already looming workforce shortage. Comprehensive strategies to prevent attrition and burnout are required to sustain the pediatric nephrology workforce during recovery from the COVID-19 pandemic.
important role in treating severe COVID-19 patients with MHD. Cardiovascular disease is the leading cause of death in ESRD patients. The cardiovascular events of this patient might be combined with COVID-19 associated heart injury and worsen of pre-existing CHD. We suggested lack of family support during quarantine might be a reason of psychiatric symptom. In conclusion, personalized immunomodulation therapies might be helpful in treating severe COVID-19 patients with MHD. Cardiovascular events were associated with poor outcome.

Clinical Presentation of Hemodialysis Patients with COVID-19: A Single-Center Study with 18 Patients

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Background: SARS-CoV-2 has affected every nation around the world. The 1st case in the Dominican Republic was reported in early March, with the most affected being the elderly. Many patients with comorbidities like cardiovascular diseases. Most hemodialysis patients share these comorbidities, in addition to a weaker immune system and health care facility exposure, it is thought to be a vulnerable population. The aim is to describe the clinical manifestation, main laboratory abnormalities, imaging findings at the moment of presentation, and the clinical course of patients on hemodialysis diagnosed with COVID-19.

Methods: Exploratory study on 18 dialysis patients with Covid-19 in a renal replacement therapy facility. Demographics, symptoms, laboratories, CT scan, hospital course, ventilation requirement, treatment and complications were described.

Results: With a population of 204 patients, 18 were diagnosed with Covid-19 in the first 2 months of the outbreak in our facility. 77.8% were males, mean age was 60 years, and 44% had known contact with infected people outside the facility. All patients had cardiovascular disease and 12 had diabetes. Cough was the most common manifestation 77.8%, dyspnea 66.7%, fever 55.6%, and malaise 44.4%, among others manifestations. Oxygen therapy was required in 66.7%, with 11.1% needing mechanical ventilation. All presented abnormal CT scan findings, 60% with a COVID-RADS grade 3. Three patients were positive and asymptomatic on a round RT-PCR test taken for all facility patients, 2 of them with CT scan graded COVID-RADS 3. Only symptomatic patients were admitted, 3 were directly admitted to the ICU, and 2 were later transferred from inpatient floor to ICU. The mean duration of hospitalization was 11 days and just 1 lethal outcome. At the moment of admission, 22.2% presented negative results on RT-PCR but had clinical and imaging findings consistent with Covid-19, with serologic conversion later.

Conclusions: Even with the increased risk of exposure, comorbidities, and a weaker immune system, these didn’t necessarily determine a higher probability of infection. We have found a high incidence of respiratory symptoms, in contrast to other case reports. Asymptomatic patients had imaging with COVID-RADS grade 3, this made us consider that the COVID-RADS grade on CT scan is a helpful tool for diagnosis of Covid-19.

Pink urine syndrome has been reported as a rare symptom described after surgery and propofol anesthesia. COVID-19 is not only manifested as a respiratory disease characterized by viral pneumonia, but also damage such as kidney, heart, blood and nervous system especially in severely ill patients.

Case Description: A 56-year-old man was diagnosed as severe COVID-19. He was admitted to ICU and underwent the tracheal intubation. During this treatment, propofol was used to sedate. He suddenly excreted cloudy pink urine on that day (Figure 1). There were some pink crystals in the urine bag and pink sediment at the bottom of the urine bag (Figure 2, Figure 3). His urine dipstick showed a specific gravity of 1.02, pH 5.5, blood (1+) and protein (1+). He had no urinary tract symptoms and his urine cultures were normal. His blood gas analysis showed pH was 7.3. His colour of urine gradually returned normal when the patient was given intravenous Sodium bicarbonate injection.

Discussion: Pink urine syndrome is a phenomenon in which uric acid precipitates into the urine due to reduced urinary pH. Propofol can increase the excretion of uric acid in the urine. Lower urine pH will reduce the solubility of uric acid, promoting the formation of amorphous uric acid crystals, which exhibit a characteristic pink color. At the same time, metabolic acidosis may aggravate this phenomenon. COVID-19 has been reported to invade cells mainly through ACE2 receptors, ACE2 receptor is strongly expressed in the proximal tubule of the kidney, causing acute tubular necrosis. It has suggested that the kidney is one of the main targets of COVID-19. While considering the pink urine syndrome might caused by propofol, we speculate that COVID-19 could damage the renal tubule which affect its reabsorption of uric acid, which may worsen the uric acid crystallinity.

Pink urine deposits observed.

Teledicine in the Care of Kidney Transplant Recipients with COVID-19

Farouk Al Ammary, Mohammad Abuzeineh, Abimereki Muzaale, Deidra C. Crews, Robin K. Avery, Daniel C. Brennan, Dorry L. Segev. Johns Hopkins University School of Medicine, Baltimore, MD.

Introduction: Kidney transplant (KT) recipients with COVID-19 symptoms are bringing challenges to providers given the risk of COVID-19 exposure to health care workers, patients, and the public.

Case Description: Three KT recipients with COVID-19 were managed using teledicine via synchronous video visits integrated with an electronic medical records system, from home to inpatient settings (Figure 1-2). Patient 1 is a 53-year-old male s/p KT in 2012; Patient 2 is a 56-year-old female s/p KT in 2019; and Patient 3 is a 53-year-old female s/p simultaneous liver-kidney transplant in 2014. Patients 1 and 3 had follow-up COVID-19 NAT testing: Patient 1 converted to be negative at 24 & 28 days, whereas Patient 2 converted to be negative at 45 & 48 days.

Discussion: Teledicine helped assess, diagnose, triage, and treat patients with COVID-19 while avoiding an ER or outpatient clinic visit. We highlight the value of teledicine in the maintenance of uninterrupted follow-up care for immunosuppressed patients with prolong viral shedding.
Table 1: Patients 1 and 2 laboratory test results during hospitalization. Patient 3 was not hospitalized.

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<th>Parameter</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Reference range (mmol/L)</th>
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</tbody>
</table>

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.

Table 2: Clinical course of the three patients with COVID-19 who were managed via telemedicine.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>COVID-19</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Treatment</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>COVID-19</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Treatment</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

Figure 1. Urinary sediment slides showing: A) a granular cast with a renal tubular cell within; B) a granular cast with several isomorphic erythrocytes.

**PUB065**

**Urinary Abnormalities and Urinary Sediment Findings in COVID-19 Patients**


**Background:** Coronavirus disease 2019 (COVID-19) is a new disease of pandemic proportions. There are only a few reports about urinary abnormalities in this disease, and to our knowledge there are no reports about the usefulness of urinary sediment on prognosis. Our aim was to describe the urinary abnormalities in COVID-19 and to assess the utility of urinary sediment on prognosis in COVID-19.

**Methods:** Prospective, single-center study, in patients diagnosed with COVID-19 (with a positive RT-PCR test), who were admitted in our hospital, from April 2020 to date, and whose urine sample could be obtained at admission to the isolation wing.

**Results:** 22 patients were included: 17 (77.3%) had proteinuria, 12 (54.5%) had microscopic hematuria, and 9 (40.9%) had leukocyturia. Granular casts (with a Chawla cast scoring index greater than 3) were present in 8 (36.4%) patients. Of the 8 patients with granular cast, 6 developed an AKI (75%), 2 required hemodiagnosis (25%) and 3 died (37.5%). Of the 14 patients whose urinary sediment was classified as bland, 5 developed an AKI (35.7%), none of them required hemodiagnosis, and 2 subsequently died (14.2%). There was a statistically significant difference between a bland urinary sediment and a sediment showing granular casts for the need of hemodiagnosis or death (p=0.02), with a positive LR of 3.5.

**Conclusions:** The urinary sediment is a cheap, available tool for the prognosis of need for hemodiagnosis or death in patients diagnosed with COVID-19, and should be taken into consideration in the assessment of these patients by the Nephrology department.

**PUB066**

**Repurposing Baby Monitors in COVID-19**

Sobia N. Khan, Sandeep K. Mallipattu. Stony Brook University, Stony Brook, NY.

**Introduction:** As of May 2, total of 1,130,075 confirmed cases resulting in 65,605 deaths were reported in US. Nearly 3.2% of individuals with COVID-19 develop AKI and have been reported to require dialysis. Initial reports from Wuhan, the burden of acute kidney injury was relatively low, about 3% -9%, subsequent analysis have demonstrated increase in the incidence to 15%

**Case Description:** In February, 376 hemodialysis and 59 CRRT while in March, 273 hemodialysis and 30 CRRT offered in our hospital. During pandemic bed capacity doubled from 650 to 1317 beds. Physical space gained by converting ambulatory surgical center and ambulatory locations. In April, observed 1,811 COVID-19 patients admitted to the hospital with 50 chronic hemodialysis patients, 30 were COVID positive. 334 hemodialysis treatments while 136 continuous renal replacement therapy offered 12.8% to the hospital with 50 chronic hemodialysis patients, 30 were COVID positive. 334 hemodialysis treatments while 136 continuous renal replacement therapy offered 12.8% increase in the incidence to 15%.

**Discussion:** To minimize the risk of exposure in COVID-19 isolation rooms we implemented telemonitoring strategy. We identified baby monitors could serve “read-to-go” telemonitoring. VTech Baby Monitor 7” display. HD camera uses WiFi connection to capture movements and sounds which helps in monitoring the patients in real-time. The camera ability to pan 360 degrees, tilts 82-degrees and zooms ten times to enable viewing of the dialysis monitor and patient. Two-way voice communication allows easy communication between patient and nursing. Before hemodiagnosis nurse sets up camera by the patient’s bedside (1 camera facing the dialysis monitor other camera facing patient and the dialysis access). Dialysis nurse visualize through the handheld monitor. Telemonitoring system COVID-19 patients undergoing hemodiagnosis we observed zero positive COVID-19 dialysis staff.
**PUB067**

**Impact of Ethnicity on COVID-19 Infection and Mortality Amongst In-Centre Haemodialysis Patients**

Gregor D. Young, Noam Roth, Kieran Mccafferty, Suzanne H. Forbes, Andrea Cove-smith. Royal London Hospital, London, United Kingdom.

**Background:** It is reported that patients of BAME origin are at greater risk of infection and death due to COVID-19. We describe outcomes in an inner city, ethnically diverse in-centre haemodialysis (HD) population during the pandemic.

**Methods:** A total of 1253 patient electronic records were analysed retrospectively. 207 infections were recorded -197 patients tested positive for Sars-Cov-2 on validated nasopharyngeal PCR analysis and 10 patients included due to high clinical suspicion. Ethnicity data is self-reported. All COVID-19 positive patients were isolated for subsequent dialysis sessions. Whole-cohort screening confirmed the rates of infection.

**Results:** Overall rate of infection amongst the group was 16.5% (n=207), hospitalisation 7.5% (n=94) and death 3.5% (n=44). Within COVID-19 infections, hospitalization rate was 45% and mortality 21%. Seven patients received critical care and two were intubated. Ethnicity data are shown in table 1: There was no significant difference in rates of COVID infection between ethnic groups. The risk of infection in BAME patients was not significantly greater than in white patients (p=0.24, OR 0.79, 95%CI 0.55-1.14). The mean age of those who died from COVID did not differ from the entire cohort (62 vs 63.2 years). Males made up the majority of both the baseline cohort (61.2%) and those infected with COVID (58.5%). 71% of those who died were male. Body mass index did not differ between the group as a whole and those infected with COVID. Rates of diabetes mellitus did not differ significantly between those infected with COVID and those who died.

**Conclusions:** We have defined COVID infections and outcomes within a real-life, large haemodialysis population. Hospitalisation and mortality rates were high, and patients self-reporting as black or Asian were over-represented in the infected group compared to the baseline prevalent HD population. Higher rates of death were observed in black and asian groups but conclusions are limited by small numbers. Larger collaborative studies are required to expand on these findings.

**Ethnic breakdown of HD cohort and COVID cases**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Baseline HD Patients (%)</th>
<th>% of total population (%)</th>
<th>COVID Cases (%)</th>
<th>% of cases (%)</th>
<th>COVID Deaths (%)</th>
<th>% of deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>23.5 (308)</td>
<td>26.9 (969)</td>
<td>31.8 (96)</td>
<td>30.7 (30)</td>
<td>6.7 (2)</td>
<td>18.8 (12)</td>
</tr>
<tr>
<td>Asian</td>
<td>32.6 (425)</td>
<td>31.6 (111)</td>
<td>31.8 (96)</td>
<td>30.7 (30)</td>
<td>6.7 (2)</td>
<td>18.8 (12)</td>
</tr>
<tr>
<td>White</td>
<td>25.9 (339)</td>
<td>28.2 (763)</td>
<td>27.3 (83)</td>
<td>27.3 (83)</td>
<td>7.9 (3)</td>
<td>26.3 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>15.0 (192)</td>
<td>16.4 (514)</td>
<td>31.8 (96)</td>
<td>30.7 (30)</td>
<td>6.7 (2)</td>
<td>18.8 (12)</td>
</tr>
</tbody>
</table>

**PUB068**

**COVID-19 Management in New York City Kidney Transplant Recipients: Before and After the Apex**


**Background:** Kidney graft recipients receiving immunosuppressive therapy may be at heightened risk for Covid-19 and adverse outcomes. We aimed to study how practice patterns and outcomes changed before and after the peak incidence of cases in New York City.

**Methods:** We reviewed 68 consecutive adult kidney graft recipients from our center diagnosed with SARS-CoV-2 from March 13, 2020 to May 25, 2020. We compared outcomes of those treated from March 13 until the apex of infections on April 14 (Phase 1), and those treated from April 15th to May 25, 2020 (Phase 2).

**Results:** Characteristics of both Phase 1 and Phase 2 patients are described in Table 1. Inflammatory markers were lower in the second phase as was patient mortality. Changes in management strategies between the two phases are highlighted in Figure 2. Graft loss occurred in 4 patients (6%) and there were 5 deaths (7%).

**Conclusions:** Data from our study suggest that management strategies of immunosuppressed patients changed over the course of the Covid-19 Pandemic in New York City, including less use of hydroxychloroquine, and increased use of novel agents such as remdesivir. Additional data are needed to better understand if the decrease in patient mortality during the second phase is attributable to better management or lower inflammatory response in the setting of Covid-19 illness.
COVID-19 in a G6PD-Deficient Patient

**Background:** Rituximab (RTX), a monoclonal antibody against the CD20 antigen found on B lymphocytes, is widely used for glomerular diseases. It may be advantageous in COVID19 given the exaggerated immune response and cytokine storm elicited by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) or could be detrimental given the impaired response to infections in immunocompromised patients.

**Methods:** We examined the clinical presentation and outcomes of 3 patients undergoing treatment with RTX who were infected with SARS-CoV-2.

**Results:** 2/3 patients had complication of severe hypoxemia with evidence of pulmonary infiltrates on imaging. Both had underlying ANCA vasculitis with a history of pulmonary involvement. Both were treated with remdesivir and one received convalescent plasma. The patient who received convalescent plasma was SARS-CoV-2 RNA negative at 3 weeks. The patient who received remdesivir but not plasma remained positive for SARS-CoV-2 RNA at 7 weeks and was negative for IgM and IgG antibodies at 4 weeks. The third patient recovered without hospitalization and had a first negative RNA test at 3 weeks and was positive for IgG antibodies when tested at 7 weeks despite a confirmed zero B cells by flow cytometry.

**Conclusions:** 3 out of 3 patients who developed SARS-CoV-2 infections while on RTX recovered. A larger review of individuals on RTX therapy infected with SARS-CoV-2 should be examined to study the association between B cell depletion and COVID19.

**Patient Characteristics and Outcomes**

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 58 yrs</td>
<td>Recovered with early monitoring of hemolysis parameters.</td>
</tr>
<tr>
<td>Race: African American</td>
<td>Severe AKI following HCQ therapy.</td>
</tr>
<tr>
<td>History of T2DM and arterial hypertension</td>
<td>Renal recovery could be incomplete.</td>
</tr>
<tr>
<td>COVID-19 pneumonia diagnosed</td>
<td>Severe G6PD deficiency can manifest with fava bean ingestion or other triggers.</td>
</tr>
</tbody>
</table>

HCQ: Hydroxychloroquine

G6PD: Glucose 6-phosphate dehydrogenase

*PR3-ANCA: Patient with eye, ENT, lung and kidney involvement

**Discussion:** The residual enzyme activity of G6PD deficiency determines the severity of clinical manifestations which are usually triggered either by fava bean ingestion or drugs, and are dose-dependent. This patient had a severe deficiency and he received a loading dose of an RTX-risk drug. Both induced hemolysis crisis. AKI is a rare complication of AHA related to G6PD deficiency. The need for renal replacement therapy seems exceptional. Renal recovery could be incomplete. Severe G6PD deficiency can manifest late, and HCQ should be used with caution given potential severe side effects. We then recommend early monitoring of hemolysis parameters.

COVID-19 in Kidney Transplant Recipients

**Background:** SARS-CoV-2 rapidly spread globally, imposing the need for change in nephrology practices guided by the recommendations, issued by scientific associations.

**Methods:** We conducted a nationwide virtual educational initiative with an inbuilt technological platform to enable live sharing of experiences of new modes for nephrology practice during COVID 19 pandemic, based on the adoption of current recommendations and evidences to enable indigenous, adaptive experiences of 404 nephrologists with approximately 8,000-man hours of cumulative clinical experience. The four zones across the country were represented by an individual educational task force member.

**Results:** There was a uniform consensus that suspected patients need to be treated similar to a COVID 19 positive patient, with dialysis facility provided in isolation area, to mitigate direct risk to both healthcare providers and patients and indirect risk of contamination of the hospital system. Multiple screening procedures and prohibition of eatables in dialysis area is the new mandate. Role and importance of CRRT, PIIRR and peritoneal dialysis was highlighted. Femoral catheterization is the preferred route. The experience of Tenckhoff catheter technique in peritoneal dialysis in 38 patients was discussed. Higher dose of anticoagulants is being utilised for extracorporeal procedures to reduce risk of enhanced risk of thrombus formation in COVID 19. The varied, emerging clinical presentation, including asymptomatic cases has made COVID 19 testing compulsory at most of the institutions. The nephrologists were informed about the emerging evidence for the need to continue the ongoing ARBs or ACE inhibitors. Renal transplantation with careful precautionary practice is being performed with modulation of dose of immunosuppressive agents in COVID 19 positive patients.

**Conclusions:** Safe and efficient delivery of nephrology care practices needs a uniform acceptance. Even minor liberties and deviations from established safe practice protocols could compromise the safety of the health care workers.

COVID-19 in Kidney Transplant Recipients

**Background:** Coronavirus disease 2019 (COVID-19) is caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Kidney transplant recipients are at a higher risk for complications due to comorbid conditions and concurrent immunosuppression. We like to describe a small cohort of kidney transplant recipients with COVID-19.

**Methods:** A single-center, retrospective observational cohort study describing short term outcomes of COVID-19 infection in kidney transplant recipients.

**Results:** A total of 8 kidney transplant recipients were diagnosed with COVID-19 with a mean age of 58 yrs (26-78), predominantly African American (7/8), mean duration of immunosuppression of 3 weeks and was positive for IgG antibodies when tested at 7 weeks despite a confirmed zero B cells by flow cytometry.
from transplant 3.5 yrs (1.5-11 yrs). All patients have HTN (8/8), half the patients have Diabetic mellitus-2 (4/8). Common presenting symptoms are fever and shortness of breath. 6/8 patients required hospitalization. 8/8 patients were managed with a reduction of immunosuppression, primarily by decreasing the dose or holding the anti-proliferative agent. 1/8 patients died, 4/6 discharged from hospital, 1/6 still admitted to the hospital with renal failure. 1/6 patients required supplemental oxygen. 2/6 patients required ICU stay and 1/6 required mechanical ventilation and renal replacement therapy. 3/6 hospitalised patients received hydroxychloroquine/ Arithromycin combination and 1/6 received Remdesivir. Median hospital stay is 5 days with a mean of 9 days. The patient who required mechanical ventilation and renal replacement is the only recipient who died from COVID-19 at our transplant center.

Conclusions: COVID-19 is a novel infection primarily presenting with fever and shortness of breath. The course of illness appears to be severe with the majority of patients requiring supplemental oxygen and a third of hospital admitted patients required ICU stay and 1/6 required mechanical ventilation and renal replacement therapy. 3/6 hospitalised patients received hydroxychloroquine/ Arithromycin combination and 1/6 received Remdesivir. Median hospital stay is 5 days with a mean of 9 days. The patient who required mechanical ventilation and renal replacement is the only recipient who died from COVID-19 at our transplant center.

Introduction: Patients with COVID-19 typically present with respiratory illness. AKI is a common complication of COVID-19. The etiology of AKI remains unclear, thought to be secondary to hemodynamic changes, cytokine release and/or direct viral (SARS-CoV-2) cytotoxicity. The following case describes a patient who presented only with GI symptoms, which led to the diagnosis of COVID-19 and AKI.

Case Description: 71 year-old white male, a nursing home resident, was admitted to the hospital with a diagnosis of COVID-19. On the following day he was brought to a local ER after 3 large projectile emesis. Labs revealed BUN/Cr 80/9.4. He was given IV levofloxacin and was transferred to our hospital. He had watery brown-greenish stools, although he denies diarrhea or abdominal pain. Meds included Insulin, statins, heparin, SSRI, and doxepine. At our ER, the patient was awake, alert, orientated to self and year. T 98.3, BP 119/71, P 119, RR 18, SpO2: 99% on RA, PE was unremarkable. Bladder scan: 150 mL. Lab: WBC 10.9, Hb 13.3, Plt 207. Na 130, K 4.0, Cr 75, bicarb 17, BUN 85, Cr 8.6, Ca 7.3, Phos 6.6, Alb 3.2. LFT was normal. FeNa = 1.5%. UA: pH 5, prot 1+. Glu 50, RBC 5, WBC 4, with amorphous sediments. These findings were clear. Renal ultrasound: kidneys with normal size and echogenicity. No obstruction. Patient was admitted to the COVID ward. Patient’s nausea and vomiting stopped upon his admission, although his watery stools continued. He was treated with iv fluid to optimize his hemodynamics. Over the next 5 days patient’s serum Cr decreased to 5.4.

Discussion: Since the COVID-19 pandemic, GI symptoms and AKI are often regarded as complications of the overall respiratory illnesses. Patients with only GI symptoms were often not suspected for COVID-19. The causes of this patient’s AKI included hemodynamic nor cytokine mediated. ATN - possible cytokine release. Regarding direct viral cytotoxicity, postmortem data has shown the presence of coronavirus-like particles in podocytes and tubule cells. While the direct viral effect to the kidneys is still not understood, treatment with conventional approaches may significantly improve renal outcome.

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Underline represents presenting author.

813
In contrast, the starting USCs lack PAX2, SIX2 and CITED1. [MOU1] We will next quantify the expression of these and other nephron progenitor markers over the time course of 3D culture.

**Conclusions:** Our results suggest a new method to derive patient-matched SIX2+ CITED1+ cells from non-invasive urine samples.

**Funding:** Private Foundation Support

PUB077

**Comparative Evaluation of Orthostatic Hypotension in Patients with Diabetic Nephropathy**


**Background:** Orthostatic Hypotension (OH) affects 5-20% of our population. Our study investigated the presence of OH in diabetic nephropathy patients (DNP) and the factors affecting OH in comparison with other chronic kidney disease patients (CKDP).

**Methods:** Patients presented to the nephrology clinic and consented were included in the study. DNP were defined by renal biopsy and/or clinical criteria. CKDP of same sex, age and eGFR were matched to DNP. Demographic parameters and medications were obtained from the records. OH was determined by mayo clinic criteria. Same researcher used the electronic device to measure the blood pressures (BP). All samples were taken and analyzed the same day for biochemical and hematological parameters and albuminuria. Statistical analyses were performed with IBM SPSS2.0 program.

**Results:** 112(51F,61M, mean age:62.56±9.35 years) DNP and 94(40F,54M, mean age:62.23±10.08 years) CKDP were included. 70.5% DNP vs 61.7% CKDP had OH (p=0.181). The mean change in systolic BP in DNP was 21.50±16.10mmHg and it was 13.76±9.03mmHg in diastolic BP. In CKDP mean change in systolic BP was 22.1±13.90mmHg and it was 9.56±6.80mmHg in diastolic BP. There was no difference between the groups in systolic BP (p=0.797), but it was present for diastolic BP (p=0.025). 60.0% DNP and 74.7% CKDP patients had OH (p=0.028). Uric acid levels were 7.18mg/dl in OH patients and 6.36mg/dl in non-OH (p=0.017). Blood albumin level was not different in two groups (p=0.902). 73.7% of patients on calcium channel blockers developed OH (p=0.015) and OH developed in 80.6% of 36 patients on alpha blockers (p=0.049).

**Conclusions:** Our study demonstrated OH is frequent among DNP and there was no difference compared to CKDP. It is important to check OH in all CKDP as it is more common than thought.

**Blood Pressure Results**

PUB078

**Clinical Practice Gap Analysis of CKD in Type 2 Diabetes from Identification to Diagnosis to Management**

Amy Larkin,1 Kelly L. Hanley,2 George L. Bakris.3 1Medscape LLC, New York, NY; 2UCincinnati Medicine, Cincinnati, OH; 3UCHicago Medicine, Chicago, IL.

**Background:** Understanding clinical practice gaps in the identification, diagnosis and management of CKD in patients with T2D can inform development of tools to improve physician practices.

**Methods:** A survey instrument of 25 multiple choice, knowledge- and case-based questions allowed participants to assess their knowledge, attitudes, and confidence with regard to CKD in T2D. The survey was available online to physicians across the globe without monetary compensation or charge. Respondent confidentiality was maintained regarding to CKD in T2D. The survey was available online to physicians across the globe without monetary compensation or charge. Respondent confidentiality was maintained.

**Results:** A total of 113 charts were reviewed. Only 18 patients(15.9 %) were on either SGLT2/GLP1A at the end of prospective phase. By the end of prospective phase, 25 patients (22.1%) were on one of these agents. Out of 28 patients with HbA1c more than 8 at the end of prospective phase, percentage of patients on SGLT2/GLP1A at the end of prospective phase remained the same. Utilization of SGLT2/GLP1A ranged 11% to 28.9%. There was no statistically significant difference between the groups treated with SGLT2/GLP1A compared to group not treated with these agents in terms of HbA1c (P value 0.94) or eGFR (P value 0.35).

**Conclusions:** Despite the new recommendations, a substantial number of patients are not on SGLT2/GLP1A even if the diabetes is not controlled adequately. However this lack of adherence to protocol doesn't seem to affect the diabetes control or change in renal function. We need larger studies to further explore the practice patterns of physicians and its impact on outcomes.

**Funding:** Commercial Support - Bayer Global

PUB079

**Practice Patterns of SGLT2 Inhibitor and GLP-1 Agonist Treatment in Eligible Type 2 Diabetic Patients Before and After the Publication of the 2018 ADA/EASD Position Statement**

Bijn Thajudeen, Wei Xiang Wong, Saeed Bidar, Sevag C. Boyadjian, Wina Yousman, Amy N. Sussman, Frank C. Brosius. Banner University Medical Center Tucson, Tucson, AZ.

**Background:** The ADA/ EASD published a position statement in October, 2018 on the prevention of atherosclerotic CVD events in diabetic patients focusing on the use of sodium glucose cotransporter 2 inhibitors (SGLT2I) and GLP-1 agonists(GLP1A). The objective of this study is to determine the practice patterns of endocrinologists and nephrologists in implementing current societal recommendations for use of SGLT2I and GLP1A.

**Methods:** This study had two phases, a retrospective phase and prospective phase to determine utilization of SGLT2I/GLP1A before and after the publication of ADA/EASD position statement. All subjects with type 2 diabetes and CVD/CKD who were at least 18 years of age and who were followed at the endocrinology and/or nephrology clinics were included in the study. Eligible patients had a minimum of two clinic visits in either endocrinology and/or nephrology clinics during either the retrospective phase (October 2017-September 2018) or prospective phase (October 2018 – September, 2019). Information collected included utilization of SGLT2I/GLP1A, HbA1c, eGFR, new CVD events and adverse effects of SGLT2I/GLP1A therapy. Primary outcomes measured was the change in percentage of eligible patients treated with an SGLT2I/GLP1A.

**Results:** A total of 113 charts were reviewed. Only 18 patients(15.9 %) were on either SGLT2I/GLP1A at the end of retrospective phase. By the end of prospective phase, 25 patients (22.1%) were on one of these agents. Out of 28 patients with HbA1c more than 8 at the end of retrospective phase, percentage of patients on SGLT2I/GLP1A at the end of prospective phase remained the same. Utilization of SGLT2I/GLP1A ranged 11% to 28.9%. There was no statistically significant difference between the groups treated with SGLT2I/GLP1A compared to group not treated with these agents in terms of HbA1c (P value 0.94) or eGFR (P value 0.35).

**Conclusions:** Despite the new recommendations, a substantial number of patients are not on SGLT2I/GLP1A even if the diabetes is not controlled adequately. However this lack of adherence to protocol doesn’t seem to affect the diabetes control or change in renal function. We need larger studies to further explore the practice patterns of physicians and its impact on outcomes.

**Funding:** Private Foundation Support, Government Support - Non-U.S.
**Results:** 3 male and 7 female patients with diabetic nephropathy were included, aged 51-80 years, with eGFR 60-4.6ml/min, and 3 patients presented with cardiac insufficiency. Sodium excretion <90mmol followed by Dapagliflozin/Canagliflozin once a day for 7 days, with follow-up. Sodium excretion increased by 30% ± 150 ml/day. Urine volume was 800±500ml/24 hours after treatment. The Scr increased by 30% after 7 days of treatment, and returned to the level of Scr before the initiation of Dapagliflozin/Canagliflozin. Electrolyte levels were comparable before and after treatment.

**Conclusions:** The diuretic regimen based on SGLT2i could significantly improve the resistance of diabetic nephropathy patients to diuretics, increase urinary sodium excretion, and slightly elevate renal function in the short term without affecting blood electrolyte level. The efficacy and safety of long-term use of SGLT2i in diabetic nephropathy patients at CKD3-4 stage need further investigate in larger sample size.

**PUB083**

Peripheral Neuropathy in a Hemodialysis Patient with a Normal Serum Vitamin B12 Level: Possible Vitamin B12 Deficiency in Target Tissues

Yadanar W. Le,

Thinn E. San,

Hun M. Aung,

Aye M. Thida,

Myat E. Mon,

Kyaw M. Thein,

Kyaw Hla,

Alexander M. Swan,

Nephrology Hypertension Renal Transplant & Renal Therapy, LLC, Avenel, NJ; 2Icahn School of Medicine at Mount Sinai Elmhurst Hospital Center, Elmhurst, NY; 3Interfaith Medical Center, Brooklyn, NY; 4Woodhull Medical and Mental Health Center, Brooklyn, NY; 5South East Regional Health Authority, Kingston, Jamaica; 6Rutgers New Jersey Medical School, Newark, NJ.

**Introduction:** Many hemodialysis patients suffer from vitamin B12 deficiency, usually due to inadequate nutritional intake. Besides, food sources of vitamin B12 contain high concentrations of electrolytes, which are harmful to these patients. Thus, they are restricted to foods with low vitamin B12 content. Moreover, high-flux dialyzers remove vitamin B12 molecules from circulation, leading to vitamin B12 deficiency. We report a hemodialysis patient presenting with peripheral neuropathy and a normal serum vitamin B12 level whose symptoms improved with monthly vitamin B12 injections after excluding other differential diagnoses of peripheral neuropathy.

**Case Description:** An 80-year-old man with a history of ESRD on hemodialysis for 3 years along with HTN and CAD presented with fatigue, muscle weakness, and numbness of his extremities for 3 weeks. He was taking aspirin, dipyridamole, finasteride, tamsulosin, and pravastatin. His dietary history was significant for poor nutritional intake. Laboratory findings showed HD 10.6 g/dL, MCV 102 fL, RBS 87 mg/dL, potassium 4.6 mmol/L, and BUN 42 mg/dL. Common causes of peripheral neuropathy in ESRD patients, such as uremic neuropathy, diabetic neuropathy, and hyperkalemia were excluded. Further evaluation revealed a normal serum vitamin B12 level of 421 pg/dL and a normal folic acid level of 14.4 ng/mL. Given his risk factors for possible vitamin B12 deficiency in target tissues, he was treated with monthly vitamin B12 1000 mcg injections and followed up regularly. His symptoms improved significantly after four months of injections.

**Discussion:** In hemodialysis patients, chronic inflammation impairs uptake of circulating vitamin B12 by peripheral tissues leading to decreased production of transcobalamin II, increased synthesis of transcobalamin I and III with further accumulation of vitamin B12 in blood. In addition, despite normal or high serum vitamin B12 levels, these patients may suffer from vitamin B12 deficiency in target tissue and show symptoms such as fatigue and peripheral neuropathy. Therefore, it seems reasonable to consider vitamin B12 supplementation in these patients after excluding other causes of peripheral neuropathy. Further studies are highly recommended.

**PUB084**

Hemodialysis Prescription in Ethylene Glycol Overdose: A Mathematical Approach

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**Introduction:** The timely management of Ethylene glycol (EG) overdose is essential. Hemodialysis (HD) is indicated for rapid elimination of its toxic metabolites. We introduce a case diagnosed shortly after presentation prior to the availability of the blood EG level and share calculations that were used to precisely and accurately estimate the clearance of EG through HD.

**Case Description:** A 61-year-old male presented with unresponsiveness. Labs were notable for anion positive metabolic acidosis with anion gap 28, osmolar gap 57, along with stage 2 AKI. His whole blood lactate was >17.1 meq/L, with a venous lactate of 0.5 meq/L. EG intoxication was diagnosed based on high lactate gap (16.6) and calcium oxalate monohydrate crystals in his urine sediment. He was given fomepizole and hemodialysis for EG toxicity to normalize. We calculated HD prescription based on the metabolite calculation which we have been using reliably to calculate HD duration and post HD EG level. His predialysis EG level was 71 mg/dL. To calculate the EG removal via HD, we need patient's predialysis EG level and share calculations that were used to precisely and accurately estimate the clearance of EG through HD.

**Discussion:** The timely management of EG intoxication is delayed and calculation of HD prescription remains a challenge due to lag in obtaining serial EG assays in clinically useful time frame. We present a case of EG toxicity that we were able to diagnose promptly with laboratory workup to wait for EG blood levels, and we present a simplified approach to determine the duration of HD based on a single EG assay. This calculation can be used to individualize HD treatments and avoid over or undertreatment of intoxication.
The Excretion Formula of Phosphorous, Potassium, and Salt Amounts

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Background: We elucidated the contribution of residual renal function (RRF) to the phosphorous, potassium and salt excretion and established the estimation formula of these amounts which are excreted into urine by RRF of hemodialysis patients.

Methods: We collected the 24 hours urine from 22 hemodialysis patients (mean age: 73.1±12.1 years old, dialysis history: 31.4±29.3 months, 15 males, 12 diabetics). The urine volume, phosphorous, potassium and salt amounts in the 24 hours urine and creatinine clearance were determined. The correlation coefficients among the urine volume, amounts of phosphorous, potassium and salt, and creatinine clearance (Ccr) were calculated.

Results: The mean urine volume was 6626±421/mL/day. The mean phosphorous amount in the urine was 114.5±55.9 mg/day, potassium 418.2±2212.4 mg/day, and salt 4.7±2.6 g/day. Ccr was 3.7±1.8 mL/min. There was a significant positive correlation: urine volume vs phosphorous amounts (r=0.759, p<0.001), urine volume vs potassium amounts (r=0.662, p=0.001). (Phosphorous amounts in the urine=134x[24 hours urine(L)]-130). There was a significant positive correlation between urine volume and salt amounts excreted into urine (r=0.915, r2=0.84, P=0.001). (Salt amounts in the urine=5.7x[24 hours urine(L])-0.2). The amount of urinary excretion of phosphorous and potassium can be roughly estimated.

Conclusions: As for phosphorous and potassium, if 24 hours urine volume is known, the amount of urinary excretion of phosphorous and potassium can be roughly estimated. As for salt, if 24 hours urine volume is known, the amounts of urinary excretion of salt can be estimated with 84% accuracy. Measuring urine volume in hemodialysis patients can estimate solute excretion roughly.

Treatment of Uremic Tumoral Calcinosi in Maintenance Hemodialysis Patients

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Background: Uremic tumoral calcinosi (UTC) is a rare disease with metastatic tissue calcification in maintenance hemodialysis (HD) patients. However, limited data are available on treatment of UTC in HD patients. This article mainly discusses the diagnostic findings and efficacy of treatment in HD patients with UTC.

Methods: A retrospective analysis was conducted on the data of 13 cases of UTC, including their clinical features, biochemical indicators, imaging findings, diagnosis, therapeutic methods and follow-up results. Parathyroidectomy (PTX) or drug treatment were determined based on intact parathyroid hormone (iPTH) levels and clinical symptoms.

Results: All of 13 patients were diagnosed as UTC definitely by imaging examination. The predominant areas involved were the buttocks (4 cases, 30.77%), shoulders (4 cases, 30.77%), and elbows (3 cases, 23.08%). Based on the levels of iPTH, cases were categorized into two different groups: PTX treatment group was associated with high levels of iPTH, while drug treatment group (lanthanum carbonate or sevelamer with STS) was lower iPTH. After PTX treatment, there was a significant decrease in serum iPTH, calcium (Ca), phosphate (P) and alkaline phosphatase (ALP) levels (p<0.05). In drug treatment group, the serum P levels was decreased significantly, along with a finding that hemoglobin levels was increased (p<0.05). All the UTC had lessen or even disappear after treatment 4 to 6 months.

Conclusions: Although most UTC patients have an increased iPTH, a small number had lower iPTH levels. Based on iPTH levels and clinical symptoms, the patients were treated with PTX or drug therapy. With proper treatment, UTC disappeared without the need for surgery to remove calcinosi tissue.
Conclusions: It has been demonstrated that flow balance error and fluid removal attainable with SC lies well within the acceptable standards permitted for haemodialysis machines, demonstrated across a range of clinically relevant parameters at dialyse flow rates of up to 500ml/min.

Funding: Commercial Support - Quanta Dialysis Technologies

PUB089

Clinical Performance of the Optiflux® F160NR Dialyzer

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Background: Subjects in the clinical trial (NCT# 03536663), An Open-Label Clinical Study to Assess the Performance of the Dialyzer with Endexo10 in End-Stage Renal Disease Subjects, were dialyzed with the Optiflux® F160NR dialyzer, followed by the new dialyzer with Endexo. This sub-analysis reports the safety and performance of the Optiflux® F160NR dialyzer.

Methods: Subjects prescribed three-weekly HD for at least 30 days at three US study sites were enrolled in the study. The Optiflux F160NR dialyzer study period included 12 HD treatments. Performance and safety assessments included URR, spKt/V, serum albumin and β2-microglobulin levels with removal rates measured pre and post HD, complement activation, and Adverse Events (AEs).

Results: Twenty-six subjects were screened. Twenty-three subjects were enrolled in the study (median age 64 years, females 73.91% and white 73.91%) and completed 268 HD treatments with the Optiflux F160NR dialyzer. Four subjects discontinued the study due to missed visits, not related to adverse events. 19 subjects completed all 12 HD treatments per protocol (n = 228 dialysis sessions). Delivered HD treatments are presented in Table 1. No SAEs were reported during the study. Four subjects reported at least one adverse event not device related. Mean (SD) for enrolled subjects were: 80.5% (4.5) for URR, 1.9 (0.3) for spKt/V, 47.1% (7.4) for corrected β2-microglobulin removal rate and an increase of 8.3% (8.2) post HD for serum albumin. Complement activation was measured Pre HD and 30 min Post HD start and showed no overt activation for C3a, C5a and SC5b-9.

Conclusions: HD treatments were well tolerated and URR and spKt/V were high with Optiflux® F160NR dialyzer. Serum albumin levels increased post HD. Complements showed no overt activation.

Funding: Commercial Support - Fresenius Medical Care North America

Table 1. Delivered HD for completed subjects (n=19, 228 HD sessions)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>HD Delivered</th>
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<td>20</td>
<td>228</td>
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PUB090

Diabetes Disequilibrium Syndrome: Severe Irreversible Brain Injury Following Hemodialysis

Fatima Ballout, Pravir V. Baxi, Roger A. Rodby. Rush University Medical Center, Chicago, IL.

Introduction: Diabetes disequilibrium syndrome (DDS) is a clinical complication of hemodialysis characterized by neurological symptoms attributed to cerebral edema that rarely occurs in ESKD patients following their first HD treatment. Treatment is primarily preventative, aimed at decreasing the rate of urea clearance to reduce subsequent osmotic fluid shifts. We describe a case of DDS with severe neurological sequelae in a patient with acute on chronic kidney disease.

Case Description: A 39 yo man with CKD 4 presented with dyspnea, lethargy and confusion. Initial labs showed a Na 133 mmol/L, K 7.9 mmol/L, BUN 281 mg/dl and creatinine 38.6 mg/dL. HD was initiated for treatment of uremia and hyperkalemia. Two hours after the start of HD, the patient had a tonic-clonic seizure followed by cardiopulmonary arrest. Lab data post-arrest showed a Na 133 mmol/L and BUN of 112 mg/dL (Fig 1). In the subsequent days, the patient remained in a comatose state. MRI of the brain revealed cortical restricted diffusion in both cerebral hemispheres and bilateral basal ganglia, concerning for hypoxic-ischemic injury. His clinical status did not improve over 3 months. He required a tracheostomy and PEG tube placement with HD dependency on discharge.

Discussion: DDS remains a rare clinical phenomenon which typically occurs with initiation of HD in those with severe azotemia and advanced CKD. Risk factors include pre-existing neurological conditions, hypotension, and higher starting BUN levels. While the pathogenesis remains debated, DDS is believed to be due to a reverse osmotic effect that occurs due to a faster decline of urea within the blood versus the brain creating osmotic disequilibrium with subsequent movement of water into the brain causing cerebral edema. Idiogenic osmolytes may also be involved. Recognition of patients at high risk is crucial as it provides an opportunity to implement preventative strategies including reduced HD treatment time with lower blood flows aimed at more gradual clearance of urea.

PUB091

Sustained High-Dose Chronic CRRT Fails to Attenuate Severe Lactic Acidosis in an Immunotherapy-Resistant Case of Malignant Melanoma with Liver Visceral Crisis

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Introduction: Lactic acidosis is the most common cause of metabolic acidosis in hospitalized patients. Though of little proven benefit, continuous renal replacement therapy (CRRT) has been suggested as treatment in some patients. We describe a rare case of a patient with lactic acidosis who received nineteen days of high dose CRRT.

Case Description: A 60-kg Asian female with melanoma and extensive liver metastasis presented in a visceral crisis. She was given combination of nivolumab and ipilimumab which was projected to take 1 month to work. She had severe lactic acidosis with serum lactate of 17mmol/L on admission despite normal renal function. After a failed trial of medical therapy, CRRT was started purely for lactic acidosis. A spot measurement of effluent lactate was 15mmol/L while the corresponding plasma lactate was 16.3mmol/L, suggesting sieving coefficient of 0.92. Switching to a lactate free dialysate fluid multilic did not help. Despite uninterrupted CRRT for 19 days, and repeated increase of effluent dose to peak of 5L/hour, giving lactate clearance of 76.7ml per minute, there was no improvement. She eventually demise 4 days after cessation of CRRT.

Discussion: We describe an unfortunate case where 2 specialties tried hard to save this young patient from the fatal complications of her aggressive tumor. Type B lactic acidosis is better described in hematological malignancies but there are increasing reports in solid organ tumors, most with extensive hepatic involvement. We present the first case of melanoma causing lactic acidosis reported in literature till date. While CRRT, convective therapies, bicarbonate-based dialysis fluids have been suggested as treatment for lactic acidosis, there is little proven benefit. In our case, we combined all 3 strategies, persisted at high dose for 19 days with no success. 2 learning points: Firstly, lactic acidosis in the absence of hyperperfusion (Type B) is not uncommon and equally dangerous. Secondly, while dialysis removes lactate to some extent, it is at best a temporizing measure. Addressing the underlying cause takes priority. Dialysis, regardless of dose, modality and timing is less likely to affect outcome.

PUB092

Primary Caregiver Burden in a Hemodialysis Clinic in Mexico: Prevalence and Caregiver-Related Risk Factors

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Background: Dialysis treatment is defined as a family disease. Primary caregiver is the main person who takes the responsibility for and supports the patient; caregiver burden can be defined as the strain or load borne by a person who cares for a chronically ill family member. The Zarit survey is a psychometric instrument designed to grade caregiver burden, recommended and validated among caregivers of patients in hemodialysis.

Methods: A descriptive study was conducted among primary hemodialysis caregivers from a dialysis clinic in Guanajuato, Mexico. Zarit Scale (A validated 22-item questionnaire with five item ranged from 0=never to 4=always) was applied in order to identify presence and level of caregiver burden. Caregivers of patients less than 3 months were excluded. Social and demographic data related were also collected. Data was analyzed for descriptive statistics using T-test and Chi square for comparison between groups.

Results: A total of 86 primary dialysis caregivers answered the survey via personal interview with one of the investigators. Most respondents were female (77%) with a mean age of 47±15 years old. Seventy seven percent were married and almost all had an occupation (95%): homemaker (43%) was the most common. We found that couples take care of patients in 42% of cases, followed by parents (27%). Interestingly, 46% of responders did not take own recreational time and some of them (38%) were diagnosed with some chronic illness. More than half (56%) usually take care of 1 to 3 more persons along with the patient and meantime of life spent caring was 2 years. Any level of caregiver burden was identified in 67%, most of them (86%) in a slight level. There were not statistical differences between groups with none and any burden.

Conclusions: ESRD affects not only patients but also the people who takes care of them. Caregivers burden is prevalent in our clinic. Caregivers are predominantly female
partners who have to cope with patients care along with attendance of other relatives and often the need to work for economic support of their families. These results should be added to the public health burden of ESRD in Mexico.

**Conclusion:** Everyone of us should be aware how our daily activity influence on the environment. Both, medical industry and nephrologists are responsible for decreasing the quantity and weight of medical waste produced during dialysis treatment. Careful proceeding with the disposables (proper procedures, medical staff training and awareness) will directly help to make the HD treatment more cost-effective and help to protect our planet.

**PUB095**

**Early Intervention of Continuous Hemodialysis Filtration Is Effective to Improve Acute Kidney Injuries and Mortality in Patient with Propofol-Related Infusion Syndrome**

**Introduction:** Propofol related infusion syndrome (PRIS) is a fatal syndrome that often develops under the long-term propofol infusion at high doses. The main features of the PRIS consist of cardiac failure, rhabdomyolysis, acute kidney injury, and severe metabolic acidosis. High dose propofol, but also supportive treatments with catecholamines and corticosteroids, act as triggering factors. Propofol is usually administered at 0.3–4.0 mg/kg/hr or less to the sedation of adult patients, and is not administered beyond 7 days to prevent PRIS. We report here a case of PRIS developed rhabdomyolysis, acute kidney injury, and severe metabolic acidosis under the dose of propofol within the safety dose.

**Case Description:** A 41-year-old woman was operated cervicopharyngeal posterior longitudinal ligament ossification. After the operation, maximum 3.5 mg/kg/hr of propofol was used for sedation for treatment of severe pneumonia under the mechanical ventilator. Catecholamines was also used to support hemodynamics. However, unidentified hypoxemia and impaired blood pressure were prolonged, then administration of propofol was discontinued on POD6. Acute kidney injuries (sCr 2.3 mg/dL), metabolic acidosis and high serum CK (79300 U/L) due to rhabdomyolysis were observed on POD8. Continuous hemodialysis filtration (CHDF) therapy was initiated, and hyperthermia, oxygenation, impaired hemodynamics and renal dysfunction were gradually improved. Finally, cardiac failure and renal function were totally recovered.

**Discussion:** Propofol impairs free fatty acid utilisation and mitochondrial activity. Imbalance between energy demand and utilisation is a key pathogenetic mechanism, which may lead to cardiac and peripheral muscle necrosis. CHDF may effective to maintain renal function and acid-base equilibrium through removal of metabolites induced by mitochondrial damage, such as lactate and creatine kinase. PRIS particularly when combined with catecholamines can be lethal and we suggest early intervention of CHDF is effective to improve renal injuries and mortality.

**PUB096**

**The Conduct of Sponsored Trials Has No Association with Dialysis Facility Clinical Quality Outcomes**

**Background:** There is a paucity of clinical trials conducted in nephrology vis-à-vis other fields (Baigent, et al. 2017). The lack of knowledge on impacts of trial conduct on dialysis facility operations can create barriers between stakeholders. We aimed to assess for clinical quality target achievement in dialysis facilities conducting trials versus matched facilities not involved in research activities that are necessary for advancing the state of the art.

**Methods:** We used data from adult (age ≥18 years) hemodialysis patients treated at a single provider network in the United States during 2017 to 2018. Facilities that did not participate in trials were matched to research facilities using 1:1 matching on logit of propensity score for patient years of follow-up, years of certification, % of Medicare patients, % of ESCO facilities and geographical region. We cross-sectionally compared mean facility-level quality metrics for: anemia (%Hgb a10 & <10g/dL), mineral bone disorder (%calcium c10.0mg/dL & %phosphate c4.5mg/dL), and event outcomes (%catherer exposure >90 days, % treatment non-adequacy, 30 day readmission rates, hospital days/patient year).

**Results:** We found no significant differences between mean facility-level quality metrics in dialysis facilities that conducted trials versus matched facilities not involved in research (Figure 1).

**Conclusions:** We found the conduct of trials in dialysis facilities had no association with achievement of quality targets, as compared to matched facilities not participating in trials. These insights are of importance to providers and stakeholders participating in considering nephrology research activities that are necessary for advancing the state of the art.

**Funding:** Commercial Support - Fresenius Medical Care
Impact of Major Surgical Operations on Clinical Outcome in Dialysis Patients

Methods: We retrospectively evaluated the records of all patients on HD and PD, who had been treated for at least 3 months at our outpatient clinics between January 1, 2014 and December 31, 2018. In addition to clinical and laboratory parameters, data on all major surgical operations were recorded.

Results: Among the 202 patients, 133 (66%) were on HD and 69 (34%) on PD. The mean age (±SD) was 58.3±14.5 years, 48% were female and 28% had diabetes mellitus. Forty-seven patients (23%) had a major surgical operation. The operation types were cardiovasculary in 14 patients, orthopaedic in 11, gastrointestinal in 8, genitourinary in 7, and breast in 1 patient. Operations were emergent in 10 patients (21%) and elective in the others (79%). Among the whole study population, 59 patients (29%) died during the study period. In Kaplan-Meier analysis (Figure), mean (±95% CI) survival time in operated patients was 43 months (±7 to 49 months), while it was 49 months (±6 to 52 months) in the others (p=0.001). Fifteen out of 23 deaths (65%) among the operated patients occurred in the first month after surgery. Severe perioperative complications (arrhythmias, hypervolemia, hypotension, bleeding, acute coronary syndrome, respiratory failure and cerebrovascular event) were recorded in 17 (36%) of the operated patients, of whom 16 died (p=0.001). Although did not reach a significant level, mortality rate tended to be higher after emergent operations than that after elective operations. Cox regression analyses revealed that age (RR 1.007, 95% CI 1.002-1.007, p=0.001) and diabetes (RR 2.581, 95% CI 1.474-4.521, p=0.001) were independent predictors of mortality.

Conclusions: Although prospective studies with a higher patient number are needed to confirm, our study shows that, in addition to age, diabetes and inflammatory status, having a major surgical operation is an independent risk factor for mortality in dialysis patients.
Achromobacter Xylosoxidans, Subspecies Denitrificans, Exit Site Infection, and Aeromonas Hydrophilia Peritonitis: Rare Infections in Peritoneal Dialysis Patients


Background: Achromobacter xylosoxidans, subspecies denitrificans, exit site infection in peritoneal dialysis patient is rare and will be reported. A second case of rare peritoneal infection caused by Aeromonas hydrophilia peritonitis will also be reported. Both are gram-negative microorganisms and are usually found in wet environments, causing infections in immunocompromised patients. Both cases occurred in the same rural city and in the same dialysis facility.

Methods: The cases involved conducting interviews with patients and documenting each visit. All observations and visitations were assessed in the dialysis center of a rural area. Previous data of cases with similar rare pathogen caused peritonitis were also analyzed.

Results: The patient with exit site infection, Achromobacter xylosoxidans, was treated with oral ciprofloxacin for 3 weeks resulting in a slow improvement of the exit site. During treatment the patient experienced erythema, discomfort, and discharge. At the end of the treatment, repeat cultures drawn from the exit site were negative. The patient with Aeromonas hydrophilia peritonitis is currently being treated with intraperitoneal gentamicin.

Conclusions: Achromobacter xylosoxidans and Aeromonas hydrophilia are both rare bacterial infections that have a history of causing infections in immunocompromised individuals exhibiting multiple risk factors. We reported exit site infections and peritonitis in end stage kidney disease patients. Both infections have been treated without any adverse effects or removal of peritoneal dialysis catheters.

Bicarbonate-Rich Peritoneal Dialysis as Salvage Therapy for Metabolic Acidosis

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Introduction: Use of peritoneal dialysis (PD) in ICUs in developed nations is limited. The need for emergent dialysis is often considered a contraindication for peritoneal dialysis and the large peritoneal surface area is often neglected in the resuscitation of critically ill patients. We report a case of successful emergent PD with high bicarb dialysate in an actively dying patient not tolerating standard renal replacement therapies.

Case Description: A 36 yo male with no medical history sustained multiple gunshot wounds. He was found to have multiple injuries in the small bowel including the duodenum. Two 15-french drains were placed at the time of surgery. While initially stable, he gradually developed worsening hypotension and a declining hematocrit requiring a bedside laparotomy that evening. A severe metabolic acidosis remained refractory to standard therapy. CRRT was started briefly but he was unable to tolerate due to worsening hypotension. His pH worsened (pH 6.97) with bicarb 6mmol/L and lactate (LA) 26.9mmol/L. Family said their goodbyes and he was made DNR. Methylene blue was given without hemodynamic change. Given his young age, inability to tolerate CRRT and intraperitoneal access already available, decision was made for emergent PD as a final effort to control refractory acidosis. Approximately 1L of 1.5% peritoneal dialysate with an additional 300 mEq sodium bicarb/2L bag was instilled for a 30 minute dwell time. Within an hour, his labs showed pH 7.12, bicarb 15mmol/L, LA 16mmol/L and his vasopressor requirements decreased. After four exchanges, CRRT was initiated. His acidosis resolved within 24 hours and he was vasopressor free by 36 hours. He was extubated, dialysis dependent and continues to recuperate.

Discussion: PD in developed nations is often a forgotten modality for acute renal failure. We found only 2 published reports since 1980 using PD in the ICU for metabolic control. Our case describes successful use of high bicarbonate PD in the ICU to control refractory acidosis and achieve hemodynamic control. Data is lacking on the use of emergent PD in trauma patients and within ICUs despite its relative case and low cost. High bicarbonate PD is an option for refractory acidosis in the critically ill.

Myoclonic Seizures and Altered Mental Status in a Patient on Peritoneal Dialysis Treated with Piperazine

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Introduction: Here we present the case of a man on automated peritoneal dialysis (APD) with altered mental status and myoclonus after the self-administration of piperazine as antihistamine. This case illustrates how dangerous self-medication can be in patients with chronic kidney disease. Additionally, it shows that neither peritoneal dialysis nor hemodialysis appear effective methods for piperazine clearance in patients on renal replacement therapy (RRT).

Case Description: A 66-year-old man was brought unresponsive and with myoclonus to the ER. His past medical history included diabetes mellitus, with diabetic nephropathy that lead to ESRD. He was started on RRT 1 year before presentation; initially hemodialysis (APD) with altered mental status and myoclonus after the self-administration of piperazine as antihistamine. This case illustrates how dangerous self-medication can be in patients with chronic kidney disease. Additionally, it shows that neither peritoneal dialysis nor hemodialysis appear effective methods for piperazine clearance in patients on renal replacement therapy (RRT).
suspected bacterial infection as the cause of the altered mental status, empirical antibiotic treatment was initiated. However, the patient’s symptoms persisted, requiring care at the ICU and intubation. Further interrogation of the patient’s family revealed that he had self-administered a full bottle of piperazine hexahydrate. An infectious cause was ruled out and no clinical improvement was achieved with antiepileptics. At this point, piperazine intoxication was our most likely diagnosis. After a week of APD we decided to switch RRT to sustained low efficiency hemodialysis (SLED). He received two sessions. Gradually the patient’s mental status improved and was discharged with his usual APD.

Discussion: The most common symptoms of piperazine intoxication are myoclonus, decreased level of consciousness and ataxia. Few data is available regarding the diazilabilty of this medication, and neither PD nor HD seem effective treatment options. Hemoperfusion seems a suitable alternative. Clinical improvement in this case may be due drug metabolism, independent of treatment. We want to highlight the importance of education in renal patients, specially in the dangers of self-medication. Fortunately, our patient had a full recovery. But that may not be the case of other patients who inadvertently poison themselves with “safe” medications; like piperazine.

**PUB106**

Two-Year Follow-Up of Quality Indicator Compliance in a Large International Peritoneal Dialysis Institution


**Background:** Peritoneal dialysis (PD) practice is not universally homogeneous, best clinical practices are not completely understood as reference values are often obtained from small sized populations and/or frequently based on chronic kidney disease (CKD) and/or hemodialysis data. **Objectives:** To evaluate two years of follow up of compliance with PD-related quality indicators (QIs) following definition of new targets in an international PD network.

**Methods:** All English and Spanish language CKD and PD guidelines were reviewed. Twelve QIs were considered being of significant relevance and targets for these QIs were defined (see table). Retrospective data analysis

**Results:** Achievement of QI targets for years 2017-2018 is shown in table (image). Variability among countries not shown.

**Conclusions:** There was a significant increase in QIs achievement in 2018 vs. 2017. 75% of patients met the target for the following variables: total weekly Kt/Vurea, 24 h fluid removal, mean arterial blood pressure and serum albumin. Peritonitis rates are clearly over International objectives and were improving. Due to the lack of referral source data, these series may help to understand PD practice and outcomes in a global setting.

**PUB107**

Acyclovir-Induced Encephalopathy in a Patient on Peritoneal Dialysis

Areen Kate M. Kuan, Shamir Hasan, Yuri Khanin, Hugo Andrade paz, Nupur N. Uppal, Mala Sachdeva. *Northwell Health, Great Neck, NY.*

**Introduction:** Acyclovir is an antiviral agent that is used for treatment of diverse viral pathologies. The regular pharmacokinetics for acyclovir is altered with kidney dysfunction. At present, our knowledge regarding treatment of acyclovir neurotoxicity in patients undergoing peritoneal dialysis (PD) is limited, as only few case reports have been published. We describe a case of acyclovir induced encephalopathy in a PD patient that was successfully treated with hemodialysis.

**Case Description:** 34F with a history of systemic erythematous lupus (on prednisone, celcept and plaquenil), ESKD on peritoneal dialysis (PD), subclinical hypothyroidism, anemia and hypertension was admitted for her lips and right eyelid. She was initiated on intravenous acyclovir at a dose of 500mg daily. 24 hours later, she developed acute confusion which progressed to include myoclonus, lethargy and coma. Labs on admission revealed hemoglobin 10, Na 137, K 4.6, Cl 92, CO2 22, BUN 64, Cr 20.85. CT head was negative. EEG did not reveal any epileptiform activity. Lumbar puncture and brain MRI did not show any evidence of viral encephalitis. Acyclovir neurotoxicity was considered as the etiology for her severe encephalopathy. Acyclovir was held and her CCPD prescription was increased but she continued to remain encephalopathic. A decision to initiate hemodialysis (HD) was made. After the first HD session, her mentation slightly improved. She received a total of 3 HD sessions, after which her mental status completely returned to baseline. Given that she improved after discontinuation of acyclovir and with HD this confirmed her diagnosis of acyclovir induced neurotoxicity. She was switched back to PD after recovery.

**Discussion:** Dose adjustment for acyclovir is recommended in patients with ESKD. Even when the acyclovir dose is adjusted for these patients, it can still cause neurotoxicity. This complication seems to be more common in those on PD likely due to the slower removal of the medication with PD. Clinicians need to be aware of this potential adverse event, as this diagnosis needs prompt recognition and treatment. Clearance of acyclovir with PD is not completely understood and in fact PD was not adequate to help with clearance in our patient despite increasing her prescription. The modality of choice for clearance of acyclovir in toxicity is hemodialysis.

**PUB108**

The Analysis of Risk Factors for the Patients with Venous Needle Dislodgement and Bleeding During Hemodialysis

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**Background:** A puncture of vascular access is commonly used in clinical treatment, such as hemodialysis or central venous catheters. Leakage or infection associated with Venous needle dislodgement (VND) is a high risk of fatality. However, only a few studies are focusing on patient disease, medication, and other risk assessments. Therefore, this study aims to explore the risk factors of patients with venous needle dislodgement and bleeding and hope to establish the risk classification.

**Methods:** This study was a prospective study conducted in the hemodialysis unit of Tainan Regional Hospital. During three months from July 2019 to Sep 2019, we collected clinical data, including patient sex, gender, diseases, records of dialysis access leakage, anti-coagulant dose, and a risk assessment form. We compared the data between the two groups of patients who have at least one risk in the risk assessment form. We analyzed the data with STATA™. P<0.05 was defined as significant.

**Results:** In the study period, seventy-one patients were included in this study, with an average age of 63.0 (± 1.19 years) and 46 males (64.79%). The patients with any risk in the risk assessment form were considered the high-risk group. There were 72 venous needle dislodgement and bleeding in 32 patients during the study period. In the below feature, gender, high-risk group or not, diabetes, high blood pressure, exposure to Benzodiazepine, the experience of Intradialytic hypotension, exposure to warfarin, or dosage of anti-coagulant, there was no statistic significant between the patients experienced at least one episode of VND and others.

**Conclusions:** Between patients experience VND or not, we did not find any significant association in not only conventional factors or other factors. However, this study provides a reference for future research.

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**Results:** Total number of patients studied were 16. The average age was 66.6 years. All were hypertensive and diabetics comprised 75% of study group. Coronary artery disease was established in 81.25%, and two patients were known to have chronic liver disease. Most common type of AVF was the left brachio-cephalic (62.5%), followed by radio-cephalic (37.5%). Average dialysis vintage of AVF at the time of procedure was one year. Previously failed AVF was present in two patients. There were 18 vascular stenosis in 16 patients. The most common site of stenosis was the venous cannulation zone (62.5%), followed by anastomotic site stenosis (31.5%) and central vein stenosis (18.75%). Successful PTA was done in 12 patients. There were no complications; hemodialysis was resumed within one week after the procedure. The primary patency rate at three months was 100%, six months was 75% and at one year it was 37.5%. Four patients were lost to follow up. Mean follow up was 9.41 ± 7.79 months. None underwent a repeat PTA.

**Conclusions:** Percutaneous transluminal angioplasty is effective for salvaging arterio-venous fistula in majority of hemodialysis patients.

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**PUBLII**

**A Tale of Two Accesses: The “Less Is More”**

Sherif Metwalli, Anil K. Agarwal, Khaled Boubes. The Ohio State University, Columbus, OH.

**Introduction:** Well-functioning dialysis access is of utmost importance as the lifeline of those with end stage kidney disease (ESKD). We present 2 patients with ‘imperfect’ accesses where a conservative approach avoided potentially problematic interventions.

**Case Description:** Case 1: A 24 year old man started hemodialysis (HD) in 1992 due to IgA nephropathy. He received a kidney transplant in 2000 which failed in 2005 requiring hemodialysis again. His vascular access consisted of multiple bilateral failed arteriovenous (AV) fistulae and AV grafts requiring numerous access interventions including tunneled HD catheter placements, angioplasties, and thrombectomies. He has also developed severe contrast allergy, making any further vascular interventions difficult. Since 2005 he has been dialyzing through a right upper extremity AVF complicated by central venous occlusion causing mild right arm swelling. Last resort vascular access options including a femoral AVG and a HeRo graft were contemplated. However, clinical decision making based on the presence of extensive collateral circulation, we opted for a conservative approach instead utilizing low blood flow rates. He has been doing well on this prescription for the last 3 years with adequate dialysis and swelling resolution. Case 2: A 67 year old woman with ESKD started peritoneal dialysis (PD) 2 years ago. PD was complicated by recurrent malpositioning of PD catheter with the catheter tip repeatedly migrating to the right upper quadrant. Changing the catheter insertion site and suturing it to the bladder wall did not prevent tip migration. Transition to HD was contemplated but she was able to continue with PD albeit with position changes to allow for complete drainage of PD fluid. Despite occasional sluggish drainage of PD fluid, the patient continued on PD for a total of 15 months before receiving a kidney transplant.

**Discussion:** These 2 cases illustrate the importance of dialysis access function as well as the dilemma of both the patient and provider when it becomes dysfunctional. The cases, however, also demonstrate that anatomical perfection is not always necessary to achieve adequate function. In both cases, a conservative approach allowed the patient to optimize dialysis through their existing ‘malfunctioning’ access and avoided further interventions that could result in worse complications, proving the adage ‘Less is More’ still true for dialysis access.

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**PUBLII**

**What Are Nephrologists' Preferences Related to Continuing Medical Education?**

Amy Larkin, Donald Blatherwick. Medscape LLC, New York, NY.

**Background:** Understanding how clinicians prefer to learn and participate in continuing medical education (CME) can help providers of such education design more engaging and effective activities that can potentially further improve nephrologists’ clinical performance.

**Methods:** Medscape conducted a 10 question, online, incentivized survey in November 2018. Respondents’ confidentiality was maintained and responses were de-identified and aggregated prior to analysis.

**Results:** Most preferred duration for a CME activity: 30 minutes (51%) Followed by 15 minutes (31%) Most preferred format for a CME activity: online (70%) Followed by live events at a medical conference (13%) Most preferred format for an online CME activity: video and text (45%) For online CME: Most preferred instructional design format: case-based (56%) Most important factors in selecting online CME/CE activities: content description (60%) and learning objectives (56%) The most important factors in selecting which symposia to attend at a scientific congress were content coverage (60%), learning objectives (41%), and faculty (33%). Most common ways of becoming aware of available professional education activities: invitation from online providers (79%) and societies (74%) The majority of participants reported that in the past 12 months they have learned something from CME that changed their practice (86%) Most learning is more impactful and clinically meaningful than a single activity (80%)

**Conclusions:** CME activities have an impact on changing clinician practices. Learner preferences for nephrologists related to live and online CME were identified. Most prefer participation in multiple activities that are online, 15-30 minutes, case-based, video and text description, learning objectives, and faculty play an important role in learner participation. These data should inform development of future CME activities that are engaging and impactful.

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**PUB109**

**Catheter Malposition: Unacceptable Reason for Access Dysfunction**

Yuliya Sharakova, Mohamed Hassanein, Evamaria Anvari, Tushar J. Vachharajani. Cleveland Clinic, Cleveland, OH.

**Introduction:** In 2017, 80% incident and 20% prevalent patients in the US received hemodialysis (HD) with a catheter (CVC). CVC placement with ultrasonography and fluoroscopy guidance (FG) is an accepted standard of care to avoid early mechanical complications. Early dysfunctional CVC (dCVC), defined as malfunction in <1 week of insertion is often due to a malpositioned tip leading to inadequate HD and a higher risk of bacteremia. We present a series of early dCVC, a preventable complication.

**Case Description:** Case 1: 42 y/o male had left IJ non-tunnelled CVC placed for discontinuous dialysis therapy. Encountered multiple episodes of circuit clotting soon after initiation of therapy despite heparinization. The CVC tip was found to be abutting against the innominate vein wall preventing adequate blood flows. An attempt to place a tunneled right subclavian vein catheter at bedside, without fluoroscopy was unsuccessful. Chest XR showed the CVC tip in the left IJ. Case 2: 30 y/o male with a pre-existing right portacath presented with several episodes of non-sustained ventricular tachycardia, 2 days after a newly placed left dialysis CVC. Chest XR showed portacath had disconnected and migrated to the right ventricle. Removal of the dislodged portacath led to resolution of arrhythmia. Dialysis CVC was preserved. Case 3: 49 y/o obese female had poor blood flows (300 ml/min) in catheter and frequent alarms that failed to improve despite tPA and port reversal. dCVC resulted from tip retraction from right atrium into SVC requiring replacing with a longer CVC. Case 4: 65 y/o female with left IJ tunnelled CVC, placed under FG, had poor blood return 2 days after placement. The CVC tip had migrated to the right innominate vein. Catheter was replaced successfully. Case 5: 70 y/o male encountered clotting of the continuous dialysis circuit soon after initiation with a left IJ CVC, requiring replacement of circuit to continue with therapy. Evaluation showed a short CVC with tip abutting against superior vena cava (SVC) wall and required replacing with a longer CVC

**Discussion:** Recognizing and troubleshooting early dCVC is an essential learning milestone for a nephrology trainee. Evaluation of a dCVC includes chest XR, forceful saline flush and appropriate use of tPA. Most of these mechanical complications are preventable with proper training and utilizing imaging tools during the procedure.

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**PUB110**

**Percutaneous Transluminal Angioplasty in Arteriovenous Fistula**

Ahmed Khan, Mohamed J. achharajani.

**Results:** Among 290 patients receiving hemodialysis in the hospital radiology archive system. Demographic characteristics, duration of dialysis, symptoms and laboratory values were compared between patients with and without impaired catheter function. A total of 30 patients were included in the study. The average age of the study population was 60.7 years (range 25-85). Male patients represented 56.7% of the study population. The average duration of dialysis was 6.79 months. None underwent a repeat PTA.

**Conclusions:** Percutaneous transluminal angioplasty is effective for salvaging arterio-venous fistula in majority of hemodialysis patients.

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**PUB111**

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Amy Larkin, Donald Blatherwick. Medscape LLC, New York, NY.

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Underlines represent presenting author.

822
Online Education Effectively Improves Nephrologists' Knowledge, Competence, and Confidence Related to Hyperkalemia Management


Background: To improve outcomes for patients, clinicians must be able to implement evolving standards of care and apply relevant data on hyperkalemia management. We sought to determine if an online continuing medical education (CME) curriculum could improve hyperkalemia management.

Methods: The online CME curriculum consisted of 4 activities. Of these, 3 were 30-minute video panel discussions. A repeated pairs pre-/post-assessment study design was used and McNemar's test assessed educational effect for each activity. The last activity comprised two patients presenting in a VPS platform that allows learners to order lab tests, make diagnoses, and prescribe treatments in a manner matching the scope and depth of actual practice. Tailored clinical guidance (CG), based on current evidence and expert recommendation, was provided following each decision, followed by the opportunity for the learner to modify to their decisions. Decisions were collected post-CG and compared with each user’s baseline (pre-CG) decisions using a 2-tailed paired t-test to determine P values. The activities launched in 2019 and data were collected for 4-12 weeks.

Results: Education significantly improved physicians’ knowledge, competence, and performance managing and treating hyperkalemia. A 40% relative increase was observed among nephrologists related to knowledge of clinical trial data related to hyperkalemia. Nephrologists also significantly improved their knowledge and competence regarding the use of therapies in practice, with a relative increase of 16% observed. Case based simulation had a strong and significant positive impact on physicians’ performance in the treatment of hyperkalemia. The % of physicians who decided to start preferred potassium-binder more than tripled after education.

Conclusions: Some gaps still remain after education. Over 40% physicians are still not equipped with the right information regarding clinical trial data and the use of therapies in practice. In addition, an average of 40% physicians are still not making the right decision to start preferred potassium-binder. As such, further education needed in these areas.

Funding: Commercial Support - independent educational grant from Astrazeneca and Fibrogen

Renal Clinic Quality Improvement Education Initiative

Rui Song,1 Iryna Danyluk,1 Colleen Rabitt,1 Diane Y. Woodford,1 Wayne A. Satz,2 Mark G. Weiner,3 Suma Prakash,1 1Lewis Katz School of Medicine at Temple University, Philadelphia, PA; 2Weill Cornell Medicine, New York, NY.

Background: Benefits of timely CKD modality education include increased knowledge and home dialysis. At our centre, attendance of scheduled CKD 4/5 patients to education sessions was low. This quality improvement study was initiated and aims to increase the prevalent percentage of CKD 4/5 patients who received CKD modality education from 40% to 55% over one year.

Methods: Outcome measure was prevalent weekly percentage of CKD 4/5 patients who completed education. Process measures were 1) weekly percentage of scheduled patients in attendance and 2) weekly number of incident CKD 4/5 patient education referrals by nephrologists. Ishikawa diagram was utilized to determine system gaps and develop changes to test in plan-do-study-act (PDSA) cycles. Changes tested were: a) NPs tracking weekly class attendance, b) NP reminder calls, c) information letter mailed to patients, d) referral data presented to nephrologists, e) reminder emails to nephrologists on education eligible patients. Discussion with primary care colleagues and 5-whys tool resulted in developing an information webpage for patient education including NPs’ zoom recorded sessions. Median outcome and processes were calculated and plotted on run charts.

Results: Prevalent percentage of CKD 4/5 patients educated decreased from 40.6% to 29.4%. All referred patients have not yet been educated due to COVID19 and number of new patients increased over time. Median weekly session attendance increased from 60-67% with PDS A cycles a–e (Figure 1). Monthly incident education referral numbers increased from 5-18/month.

Conclusions: Weekly session attendance and incident education referrals increased. Prevalent percent patients educated decreased but number of incident referrals increased. To provide a virtual information option for patients with barriers to attending sessions and for use during COVID19 pandemic, the webpage described is a helpful resource developed as a result this project. We anticipate this tool will increase the outcome and both process measures over time.

Optimizing On-the-Go Learning Utilizing Short Modules on Topics Related to Nephrology

Kirin Munir, Farah Daccueil, Stony Brook University Hospital, Stony Brook, NY.

Background: Residents and medical students are expected to formulate evidence-based treatment plans by keeping up with the most recent guidelines but that can be difficult given our schedules. In such circumstances, it is ideal to learn bite-sized pieces on the go.

Methods: We created two modules about Phosphorus Binders and Oral Hypoglycemic Agents using a friendly graphic interface called Prezi. These modules were estimated to take 10-15 minutes and were accompanied by a total of seven content related questions that were compiled from Uworld Step 3 Question Bank, John Hopkins Primary Modules, and hospital courses of patients seen at Stony Brook. Survey monkey was utilized to create the pre and posttest. The modules were sent to third and fourth year medical students. Data was collected for 10 days.

Results: Wilcoxon signed rank test was utilized to evaluate the effectiveness of the modules. Unfortunately, only six students completed the hypoglycemic module of which two had no improvement in scores, so no statistical significance was achieved. However, four of the six students had improvement in posttest scores by at least one point. Improvement in the posttest scores for the phosphorus module was significant as of the nine students who completed the phosphorus module, eight had an improvement by at least 1 point (W 36, p=0.008).

Conclusions: The observation of improved posttest scores for the phosphorus module supports the use of short lessons using a friendly graphic interface such as Prezi.
Ethylene Glycol Poisoning with Near-Normal Osmotic Gap: A Diagnostic Challenge
Moeed Ahmed, Cliff Janikowski, Aiza Ahmad, Lee E. Morrow. Creighton University School of Medicine, Omaha, NE.

Introduction: Ethylene glycol poisoning is classically associated with a high anion gap metabolic acidosis (HAGMA). Neurological and gastrointestinal symptoms predominate early while renal failure and death occur if not diagnosed and treated promptly. The diagnosis is usually suggested by HAGMA and an elevated serum osmolal gap in the setting of a suspected ingestion. Rarely, the serum osmolal gap may be close to normal which can delay the diagnosis or lead to a misdiagnosis. We report a case of ethylene glycol ingestion with near-normal serum osmolal gap.

Case Description: An 85-year-old man with a past medical history of Dementia presented to the Emergency Department with altered mental status, restlessness and serum osmolal gaps. Additional history obtained later from his family increased the suspicion for toxic alcohol ingestion. Ethylene glycol level, a send out lab, eventually resulted at an elevated level.

Discussion: The workup for a HAGMA should include evaluation of the serum osmolal gap in the setting of a suspected toxic alcohol ingestion. Although uncommon, the absence of an elevated serum osmolal gap should not prohibit treatment for toxic alcohol ingestion when the clinical suspicion is sufficiently high.

Hypernatremia Three Ways
Jordan R. Evans, Shweta Bansal. US Army Brooke Army Medical Center, Fort Sam Houston, TX; University of Texas Health Science Center at San Antonio, San Antonio, TX.

Introduction: Hypernatremia is a disorder commonly seen in hospitalized patients. It is often caused by dehydration from low water intake, GI, or urine losses. We present a case in which there were 3 distinct etiologies of hypernatremia that developed during the same admission.

Case Description: A 55 year old male with Down Syndrome and epilepsy was admitted from his nursing home for altered mental status and a 2 day history of lethargy and low oral intake. On admission, he had hypotension, tachycardia, and altered cognition from baseline but otherwise had unremarkable exam. He was diagnosed with klebsiella UTI, acute kidney injury, and hyponatremia. He was started on ceftriaxone and given 1 L of normal saline for hypovolemic hypotension, later switched to a continuous DSW infusion. Pertinent blood and urine chemistry after a liter of saline is shown in table 1. Over the next 4 days, sodium corrected slowly to 144 mEq/L, creatinine returned to baseline, and the D3W infusion was replaced with tube feeds. On day 6, he was again found to be hypernatremic but with polyuria. Urine chemistry (table 1) suggested osmotic diuresis which was attributed to high protein tube feeds. The polyuria and hypernatremia resolved with a change in feeds and D5W infusion. Meanwhile, he found to be in status epilepticus and intubated for prolonged hypoxia. Despite maximal anti-epileptic treatment, he continued to have frequent seizures. On day 9, he again had polyuria and hypernatremia but this time with lower urine osmolality (table 1). A central DI process was considered due to hypothalamic injury from status epilepticus, which has been reported seldomly. The urine osmolality increased to 413 mOsm/kg. A central DI process was considered due to hypothalamic injury from status epilepticus, which has been reported seldomly. The urine osmolality increased to 413 mOsm/kg.

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Underline represents presenting author.
underline represents presenting author.

**Case Description:** A 25-year-old female with Cronh’s disease presented with one month of worsening abdominal pain, diarrhea, and anorexia with reported 20 kg weight loss. She developed septic shock secondary to sigmoid colon perforation and underwent sub-total colectomy and end-ileostomy. Her hospital course was complicated by stage 2 acute kidney injury (AKI) secondary to acute tubular necrosis with a peak creatinine of 0.8 mg/dL from baseline of 0.3 mg/dL. Her AKI gradually resolved with supportive treatment. Over a 10-day period, she received a total of 20 g of acetylsalicylic acid with a total daily dose of 2 g. It was also noted that she had a persistent non-renal high-anion gap metabolic acidosis developed with serum bicarbonate levels as low as 11 mmol/L and a corrected anion gap of 26 mmol/L. Further laboratory data showed normal serum osmolality, blood urea nitrogen, beta-hydroxybutyrate, L-lactate, D-lactate, acetoaceton, and salicylate levels. A urine analysis showed a urine 5oxoproline level was markedly elevated at 26,740 mmol/mol creatinine. The patient’s severe metabolic acidosis resolved with discontinuation of acetylsalicylic acid and oral bicarbonate supplementation.

**Discussion:** Pyroglutamic acidosis is an often underrecognized condition requiring a high index of clinical suspicion for diagnosis. Urine or serum 5oxoproline levels are needed for diagnosis, which may not always be readily available. Chronic acetylsalicylic acid depletes intracellular glutathione resulting in increased levels of 5-oxoproline. Patients, like the one reported here, with malnutrition, female gender, sepsis, and kidney dysfunction are especially vulnerable as they have lower intracellular glutathione and therefore faster 5-oxoproline accumulation despite standard dosing of acetylsalicylic acid. Prompt recognition is essential for treatment with acetylsalicylic acid cessation and bicarbonate supplementation. The use of acetylsalicylic acid as an analgesic alternative to opioids is growing, especially in post-operative and critical care settings. Clinical awareness of predisposing conditions and close monitoring of patient’s acid-base and kidney status can help us mitigate this underrecognized complication of acetylsalicylic acid use.

**PUB123**

**Treatment Pattern of Hyperkalemia Among Patients Presenting Emergency Department in China**

Jianming Bian, Li Zuo, Houyu Zhao, Xu Han. Department of Pharmacology, Chinese People’s Liberation Army General Hospital, Beijing, China.

**Background:** In China, the treatment pattern of hyperkalemia (HK) among patients presenting emergency department (ED) is not well described.

**Methods:** Data containing hospital information system (HIS) records of 157 hospitals covering 30 provinces in China were extracted from Beijing Data Center for Rational Use of Drugs. Patients (aged ≥18 years old) in ED with record(s) of HK, defined as serum potassium (S-K) ≥5.5 mmol/L, were included in this study. The diagnosis rate was defined as the proportion of HK episodes that have diagnoses records. Treatment rate was defined as the proportion of HK episodes that have records of any HK treatment including diuretics, glucose injection + insulin (G+I), calcium injection, sodium bicarbonate, potassium binder or dialysis. Retesting rate was defined as the proportion of HK records that have potassium retest records within 1 day.

**Results:** A total of 36,015 HK cases were included. The overall HK diagnosis rate was 9.2%. Diagnosis rates increased by the severity of HK, patients with S-K >7.0 mmol/L showed the highest diagnosis rate of 31%. The overall treatment rate within 2 days was 45.2%, treatment rates increased by the severity of HK. Analyzing the HK episodes with HK treatment, G+I (used in 72.4% of HK episodes), loop diuretics injection (used in 50.36% of HK episodes) were most commonly used, while oral potassium binders, including sodium polystyrene sulfonate and calcium polystyrene sodium, were used in only 0.2% of HK episodes. Combined treatments were observed, among which a combination of G+I and loop diuretics injection was used in 10.4% of episodes and a combination of G+I, diuretics injection, calcium injection and sodium bicarbonate was used in 7.4% of episodes. Subgroup analysis of HK treatment in patients with chronic kidney disease showed that, G+I (used in 71.7% of episodes), loop diuretics injection (used in 61.2% of episodes) were most commonly used. The overall retesting retest rate within 1 day was 19.36%. Patients with S-K 5.0-5.5 mmol/L were retested less frequently (15%) than those with S-K >5.5 mmol/L (22.3-30.6%).

**Conclusions:** In China, the diagnosis and retreating rates of HK in ED patients was relatively low. Glucose injection + insulin was commonly used to treat HK in ED, while oral potassium binders were rarely used. Combination of treatments was common.

**PUB124**

**Factors Associated with Volume Overload in Pulmonary Arterial Hypertension**

Shweta Bansal, Ahmad Altarawneh, Chakradravti Vagapudi. The University of Texas Health Science Center at San Antonio Long School of Medicine, San Antonio, TX.

**Background:** Knowledge about the pathophysiology of volume overload in pulmonary arterial hypertension (PAH), a frequent and early complication, and major contributor to the development of right heart failure, is scant. We aimed to identify factors associated with volume overload in PAH patients.

**Methods:** We reviewed medical charts of consecutive 32 patients with PAH. Patients on loop diuretic were considered volume overloaded. Repeated measures of clinical and lab variables were recorded at the time of each right heart catheterization (RHC) were included for analysis. For comparisons between diuretic and non-diuretic groups, we used independent t-test for normally distributed and Mann-Whitney U test for nonparametric variables.

**Results:** Mean age at last follow up was 51.2 ± 11.6 years, 100% were white, 94% were female, and mean estimated glomerular filtration rate (GFR) was 91 ± 30 mL/min. Median follow-up was four years. Four patients were on loop diuretic. In PAH patients on diuretic were significantly more edematous (1.24 ± 0.7 vs. 0.63 ± 0.7 mg/kg, p<0.005), had higher BMI (30.5 ± 6.3 vs. 25.1 ± 4.9 kg/m², p=0.002) and covered less distance on 6 minute-walk test (360 [300;413] vs. 420 [385;464] meters, p=0.012) than patients not on diuretic. No difference was noted in age, gender, BP, NYHA class, or oxygen saturation. RHC were performed 2 times more often in diuretic vs. non-diuretic group (68% vs. 28.6%, p=0.03). On RHC, right atrial pressure (RAP) was significantly higher (7.9 ± 4.2 vs. 3.8 ± 3.2 mmHg, p=0.006) and there was trend towards higher mean pulmonary artery pressure (49 ± 13.3 vs. 41.2 ± 12.1 mmHg, p=0.08) in diuretic group with no difference in cardiac index or pulmonary vascular resistance. Serum alkaline phosphatase was higher (106.8 ± 34.3 vs. 76.2 ± 35.3 U/L, p=0.02) in diuretic group with no difference in other blood work including BNP and estimated FGR. There was no difference in proportion of patients on PAH-specific therapies. On follow-up, four patients in diuretic vs. non-diuretic group were lost follow-up.

**Conclusions:** High BMI and RAP, well-known factors associated with volume overload in other edematous disorders were applicable in our PAH cohort as well suggestive of presence of similar pathways of impaired natriuresis despite normal GFR. Further studies are required to confirm these pathways which can guide appropriate early-on therapeutics.

**PUB125**

**A Negative Anion Gap with a Positive Outcome**

Samantha E. Blank, Casey N. Gashti, William L. Whittier. Rush University Medical Center, Chicago, IL.

**Introduction:** The utility of an increased serum anion gap (AG) in clinical practice has long been established. A decreased or negative AG, however, often remains undiscovered or neglected. Overproduction of paraproteins, such as IgG (cationic) and
Laxative Use in Acute Hyperkalemia

A 62-year-old male patient with Mantle Cell Lymphoma presented to the emergency room with a one-day history of hemoptysis, emesis, and fatigue. Laboratory workup revealed severe anemia of 6 g/dL, marked leukocytosis of 265.27 thousand/µL, increased uric acid 15.1 mg/dL, and elevated lactate dehydrogenase of 1,261 U/L. These findings were consistent with active disease, and upon admission, the patient was initiated with aggressive hydration, alkalization, and rasburicase. Case Description: A 62-year-old male patient with Mantle Cell Lymphoma presented to the emergency room with a one-day history of hemoptysis, emesis, and fatigue. Laboratory workup revealed severe anemia of 6 g/dL, marked leukocytosis of 265.27 thousand/µL, increased uric acid 15.1 mg/dL, and elevated lactate dehydrogenase of 1,261 U/L. These findings were consistent with active disease, and upon admission, the patient was initiated with aggressive hydration, alkalization, and rasburicase.
was started on IV hydration, dexamethasone, rasburicase, and allopurinol. On the fifth hospital day, hypokalemia was noted, and white blood cell count decreased by approximately 50 thousand/μL. Two days after, laboratory values were remarkable for hyperkalemia of 6.1 mmol/L, blood urea nitrogen of 66.2 mg/dL, creatinine of 2.61 mg/dL, hyperphosphatemia of 8.5 mg/dL, and a corrected calcium of 7.1 mg/dL. These findings were suggestive of TLS following chemotherapy, along with the development of a non-oliguric stage three acute kidney injury. The next day, the patient had adequate urine output, stable blood pressures, no signs of volume overload or uremia, but laboratory values revealed worsening renal parameters and an increased calcium-phosphate product above 70 mg2/dL2. Consequently, hemodialysis was performed with good tolerance and response to treatment.

Discussion: The criteria for hemodialysis in this case of a non-oliguric euvolemic patient with acute renal failure secondary to TLS was founded on an elevated calcium-phosphate product, as opposed to more common indications such as anuria, fluid overload, or persistent electrolyte disturbances. The prognosis for complete recovery of renal function is excellent if dialysis is initiated early to rapidly reduce serum uric acid and phosphate concentration. This emphasizes the importance of a prompt assessment of the calcium-phosphate product as an indication for renal replacement therapy in the setting of tumor lysis syndrome.

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PUB131

Hypomagnesemia and Protein Pump Inhibitors

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Introduction: Proton pump inhibitors (PPIs) are commonly used for GERD. They are associated with acute intermittent nephritis, B12 deficiency, Clostridium difficile infection, gastric malignancy, atrophic gastritis, bone fractures, and rarely, hypomagnesemia. We present a case of hypomagnesemia manifesting with unexplained hypocalcemia, refractory hypocalcemia, and hyperphosphatemia. A 66 year old male with GERD and prostate cancer (scheduled for prostatectomy), was found to have abnormal electrolyte values on routine preoperative evaluation. Two months ago, they were all normal. He had copropapsial spasms, facial twitching, frequency and weak urine stream for two months. He denied diarrhea, nausea, vomiting, fever, chills, medication changes or use of supplements. He drank alcohol socially. Trousseau sign was positive. Labs showed potassium 2.8 mmol/L, bicarbonate 1.5 mmol/L, calcium 1.3 mg/dL, albumin 4 mg/ dL, magnesium 0.9 mg/dL, and phosphorus 3.2 mg/dL. 25-OH vitamin D was 9 ng/mL, whereas 1,25(OH)2 vitamin D was ele vated. During hospitalization, Fractional excretion of magnesium (measured after changing his PPI to an H2-receptor antagonist) was 2.5%. It was suspected that PPI use may have driven hypomagnesemia (which accelerated renal K+ losses), associated with PTH resistance and vitamin D deficiency (causing hypocalcemia). Symptoms resolved with electrolyte supplementation.

Discussion: Hypomagnesemia can result from gastrointestinal or renal losses. The presumably mechanism for PPI-induced hypomagnesemia involves impaired absorption of magnesium by intestinal epithelial cells caused by PPI-inhibited inhibition of transient receptor potential melastatin-6 (TRPM6) and melastatin-7 (TRPM7) channels. The aim of treatment is correction of magnesium and vitamin D first, resulting in rapid improvement of potassium and calcium. Our case is unique, as he developed the abnormalities so acutely. He was also restarted back on his PPI, along with magnesium supplements, and repeat electrolytes over the ensuing 4 months have been normal.

PUB132

Analysis by Bioimpedanciometry of Three Cohorts with Expanded Extracellular Volume: Critically Ill, Nephrotic, and Hemodialysis Patients

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Background: By applying, bioimpedanciometry provides information on body composition, estimating total body water (TBW) and extracellular water (ECW) with formulas. However, these estimates are imprecise in edematous patients. Fortunately, there are variables that are directly measured: resistance (R), reactance (Xc) and phase angle (AF), which in theory reflect the cells’ ability to maintain adequate function. In our work, we mainly wanted to analyze this second group of variables in patients with increased ECV and additionally compare them with a group of healthy volunteers.

Methods: Using a multifrequency bioimpedanciometer, we performed measurements on edematous patients in the ICU, edematous patients with nephrotic syndrome (NS), and anuric patients on hemodialysis (HD) before starting a random session. The control group were healthy volunteers (V) of the same age as the studied patients. A two test was performed to compare each group against V and a pearson’s correlation test was performed to assess correlation between variables.

Results: During 6 weeks measurements were made getting data of 14 V, 11 HD, 13 SN and 11 ICU. When comparing against V, significant differences were obtained in R, Xc and AF (p<0.05) in all groups except HD group. When comparing among them the most edematous groups (ICU and NS), surprisingly no differences were obtained (p>0.05). In the estimated variables related to water distribution (ECW, TBW and ECW/TBW), the 3 groups show significant differences compared to V, except in TBW. Finally, when using a correlation to compare measured against estimated variables, we found that Xc has a high negative correlation (r: -0.75) with ECW; AF has a high negative correlation (r: -0.83) with ECW/TBW, while R has a moderate negative correlation (r: -0.67) with ECW and TBW.

Conclusion: Our results show, the studied groups have differences in measured and estimated variables compared to V, theoretically reflecting a state of cellular malfunction in addition to the expansion of the ECV. Surprisingly, patients with NS and ICU are “electrically” the same, despite their very different clinical contexts. However, we cannot rule out that it is only due to expansion of the ECV of a similar amount since the measured variables depend to some degree on the estimated variables.

PUB133

Intractable Hyponatremia, Polydipsia, and the Reset Osmostat: A Case Report

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Introduction: Water intake in excess of water excretion results in hyponatremia, the most common electrolyte abnormality in clinical practice. Typically, ADH secretion fluctuates to maintain a physiologic serum osmolality, the so called “ADH osmostat”. This threshold can be altered by multiple physiologic and pathologic stimuli. In this report, we present a case of symptomatic hyponatremia associated with polydipsia in an elderly patient with psychiatric comorbidities and chronic hyponatremia. We describe the accompanying laboratory findings that support the diagnosis of reset osmostat. We postulate that chronic hyponatremia secondary to polydipsia related to psychiatric illness could have reset this patient’s osmostat and discuss potential therapeutic strategies.

Case Description: A 71-year-old man with severe depression, type 2 diabetes mellitus and chronic obstructive pulmonary disease presented to the hospital with diffuse weakness, difficulty with focused attention and suicidal ideations. He admitted to drinking more than 15 liters of liquid daily. Home medications included metformin, insulin, lisinopril, amiodipine, metoclopromide, pantoprazole, and trazodone. Physical exam revealed hyperpneic and trunclal obesity, but was otherwise unremarkable. Laboratory investigation revealed a plasma sodium concentration of 120 mEq/L, blood urea nitrogen of 9 mg/dL, creatinine of 0.82 mg/dL, serum osmolality of 263 mOsm/kg and urine osmolality of 155 mOsm/kg with a urine sodium of 38 mEq/L. Because of neurological symptoms and worsening hyponatremia, the patient received 3% hypertonic saline infusion. Serum sodium was noted to fluctuate during periods of unsupervised access to fluid, hypertonic saline infusion and fluid restriction. Urine osmolality was also noted to fluctuate, dropping appropriately with worsening hyponatremia and rising with fluid restriction, hypertonic saline and resultant rise in serum sodium. The rise in urine osmolality occurred without normalization of serum sodium.

Discussion: In this report, we present a case of symptomatic hyponatremia associated with polydipsia in an elderly patient with psychiatric comorbidities and chronic hyponatremia. We describe the accompanying laboratory findings that support the diagnosis of reset osmostat. We postulate that chronic hyponatremia secondary to polydipsia related to psychiatric illness could have reset this patient’s osmostat and discuss potential therapeutic strategies.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.

827
Discussion: Hypercalcaemia is a known side effect of patiromer use since it exchanges calcium ion with potassium. To our knowledge, however, hypocalcemia has not been attributed to patiromer use. In this unique case, hypocalcemia was an indirect side effect caused by severe hypomagnesemia that was probably exacerbated by the use of patiromer. Hypomagnesemia can cause hypocalcemia through suppression of PTH secretion, which was seen in this case, along with increasing PTH resistance. Novel potassium binders have a myriad of useful indications; however, one should be vigilant to their effects on other electrolytes.

PUB136
Hypokalemic Periodic Paralysis
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Introduction: Hypokalemic periodic paralysis (HOKPP) is characterized by transient episodes of muscle weakness and inability of muscle movement associated with hypokalemia. The paralysis typically affects the arms and legs, though the diaphragm and the tongue may also be affected.

Case Description: A 50-year-old female with tobacco use and significant alcohol consumption presented with progressive upper and lower limb weakness, numbness, and paresthesias that worsened over the past 2-3 months. She also reported fever, sweats, and unintentional 40-lb weight loss over the past 3 months. The patient denied use of diuretics and laxatives. Labs revealed serum potassium 1.9 mmol/L (3.5 - 5.2), phosphorus 2.2 mg/dL (2.5 - 4.5), bicarb 43 mmol/L (21-30), and a venous blood gas of 7.61/50/25/50, which is consistent with metabolic alkalosis. EKG demonstrated U waves and ST depressions significant for severe hypokalemia. She was admitted for severe hypokalemia and was given oral and IV potassium. Vitamin D was 16.0 ng/mL (30-100), which is suggestive of hypovitaminosis D. TSH and cortisol were normal, thus ruling out thyrotoxicosis and Cushing’s, respectively. Serum aldosterone and renin levels were normal, thus ruling out adrenal insufficiency. The Transtubular K+ Gradient was calculated to be 4, indicating a renal tubular wasting of potassium. In addition to renal potassium wasting, the cellular shift of potassium in the setting of chronic malnutrition and prolonged alcohol use exacerbated the severe hypokalemia. The patient’s potassium was repleted, and she was discharged from the hospital with close outpatient follow up.

Discussion: Hypokalemic periodic paralysis is characterized by transient episodes of muscle weakness in the setting of hypokalemia. HOKPP manifests itself as a sudden onset of weakness ranging from mild transient weakness of the arms and legs to paralysis of the diaphragm and accessory muscles, resulting in lethal respiratory failure. HOKPP can be triggered by a stressor, such as a viral illness or by specific medications, such as insulin or beta-agonists. HOKPP is important to rule out when evaluating a patient with abrupt onset of paralysis or weakness, especially in patients with no history or risk factors of other pertinent disease, such as stroke. The failure to diagnose and properly treat HOKPP can be fatal. It is vital to address the underlying cause of hypokalemia to prevent the recurrence of HOKPP.

PUB137
Screening Fabry Disease in CKD Patients in a Single Center of Middle Taiwan
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Background: Fabry’s disease (FD) is an X-linked inherited rare, progressive, lysosomal storage disorder affecting multiple organs due to the deficient activity of alpha-galactosidase (a-Gal A) enzyme. The prevalence has been reported to be 0.15–1% in hemodialysis patients; however, the information on the prevalence in chronic kidney disease (CKD) is lacking in Taiwan. This study aimed to determine the prevalence of FD in our CKD patients.

Methods: We screen male patients older than 18 years in our dialysis, renal transplantation (RTx) and Pre-End Stage Renal Disease (pre-ESRD) program patients. A total of 611 male CKD patients were screened using an assay of a-Gal A activity by dried blood spots (DBS). A Fabry confirm test by GLA gene analysis was done for those with low enzyme activity.

Results: There were 2 cases with positive (a-Gal A activity <0.6 μmol/hr) and 6 patients with borderline (0.6–1.5 μmol/hr). Interestingly, the 2 positive cases were brothers diagnosed IgA nephropathy (IgAN) in their childhood and received RTx identified as late-onset FD with GLA mutation in c.659+910C>A; a popular mutation site found in studies of male newborns screening for cardiac variant FD in Taiwan, and their mother was the carrier of GLA mutation. We also found 3 cases with borderline of a-Gal A activity with mutation on nonfunctional region. The prevalence of FD is about 0.33 % (2 in 611) in the high-risk population group with CKD. The clinical symptoms of FD patients are nonspecific except in those with various degrees of renal failure.

Conclusions: FD should be considered in the differential diagnosis of any CKD patients even with knowing their renal disease entities without symptoms and signs suggestive of FD. Clinicians should be aware of FD might be not only renal involvement, but also affected heart and brain.
A Novel Frameshift Mutation of COL4A5 Identified by Whole-Exome Sequencing in a Chinese Family with Alport Syndrome

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Background: Alport syndrome is an inherited kidney disease caused by the defects in type IV collagen, approximately 80% of which is caused by X-linked mutations in the COL4A5 gene. This study explores a novel frameshift mutation of COL4A5 responsible for renal disorder in a 3-generation Han Chinese pedigree.

Methods: We enrolled the proband and his family members from a village in Sichuan province, and collected the family history and clinical data. Clinical examinations were performed to evaluate the phenotypes of the family. Blood samples from the proband and the other eight family members were collected for genetic screen. Whole exome sequencing (WES) was applied in the proband to find out the potential genetic variants, and then the variant within the family was verified by Sanger sequencing.

Results: The 31-year-old male proband and his elder brother had ESRD, binaural sensorineural hearing loss and ocular lesions. Further, his three male cousins received hemodialysis and all died from ESRD between 18 and 25 years old. The 90-year-old maternal grandmother, one maternal aunt and one female cousin had only microscopic hematuria without gross hematuria, proteinuria, impaired kidney function or extrarenal symptoms. Genetic analysis identified a novel deletion mutation (c.422_428del) in exon 7 of COL4A5 gene which located on the X chromosome in the proband. The c.422_428del variant was also detected in the proband’s grandmother and four other affected family members. The proband’s farther and three unaffected family members had not found this variant. This mutation was results in frameshift followed by formation of a truncated (p.Leu142Valfs*11) COL4A5 protein product with only 152 amino acids including an aberrant 10 residues. This mutation was not present neither in the Exome Variant Server of the NHLBI-ESP database, ExAC database or in the 1000 Genomes database. According to the variant interpretation guidelines of American College of Medical Genetics and Genomics (ACMG), this novel variant was classified as “likely pathogenic” variant for Alport syndrome in this pedigree.

Conclusions: Our study identified a novel COL4A5 frameshift mutation in a Chinese family with Alport syndrome, expanding the mutational spectra of COL4A5 gene, which were significant for screening and genetic diagnosis for Alport syndrome.

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Elevated Ambulatory Blood Pressure Is Associated with a Progressive Form of Fabry Disease

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Background: Published data on hypertension incidence and management in Fabry Disease (FD) are scanty and it remains to be shown how much high blood pressure (BP) contributes to organ damage in these patients. Therefore, we have assessed BP values and their correlations with clinical findings in a cohort of FD patients.

Methods: Between January 2015 and May 2019, all adult FD patients (n=32) referred to our institute were enrolled; they were Caucasians (n=24 female, n=8 males) with an average age of 50±12.2 years. Data regarding hypertension were obtained by ambulatory BP monitoring (ABPM), home self-monitoring and office measurements. Patients were defined as hypertensive according to 2018 ESC/ESH Guidelines. The severity and the stability of FD were assessed with the Fabry Stabilization Index (FASTEX). Organ involvement and hypertension risk factors were also evaluated.

Results: The ABPM revealed elevated BP in 18.75% (n=6) of the FD population and 50% (n=16) of this group was diagnosed with masked hypertension. All these patients were females with an average age of 58±9.9 years. They presented a lower (p<0.046) glomerular filtration rate compared with the normotensive patients (77±17.7 and 89.3±21.4 ml/min/1.73m², respectively) and a more advanced cardiac hypertrophy with a higher LVPWD (p=0.044) and LVMi (p=0.033). Four of them (66.7%) were classified as progressive by the FASTEX score while the majority of the normotensives (84.6%) were stable (Figure 1). No correlation (p=0.428) was found between the category of GLA mutation and the development of hypertension.

Conclusions: Newly detected hypertension is found in a restricted portion of stable FD patients, while it becomes more prevalent in clinically progressive cases. The use of ABPM is of paramount importance to reveal masked hypertension which can contribute to the progressive worsening of the organ failure. We recommend a standardised ambulatory long-term BP monitoring program and timely antihypertensive intervention to improve the outcome of FD patients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Background: Patients with primary hyperoxaluria type 1 (PH1) have an increased risk of acute or chronic kidney failure (AKF/CKF). There are two risk groups: infantile oxalosis patients with an unremarkable family history and adult patients with only an oligosymptomatic course (minor stone events), who get into end-stage renal disease (ESRD) due to oxalate-induced chronic inflammatory processes in the kidney. We were interested in the prevalence of acute kidney failure in patients with non-infantile PH1 seen in our Hyperoxaluria Center over the last 10 years.

Methods: We retrospectively analyzed the database of the German Hyperoxaluria Center for patients being seen in our outpatient clinic for AKF. AKF was defined as a sudden onset of kidney failure and the necessity of dialysis installment in patients, but a documented stable kidney function (no worse than stage 2-3 CKD) prior to onset of AKF.

Results: There were 117 PH1 patients in the center, of whom 6 had infantile oxalosis and thus early ESRD, 8 patients are currently on dialysis, and 6 patients have died. Transplantations were performed in 35 patients with PH1 (liver & kidney in 28 patients, liver-only in 4 patients, and kidney-only in 3 patients). Currently, we routinely follow up (3-4 times a year) 49 of 117 PH1 patients. Out of these 49 patients, AKF was diagnosed in 8 patients aged 11-56 years (1 pediatric patient, 3 patients 18-19 years old, and 4 patients 29-56 years old), which led to CKF and subsequently, maintenance hemodialysis in 7 patients and death in 1 patient. Non-compliance regarding medication or recommended fluid intake was the reason for AKF in 6 of the 8 patients. Acute massive diarrhea without adequate fluid substitution led to AKF in the other 2 patients.

Conclusions: AKF is not uncommon in patients with PH1. It is frequently related to either non-compliance or to situations of severe fluid losses with inadequate fluid substitution and not based on already extremely altered renal function. Therefore, interruption of medication or lack of fluid intake, even for short periods of time, can lead to severe clinical consequences in these patients.
Case Description: A 32-year-old female with prior history of gestational hypertension presented to her primary care provider with a three-day history of bilateral lower extremity edema and periorbital swelling. On exam, profound periorbital edema and 2+ pitting edema up to the knees bilaterally was noted. Labs were consistent with a creatinine level of 5.0 mg/dL up from her baseline of 0.5 mg/dL three months prior. Urinalysis and random urine testing confirmed proteinuria of almost 19 grams per day. Renal ultrasound was obtained showing normal sized kidneys with increased echogenicity. Kidney biopsy was obtained and results were consistent with collapsing FSGS. Secondary workup for etiology of FSGS came back positive for Parvovirus B19 infection. Along with diuresis, decision was made to start IVIG and prednisone therapy. Initially, patient had improvement in kidney function post treatment and patient was followed up in clinic. However, required hemodialysis for one month.

Discussion: FSGS is commonly associated with nephrotic syndrome and stems from podocyte abnormalities. Podocyte detachment and death lead to segmental sclerosis, which is the hallmark pathophysiology of FSGS. Kidney biopsy is used to diagnose FSGS and characterized by the presence of sclerosis of at least one glomerulus on histologic examination. Histologically there are five classifications of FSGS with collapsing carrying worst prognosis. Treatment is typically aimed at controlling proteinuria, edema, and cholesterol. In our patient with Parvovirus B19 induced FSGS, we used IVIG with prednisone therapy but no improvement. Further research is needed to find treatments for Parvovirus B19 induced FSGS for better outcome.

PUB145

A Whole Genome-Wide Arrayed CRISPR Screen in Primary Organ Fibroblasts to Identify Regulators of Kidney Fibrosis

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Background: Robert J. Turner, Stefan Golz, Carina Wollnik, Nils Burkhardt, Ina Sterlingberg, Uwe Andag, Hauke Cornelis Kidney fibrosis presents a hallmark of chronic kidney disease. With ever-increasing patient numbers and limited treatment options available, novel strategies for therapeutic intervention in kidney disease are warranted. Fibrosis commonly results from a wound healing response to repeated or chronic tissue damage, irrespective of the underlying etiology, and can occur in virtually any solid organ or tissue.

Methods: whole-genome-wide arrayed CRISPR screening high content imaging Results: In order to identify targets relevant for kidney fibrosis, we employed CRISPR screening in primary human kidney fibroblasts. Selected hit genes were validated. Conclusions: We demonstrate that CRISPR technology can be applied in primary kidney fibroblasts and can furthermore be used to conduct arrayed CRISPR screening using a high-content imaging readout in a whole genome-wide manner. Hits coming out of this screen were validated using orthogonal approaches and present starting points for validation of novel targets relevant to kidney disease.

Funding: Commercial Support - Evotec, Bayer Pharma

PUB146

Dual Positive Anti-Glomerular Basement Membrane Disease and ANCA Disease: A Diagnostic Challenge

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Introduction: Double-positive disease (DPD), defined as coexistence of anti-glomerular basement membrane (Anti-GBM) disease and an anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV), is rare disease associated with variable outcomes. These patients often do not have typical presentation of either anti-GBM disease or AAV, making diagnosis a challenge.

Case Description: A 59-year-old male with history of hypertension presented with 1 week of fatigue and decreased urine output. Initial labs revealed a serum creatinine of 11.6 mg/dL and blood urea nitrogen of 133 mg/dL. Urinalysis showed specific gravity of 1.025, pH 5.0, 1+ protein, large blood, and 11-20 RBCs/hpf. Serological workup including anti-nuclear antibody, complement C3 and C4, HIV, hepatitis B and C were all unremarkable. The patient then developed hemoptysis and anuria. He was initiated on hemodialysis. Renal biopsy revealed extensive cellular and fibrocellular crescents, diffuse tubular injury with RBC casts, and 30% interstitial fibrosis and tubular atrophy. Immunofluorescence was negative. Further investigation revealed an elevated Anti-GBM titer, elevated anti-myeloperoxidase antibody and negative anti-proteinase 3 antibody. He was treated with methylprednisolone 1g intravenously for 3 days then daily prednisone 60mg and one dose of cyclophosphamide 1g intravenously. He was then transferred for initiation of plasmapheresis and received 8 sessions with normalization of Anti-GBM and ANCA titers. He also received another dose of cyclophosphamide 1g. He remained dialysis-dependent upon discharge.

Discussion: The varied presentation of DPD may cause a delay in diagnosis. DPD patients have a greater tendency to recover renal function but a higher risk of relapse. Early recognition and aggressive treatment is essential.

PUB147

Transcriptomic Profiling of Collagens in Proteinuric Kidney Disease


Background: Collagen proteins are a major component of the extracellular matrix and play a significant role in kidney health and disease. In proteinuric kidney disease, increased production or altered expression of specific collagens may contribute to renal injury and fibrosis.

Methods: Adult Wistar rats were administered water (sham) or PAN (~100 mg/kg, IP) and urine protein (24-hour) was measured on Days 4, 8, 12 and 21. Animals were sacrificed on Day 21, the left kidneys retrieved, and renal COL1A1 and COL3A1 mRNA levels measured using quantitative polymerase chain reaction.

Results: The rat PAN model was associated with increased proteinuria (*, p<0.01 vs. sham). Compared to the sham cohort, renal COL1A1 and COL3A1 mRNA expression levels were increased, 1.86-fold (p<0.05) and 8.4-fold (p<0.01), respectively, in the PAN cohort. Proteinuria correlated directly (r=0.9) and significantly (p<0.01) with renal COL3A1 mRNA expression level.

Conclusions: Renal COL1A1 and COL3A1 mRNA expression levels are elevated in proteinuric kidney disease. Since COL3A1 mRNA expression is associated with increasing proteinuria, targeting type III collagen might prove beneficial. Funded By: United States Department of Defense - PR180780/ W81XWH1910448

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PUB148

C3 Glomerulonephritis: Diagnostic Challenges and Overlap Syndromes

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Introduction: C3 glomerulonephritis (C3GN) is a rare complement-mediated GN, with an incidence of 1-3:1,000,000. Spectrum of presentation can range from asymptomatic hematuria and proteinuria to a full blown acute GN with hypertension, hematuria, and renal insufficiency. Serum C3 levels are typically low. Diagnosis is confirmed by renal biopsy. The underlying mechanism appears to be dysregulated alternate complement pathway, triggered by genetic, environmental or a combination of both factors. Medical management addresses blood pressure, proteinuria, and dyslipidemia. Immunosuppression with glucocorticoids, antimalabobilites, and anti-complement agents is used alone or in combination. Here we present 2 cases of biopsy-proven C3GN mimicking infection-associated GN (IAGN) and TTP/HUS.

Case Description: Case 1: A 49-year-old man presented with 4-5 days of fevers, chills, nausea, vomiting and diarrhea. Labs revealed mild thrombocytopenia, proteinuria, microscopic hematuria and a low C3 level. Blood cultures revealed Streptococcus pyogenes. His hospital course was marked by rapidly progressive pancytopenia and hemodilisais requiring acute renal failure. He received a single dose of ecilizumab empirically due to concern for atypical HUS, but platelet counts improved too rapidly.
to be consistent with eculizumab benefit. Kidney biopsy revealed acute tubular injury with mild interstitial inflammation. EM did not show immune deposits. Sequential renal recovery followed 4 hemodialysis sessions. One month post-dialarge, he had normal renal function and hematocrit cell counts. Case 2: A 74-year-old man with CKD III was admitted with altered mental status, septic shock, and acute kidney injury. Extensive workup did not reveal direct infection or altered autoimmune status. His course was complicated by worsening renal failure, proteinuria, and hematuria. Renal biopsy demonstrated acute tubular injury and glomerular C3 deposition without immune deposits on EM. Eculizumab was deferred due to normal C3 and C4 levels. A steroid pulse was associated with an improvement in creatinine beginning on day 4 and return to baseline kidney function by day 17.

Discussion: Our cases highlight the variable presentation and complexity associated with accurate diagnosis of C3GN, including considerable overlap with IAGN and TTP/HUS.

PUB149
To Treat or Not to Treat? The Dilemma of C3 Glomerulonephritis vs. Infection-Related Glomerulonephritis
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Introduction: With a paradigm shift in the concept of disease-related glomerulonephritis (C3GN) from a post-streptococcal infection of the young in developing countries to a primary-microbial infection of the elderly in the western world, the differential has broadened. This has coincided with an evolving phenomenon of C3 glomerulopathy (C3G-C3 glomerulonephritis (C3GN) & Dense Deposit Disease (DDD)). In all these entities a common feature is C3 dominant staining. Although subtle differences have been described in the nature of these deposits, we present a case in which the clinical course & biopsy findings highlight the challenges of identifying C3GN vs. IRGN.

Case Description: A 62 y/o female with HTN, hypercholesterolemia, epidermal abscess, & recent MSSA bacteremia presents with AKI & anemia. Her creatinine was 2.9 mg/dL vs. 0.53 mg/dL (three weeks ago). Labs: Total Protein/Creaitnine 4.29 mg/mg, negative blood cultures, unremarkable ANA, ANCA, SLEP, UPEP, K/L, Antistreptolysin O (ASO) Antibodies 514 IU/mL (0-200) & C3 77 mg/dL (87-200), C4 47 mg/dL (10-50). Kidney biopsy: C3 dominant glomerulonephritis, >50% crescents, 3+4 staining for C3 in mesangium & capillary loops, EM revealed finely granular mesangial, intramembranous, & subepithelial electron-dense deposits. She was started on steroids & C3 improved to 95 mg/dL after three weeks. Creatinine plateaued ~4 mg/dL prior to discharge. Full complement profile available after one month (C1 Inhibitor 84 mg/mL (21-39), C3 Nephritic titrums/mL (0), C4Bp 136.3 (61-116), Factor H AutoAB 30 unit/mL (<=22), SCSb 313 mg/mL (>=-244).

Discussion: Classically, neutrophilic infiltration, occasional crescents (>50%) & subepithelial humps with co-deposition of C3 & IgG or IgA are described with IRGN, while mesangial & diffuse capillary proliferation exclusively with C3 deposition is expected with C3G. However biopsy alone is not specific for identifying the underlying etiology. ASO titerers are elevated in >50% cases of C3GN and 25% of IRGN cases present with only C3 staining. Based on a strong history of infection, & improvement of C3, we treated as IRGN. Although testing for complement pathway mutations is recommended, results are not readily available. The clinical significance of these mutations remain under scrutiny. Until issues of testing & treatment can be generalized a holistic approach with close follow up is needed in cases of C3 dominant glomerulonephritis.

PUB150
A Young Asian Man with Heavy Chain Deposition Disease
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Introduction: Heavy chain deposition disease (HCDD) is an exceedingly rare condition characterized by nonamyloid tissue deposition of monoclonal immunoglobulin heavy chain. It typically presents in patients above age 50. Here, we report a case of a young Asian adult who presented with acute kidney injury (AKI) and nephrotic syndrome (NS).

Case Description: A 32-year-old Chinese man presented with anasarca. He has no significant past medical history and his family history was also unremarkable. On presentation, he was afebrile with an elevated blood pressure to 205/136. Examination showed peri-orbital and 2+ lower extremity edema. Laxled skin was noted in his neck and abdomen. Laboratory studies showed an initial serum creatinine of 1.5 mg/dL with unknown baseline. It has tripped to 10.4 mg/dL over the next 4 weeks requiring dialysis support. His LFT was normal, serum albumin was 2.0 g/dL, total cholesterol was 224 mg/dL, 24-hour urine total protein was 10.9 g/m with albumin 7.7 g/m. Serologies showed negative ANA, dsDNA, hepatitis and HIV panel, SPEP and UPEP for m-splikes. His complement levels were also normal. Urine sediment revealed 360 RBC with acanthocytes and 10 WBC under high power field. His kidney ultrasound was unremarkable. Kidney biopsy revealed nodular mesangial sclerosis with membranoproliferative features. There were intense immunoglobulin G1 staining in the mesangium, glomerular and tubular basement membranes and vessel walls. Kappa, lambda, IgM and IgA immunohistochemistry were unremarkable. Thus, a diagnosis of γ-type HCDD was made. The patient was started on treatment with bortezomib and dexamethasone. Within 2 months, he came off dialysis, 24hr urine total protein improved to 5.9 mg. Four months after starting bortezomib therapy, serum creatinine improved to 1.4 mg/dL and 24hr urine protein was down to 1.6 g.

Discussion: In summary, this is a unique HCDD case diagnosed in a young Asian gentleman. He did not have detectable monoclonal serum protein. Like other reported cases, he responded well to a bortezomib based regimen.

PUB151
A Challenging Case of Renal-Limited Vasculitis
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Introduction: Anti-neutrophil cytoplasmic autoantibody (ANCA)-Associated Vasculitis (AAV) is an autoimmune disease that causes inflammation of blood vessels and has a wide spectrum of clinical presentation. It can present as multisystem or renal-limited disease. The typical renal presentations that of a rapidly progressive glomerulonephritis (RPGN). We present an interesting case of renal-limited vasculitis with atypical features.

Case Description: A 76 year old male with a past medical history of Hypertension (treated with hydralazine) and CKD Stage 3 presented with weakness and shortness of breath for about two weeks. Physical exam and vitals were unremarkable. Laboratory workup revealed AKI with creatinine of 6.5 mg/dL. Urinalysis revealed microscopic hematuria and proteinuria (urine protein/creatinine ratio of 0.9). Renal ultrasound was unremarkable. Serologic workup including ANA, C3, C4, anti-GBM Ab, HbAsg, HbsAb and HbcAb was unremarkable. However, p-ANCA titer was high (1:160). He was treated with IV fluids. Interestingly, he continued to have good urine output as well as improvement in serum creatinine to 4.8 mg/dL and was discharged from the hospital. Follow-up renal function panel in two weeks showed worsening serum creatinine of 6.8 mg/dL. The patient was readmitted to the hospital. Repeat serologic workup revealed p-ANCA, titer of 1:320 and elevated MPO IgG of 78 U/mL. Renal biopsy revealed pauci-immune glomerulonephritis. Steroids and rituximab were initiated as treatment. Due to worsening kidney function, patient was started on hemodialysis. He remained dialysis dependent with no significant renal recovery. Given atypical features of disease presentation, hydralazine was considered to be an etiologic agent hence, and was discontinued.

Discussion: We present a case of renal-limited vasculitis with atypical features making the diagnosis very challenging. Firstly, the patient remained nonoliguric through the first hospital course. Secondly, his serum creatinine improved with supportive treatment leading to his discharge with presumptive diagnosis of ATN. In summary, ANCA associated GN may present with nonoliguria as well as wanning renal function. Atypical features of AAV should raise concern for drug-induced etiology.

PUB152
Collapsing Focal and Segmental Glomerulosclerosis with Thrombotic Microangiopathy Found on Renal Biopsy in a Patient Receiving Intravitreal Afibbercept for Age-Related Macular Degeneration
Ramy M. Hanna, Gautam M. Phadke,1 Kenar D. Jhaveri,1 Ira Kurtz,2 Kamyar Kalantar-Zadeh.1 UC Irvine, University of California Irvine, Orange, CA, 2University of California Los Angeles, Los Angeles, CA. 1Northwell Health, Great Neck, NY, 2University of North Dakota, Columbus, OH.

Introduction: Intravitreal Vascular Endothelial Growth Factor (VEGF) Receptor blockers are used for a variety of retinal pathologies. These include age related macular degeneration (AMD), diabetic macular edema (DME), and central retinal vein obstruction (CRVO). Reports of absorption of intravitreal agents into systemic circulation have increased in number, and confirmation of depletion of VEGF has been confirmed. Increasingly there are studies and case reports showing worsening hypertension, proteinuria, renal dysfunction, and glomerular disease. The pathognomonic findings of systemic VEGF blockade, thrombotic microangiopathies (TMA) are also being increasingly reported. One variant of TMA’s that has been described is collapsing focal and segmental glomerulosclerosis (cFSGS). cFSGS has been postulated to occur due to TMA induced chronic glomerular hypoxia. We present the third reported case of cFSGS in the setting of intravitreal VEGF blockade, a chronic TMA component was crucially found on biopsy.

Case Description: This patient is a 74-year-old non-diabetic male receiving afibbercept for AMD of the two prior cases of cFSGS in setting of VEGF blockade, one had AMD and the other had DME.

Discussion: This case solidifies the finding of cFSGS and its association with chronic TMA as a lesion that may be frequently encountered in patients receiving intravitreal VEGF inhibitors.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underlines represents presenting author.
A Case of IgA Vasculitis in Liver Cirrhosis

Jayesh B. Patel, Swe Zin Mar Winhtuto, Daniele G. Holanda, Lama A. Noureddine. University of Iowa Hospitals and Clinics, Iowa City, IA.

Introduction: IgA vasculitis (previously termed Henoch-Schönlein purpura) is a systemic immune-complex mediated condition characterized by predominant IgA deposition in microvessels. We present a case of biopsy-proven IgA vasculitis involving skin and kidneys in a patient with known liver cirrhosis.

Case Description: A 71-year-old man with liver cirrhosis due to chronic ETOH use presented to ER with a one-month history of progressive rash and pedal edema. He denied arthralgias, melena, hematemesis, abdominal pain, or fever. Diffuse, erythematous, palpable, non-pruritic petechial lesions were noticed on bilateral thighs, arms, and anterior abdominal wall with few lesions coalescing to purpura. Laboratory evaluation revealed an elevated creatinine at 1.7 mg/dL. Urinalysis showed dysmorphic erythrocytes, leucocytes, and proteinuria. ANA was positive (1:320), C3 slightly low with normal C4, Cryoglobulin, RA factor, SPEP, ANCA, anti-dsDNA, HBsAg, antibodies to HIV, HCV, rickettsia, and syphilis were negative. Peritoneal fluid culture was sterile. Kidney biopsy revealed severe proliferative glomerulonephritis, cellular/fibrocellular crescents and mild interstitial fibrosis. Skin biopsy revealed dense perevacular neutrophilic infiltration with fibrin deposition and erythrocyte extravasation consistent with leukocytoclastic vasculitis. He was diagnosed with IgA vasculitis and treated with pulse IV steroids followed by oral cyclophosphamide tapers along with monthly IV cyclophosphamide infusions.

Discussion: IgA vasculitis, more commonly observed among children than adults, manifests clinically as palpable, blanching purpura, arthritis, intestinal perforation, and kidney injury. Adults commonly develop ESRD in one-third of cases. Similar to crescentic GN, it also manifests clinically as palpable non-blanching purpura, arthritis, intussusception, and pedal edema.

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Nephrology was consulted due to no improvement in urine output despite benzenamide and thiazide diuretic challenge. Renal ultrasound was unremarkable. Spot urine albumin was negative. She required emergent hemodialysis (HD) as her kidney function failed to recover. A renal biopsy showed chronic tubular and arteriolar changes with noted glomerular endocapillary immune-complex glomerulonephritis, concerning for post-infectious GN. She ultimately required an arteriovenous fistula for long-term HD.

Discussion: PSGN primarily occurs after an upper respiratory infection or impetigo. It is less common in adults, however, is associated with a worse prognosis compared to children, with less than 25% achieving full recovery of renal function. Unlike children, the patient was noted to present with etiologies of lower respiratory infections (LRI) and UTIs. Studies show the time between infection and renal injury may be little to none, as infections in the elderly are often nonspecific and might go unrecognized. Our patient had an AKI after a LRI, resulting in significant oliguria and lack of renal recovery leading further work up with a biopsy. It is therefore imperative that providers consider PSGN as a diagnostic consideration in elderly patients with severe AKI. Treatment is mainly supportive, and patients, like ours, might require HD.

PUB153

Poststreptococcal Glomerulonephritis in an Elderly Patient: A Rare but Often Overlooked Differential in AKI

Enoemen M. Okpoko, Navneet Kaur, Lilibeth Jauregui, Anika Bethel. Florida Atlantic University Charles E Schmidt College of Science, Boca Raton, FL.

Introduction: Poststreptococcal glomerulonephritis (PSGN) is a complication of specific Streptococcal strains. Presentation ranges from asymptomatic microscopic hematuria to acute nephritic syndrome, with oliguria, edema, hypertension, and acute kidney injury (AKI). It mostly occurs in children of developing countries. Its incidence is not well characterized in elderly individuals but is thought to be extremely rare. We report a case of PSGN in an elderly female complicated by hypertensive urgency and heart failure.

Case Description: An 89-year-old female with history of COPD, HFpEF, CKD stage 3a presented with lethargy and weakness. She was treated for bronchitis 3 weeks prior and initially improved but then developed progressive dyspnea and swelling in her lower extremities. On presentation, BP was 252/120, CXX showed cardiomegaly and pulmonary edema. Labs revealed a creatinine of 2.72 (baseline 1.4). She was started on IV diuretics, BIPAP, and nitroglycerin drip with improved BP control. She remained oliguric.

Discussion: The patient is one of the few reported cases of PSGN in an elderly patient. It is less common in adults, however, is associated with a worse prognosis compared to children, with less than 25% achieving full recovery of renal function. Unlike children, the patient was noted to present with etiologies of poststreptococcal GN. She ultimately required an arteriovenous fistula for long-term HD.

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Discussion: IgA vasculitis, more commonly observed among children than adults, manifests clinically as palpable, blanching purpura, arthritis, intestinal perforation, and kidney injury. Adults commonly develop ESRD in one-third of cases. Similar to crescentic GN, it also manifests clinically as palpable non-blanching purpura, arthritis, intussusception, and pedal edema.

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Our patient, it is an intriguing question based on new evidence. Certainly, her underlying hypothyroidism was worsened by the development of NS. Nephrologists should consider screening for hypothyroidism when diagnosing NS, as treatment has the potential to significantly improve patient symptoms.

** PUB159 **

Patient Journey, Perceptions, and Burden Associated with Immunoglobulin A Nephropathy (IgAN): A Qualitative Study

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1Novartis Pharma AG, Basel, Switzerland; 2IPSOs SA, Basel, Switzerland; 3Novartis India Hyderabad, Hyderabad, India.

Background: There is a lack of published evidence on patient perspectives in IgAN; a rare condition that can progress to end stage renal disease (ESRD). The objective of this study was to understand the patient journey, disease perceptions and burden of disease from the patients’ perspective.

Methods: This qualitative study was conducted after review board approval through a moderated online bulletin board platform and by telephone interviews, to allow comprehensive answering of pre-defined questions. Participants were recruited via physician referral and were screened to ensure eligibility and willingness to participate. Analysis was conducted using a combination of various qualitative analytical tools.

Results: Eight participants with a confirmed diagnosis of IgAN from North America and Europe, aged 29–58 years participated. Diagnosis was often incidental as symptoms were underestimated or unnoticed. Participants were overwhelmed to learn they were diagnosed with a chronic disease and many did not understand the seriousness of the outcomes associated with the same. Post diagnosis, participants were referred to a nutritionist to discuss diet changes and received blood pressure medications. Some participants also received steroids and immunosuppressants. Frequency of monitoring visits varied and created anxiety due to dependence on the same. Speed of disease progression was different among patients. Besides symptoms like fatigue and lack of energy, some participants had to deal with emotional burden of feeling alone and fearful of the future with potential dialysis, transplantation and shortened life expectation. According to the participants, the lack of standard procedures for early screening and diagnosis along with the absence of adequate information in patient friendly language and counselling were some of their needs. Additionally, participants expressed the need for a support mechanism with similar peers to learn to live with the disease and to counteract feelings of being alone.

Conclusions: This study provides insights into how differently IgAN patients perceive and live with their disease. The insights obtained can be used to inform drug development and include what matters most to patients. Finally, this study highlights that a comprehensive education program for patients and caregivers is needed.

**Funding:** Commercial Support - Novartis Pharma AG

** PUB160 **

Retinal Drusen in Antibody-Mediated and Pauci-Immune Glomerulonephritis

Philip A. Harraka,1 Heather G. Mack,2,3 Deb J. Colville,4 David Bar1, David Langford,3 Timothy J. Pianta,4 Judith A. Savige.1
1The University of Melbourne Department of Medicine, Northern Health, Melbourne, VIC, Australia; 2The University of Melbourne Department of Surgery (Ophthalmology), Melbourne, VIC, Australia; 3Department of Ophthalmology, Melbourne Health, Melbourne, VIC, Australia.

Background: Membranous and anti-glomerular basement membrane (GBM) glomerulonephritides are autoantibody-mediated diseases, where the antigens (PLA2R, TSSR, collagen IV α3 respectively) are also expressed in the retina. Drusen are retinal deposits caused by complement activation and lipid debris in Bruch’s membrane. Drusen have been described in one individual with membranous nephropathy and linear IgG deposits in Bruch’s membrane of another with anti-GBM disease. In contrast, pauci-immune anti-neutrophil cytoplasm antibody (ANCA) vasculitis triggers complement but does not produce glomerular immune deposits. This study examined individuals with antibody-mediated or pauci-immune glomerulonephritis to determine how often drusen occurred in each group.

Methods: This was a cross-sectional observational case-series of individuals with antibody-mediated (n=15, membranous n=9, anti-GBM disease n=6) or pauci-immune (n=16, granulomatosis with polyangiitis n=7, microscopic polyangiitis n=7, eosinophilic granulomatosis with polyangiitis n=2) glomerulonephritis recruited from a general medical service and an Australian tertiary-care hospital. Two-field colour fundus images were obtained with a non-mydriatic camera (CANON, Japan). Images were coded and assessed for drusen count, location and size by two trained graders using the Wisconsin Age-Related Maculopathy Grading Grid. Central drusen counts a10 were considered abnormal.

Results: Four (27%) individuals with antibody-mediated disease (membranous n=2, anti-GBM disease n=2) but only 1 (6%) with a pauci-immune vasculitis had a10 central drusen. Gender, mean age and disease duration were not different between the two groups.

Conclusions: These results suggest that retinal disease occurs together with glomerular disease when the target antigen is found in both locations. Retinal drusen may be a useful biomarker for some forms of glomerulonephritis, and drusen pathogenesis may explain in part the pathogenesis of glomerular immune deposits. In addition, treatments that target retinal drusen may also be useful in antibody-mediated glomerulonephritis.
Long-Term Therapeutic Plasma Exchange (TPE) in Management of Focal Segmental Glomerulosclerosis (FSGS) in Native Kidneys

Northwestern University Feinberg School of Medicine, Chicago, IL.

Introduction: Circulating permeability factors (CPF) may be involved in the pathogenesis of some forms of FSGS that are non-responsive to intensified immunosuppression and exhibit a rapidly progressive course. The role of CPF-mediated FSGS is indicated by the post-transplant recurrence of proteinuria and its response to TPE. Moreover, experimental animals injected with plasma from patients with FSGS can develop proteinuria. While TPE in patients with post-transplant recurrence can prevent graft failure, evidence to support its use in resistant FSGS in native kidneys is lacking.

Case Description: A 62-year-old Caucasian female presented with anasarca and nephrotic-range proteinuria (5.0 g/day) in March 2018. Kidney biopsy revealed minimal change disease. The first 14 months of her course were complicated by steroid resistance, side effects of high-dose steroids and calcineurin inhibitors (CNI), recurrent AKI, CNI/ ARB-induced hypertension, and worsening of proteinuria with CNI reduction. She received 4 doses of rituximab (375 mg/m²) during that period. Genetic testing for the steroid-resistant nephrotic syndrome was negative. In June 2019, a trial of 10 TPE sessions resulted in a significant improvement in proteinuria (UPCR= 1.8±0.6), which worsened over the following 4 months after discontinuation of TPE (UPCR=4.0). Repeat kidney biopsy revealed FSGS. Given the previous response to TPE, a central-venous port was placed for long-term TPE in December 2019. The patient received TPE twice a week for the first 6 weeks. With improved proteinuria, TPE was tapered to twice a month with maintenance removal (UPCR= 1.5) for the last 5 months. The patient is off ARB, on a minimal dose of CNI. The symptoms associated with nephrotic state and the side-effects of multiple drugs have resolved.

Discussion: This case highlights the dilemma of therapeutic decision-making in patients with resistant FSGS. Long-term TPE successfully maintained symptom-free, sustained PR and stabilized renal function. TPE has become the preferred choice of our patient to avoid the toxic effects of long-term intensive immunosuppression. More studies are required to study the efficacy and safety of TPE in patients with native kidney FSGS resistant to therapy.

PUB162
Association Between Anti-GBM Titers and Kidney Inflammation with a New Activity Score


Background: Anti-glomerular basement membrane antibody (anti-GBM) disease is a rare glomerulonephropathy characterized by rapidly progressive loss of kidney function, leading to end-stage kidney disease in a significant amount of cases. The main objective of our study is to determine whether anti-GBM titer correlate with rate of activity in renal biopsy and long-term kidney survival in patients with anti-GBM, hence identifying patients who would potentially benefit from more intensive treatments.

Methods: A retrospective analysis was performed on anti-GBM cases from 2007 to 2018 with both positive biopsy and serology. Anti-GBM levels and kidney function at admission, discharge, treatment, and kidney biopsy findings were collected. All biopsies were reevaluated by a single, blinded pathologist. Based on a recent study by Van Daalen et al, we developed an activity score. The score was divided in a glomerular and interstitial section. In the glomerular section, a sclerotic pattern (~50% of glomeruli) was given 0 pts in activity and 3 in chronicity, a mixed pattern was given 1 pt in activity and chronicity, and a crescentic pattern (~50% with cellular crescents) was given 3 pts in activity and 0 in chronicity. In the interstitial section, the presence of fibrosis and atrophy was given between 0 and 3 pts in chronicity and the presence of tubulitis or interstitial infiltrate with neutrophils were given points in activity (0 to 3 respectively). Spearman correlation was performed between anti-GBM levels, our biopsy score, and kidney survival at follow-up.

Results: Twelve cases were identified, 9 were males, mean age was 54. Anti-GBM at admission ranged from 40 to 1517 U/mL. Ten patients were treated with cyclophosphamide, 1 with rituximab plus cyclophosphamide and 1 with only rituximab. The median number of therapeutic plasma exchange sessions was 8 (range 6-12). High antibody titers correlated with greater activity on biopsy (r 0.6, p = 0.04) and lesser chronicity (r -0.7, p =0.02). Kidney loss at follow-up (35 months) was 92%.

Conclusions: These results suggest that patients who present higher titers have more acute inflammation, and therefore could benefit from more intensive treatment. It would be interesting to study this score in larger cohorts in order to produce more definitive conclusions.

PUB163
Antisynthetase Syndrome and Nephrotic Syndrome

Noe Martinez-murillo, Jorge J. Font, Jonathan Chavez, Joana G. Navarro gallardo, Jose A. Torres, Christian P. Flores. Universidad de Guadalajara, Guadalajara, Mexico.

Introduction: The presence of anti-synthase syndrome and IgA nephropathy is unusual. symptoms similar to other diseases that affect the connective tissue: Lupus, Rhematoid and other.

Case Description: A 39-year-old female patient was admitted to the hospital in 2018 with proteinuria, hematuria, and acute renal failure. Her lack of ANCA rendered her disease entity mystifying and puzzled providers in terms of how to proceed with treatment.

Case Description: A 39-year-old Caucasian female was admitted to the hospital with a one day history of shortness of breath. Her admission was complicated by pre-existing hypertensive arterial disease, pulmonary edema confirmed by a complete reliance on venovenous extracorporeal membrane oxygenation. Labs showed acute kidney injury (AKI) with a serum creatinine of 3.70 mg/dL. Urinalysis demonstrated
large blood, 4–10 red blood cells, and proteinuria > 1000 mg/dL. Urine protein creatinine ratio was 3.895 mg/g. She developed bloody endotracheal tube secretions, warranting performance of bronchoscopy that was consistent with diffuse alveolar hemorrhage. Given that serological work up, including ANCA, returned unremarkable, the etiology of her renal failure was unclear. Her AKI became oliguric and she was initiated on continuous venovenous hemodialysis (CVVHD). Given the uncertainty regarding the etiology of her renal failure, and therefore how to proceed with treatment, despite her hemodynamic instability, renal biopsy was performed. Findings were consistent with segmental sclerosis and showed intratubular red blood cell casts and mesangial hypercellularity. No evidence of glomerulonephritis or interstitial nephritis was observed. The patient was treated with IV fluids, diuretics, and eventually dialysis. She was discharged home after a month in the hospital with improved renal function.

**Case Description:** A 46-year-old male with a history of Intravenous (IV) drug use and Hepatitis C had been admitted to the hospital with shortness of breath and chest pain. Patient was found to have Methicillin Resistant Staphylococcus bacteria and tricuspid valve endocarditis. Physical examination was positive for bilateral leg edema and pan systolic murmur over left lateral sternal border. Initial serum creatinine was 1.54 mg/dL (baseline 0.4 mg/dL). Urine analysis revealed proteinuria and hematuria. The patient subsequently developed acute kidney injury with increased creatinine to 5.5 mg/dl, UPCR: 5.81g/g and INR: 1.0 as the patient by then had stopped taking warfarin. Labs showed creatinine: 5.5mg/dl, UPCR: 5.81g/g and INR: 1.0 as the patient by then had stopped taking warfarin. Additional serology tests were performed with unrevealing results. She was managed with pain medications and had conservative management.

**Discussion:** The presence of nephrotic syndrome in this patient presents a challenging scenario and MPGN secondary to hepatitis C may be considered a differential diagnosis in this case. SAGN, a form of monoclonal gammopathy associated with proteinuria, though not common, has been described in SAGN and endocardiitis-associated GN cases in variable percentages, ranging from 6-48%.

**PUB168**

Unmasking of Pancreatobiliary Carcinoma in a Patient with Fibrillary Glomerulonephritis

Avneek Singh Sandhu,1 Harold J. Duarte,1 Natallia Maroz.1 2 Kettering Health Network, Dayton, OH; 1Wright State University, Dayton, OH.

**Introduction:** Fibrillary Glomerulonephritis (FGN) is a rare disease with known malignancy correlation. Cancer can be discovered simultaneously with the diagnosis of FGN or later in the course of the disease. As per our knowledge, this case is a first description of rapidly progressing pancreatobiliary carcinoma (PBC) associated with FGN.

**Case Description:** 49 y/o white woman presented to the nephrology office with proteinuria of 1.3 g/d and hematuria. She had a past medical history of smoking (>20 years) and hysterecmy for uterine fibroids. Serologic work up was unrevealing. Kidney biopsy reported FGN with minimal intimal scarring. Oncology referral was made to rule out hidden malignancy. She had an unremarkable CT scan of the chest and abdomen, PAP smear, mammogram, colonoscopy as well as normal chemical evaluation and ultrasound of thyroid. Patient quit smoking and had conservative management. Introduction of ACE-I led to reduction in proteinuria to 0.6 g/d. Unfortunately, she had decline in creatinine from 0.6 to 1.0 mg/dl, and worsening of proteinuria to 1.3 g/d associated with edema and weight gain. Therapy with Acthar® injections was initiated at the dose of 80 units thrice weekly. Patient had rapid improvement in proteinuria and swelling, and after 12 months of therapy, Acthar® dose was reduced to 40 units twice weekly. Creatinine remained stable. 24 months after the initial presentation and 13 months from Acthar® therapy initiation, she developed acute pancreatitis. Imaging studies showed pancreatic pseudocyst. Unfortunately, her pain did not improve. During the second hospitalization, a month later, HIDA scan and FGD were performed with unrevealing results. She was managed with pain medications and Acthar® therapy was uninterrupted. Patient underwent MRCP 3 months after the initial presentation, which showed pancreatic mass and multiple liver lesions. Biopsy of the liver lesion demonstrated poorly differentiated adenocarcinoma. Palliative chemotheraphy was initiated but was not tolerated by the patient. Patient deceased 4 months after the development of pain symptoms.

**Discussion:** Consideration of a hidden malignancy is a part of FGN management. PBC is a devastating cancer with dismal survival. Conducting an aggressive and repetitive work up for malignancy in patients with a new diagnosis of FGN may improve outcomes.

**PUB169**

A Case of Proliferative Glomerulonephritis with Monoclonal IgG Deposits Following Influenza Infection

Merve Postacioglu.1,2 1Kent Hospital, Warwick, RI; 2Brown University Department of Medicine, Providence, RI.

**Introduction:** Proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) is relatively a new entity. It is a form of monoclonal gammopathy with renal significance. Our patient is presented with this rare disease triggered by very common illness, influenza infection.

**Case Description:** A 61-year-old female with a past medical history of chronic kidney disease stage IIIB, and type 2 diabetes mellitus presented to the hospital with gross hematuria for 1 week and right-sided flank pain started within last 24 hours. The patient was diagnosed with influenza A infection 10-days before her hospital admission and treated with Oseltamivir. She was started on captopril and enalapril. She had a history of hypertension for 21 years. She was hypertensive otherwise hemodynamically stable. Her physical exam was significant for right-sided costovertebral angle tenderness. BMP showed creatinine as 2.73 mg/dl which was 1.33 mg/dl at baseline. She was diagnosed with acute kidney injury and started on IV fluids resuscitation. Her urinalysis revealed 58/HPF red blood cells and 7/HPF white blood cells. The kidney ultrasound was unremarkable. CT abdomen and pelvis did not show any evidence of neoplasia. On further examination, she was found to have IgA glomerulonephritis with IgA deposits in glomeruli and interstitium. She was started on corticosteroids and IgA-depleting immunoglobulin. She had rapid improvement in proteinuria and swelling, and after 12 months of therapy, Acthar® dose was reduced to 40 units twice weekly. Creatinine remained stable. 24 months after the initial presentation and 13 months from Acthar® therapy initiation, she developed acute pancreatitis. Imaging studies showed pancreatic pseudocyst. Unfortunately, her pain did not improve. During the second hospitalization, a month later, HIDA scan and FGD were performed with unrevealing results. She was managed with pain medications and Acthar® therapy was uninterrupted. Patient underwent MRCP 3 months after the initial presentation, which showed pancreatic mass and multiple liver lesions. Biopsy of the liver lesion demonstrated poorly differentiated adenocarcinoma. Palliative chemotheraphy was initiated but was not tolerated by the patient. Patient deceased 4 months after the development of pain symptoms.

**Discussion:** Consideration of a hidden malignancy is a part of FGN management. PBC is a devastating cancer with dismal survival. Conducting an aggressive and repetitive work up for malignancy in patients with a new diagnosis of FGN may improve outcomes.
cause. cFSGS complicating HLH is rare. Excessive immune activation with release of pro-inflammatory cytokines targeting the podocytes is hypothesized to cause cFSGS in HLH. Renal prognosis appears to be poor despite therapy and most patients remain dialysis dependent. HLH has been reported post stem cell transplant and should be considered in the differential diagnosis of cFSGS.

**PUB172**

**Epidemiology of Glomerular Diseases in Minia Governorate: A 5-Year Single-Center Experience**

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**Background:** Studying the pattern of glomerular diseases gives an important insights about factors associated with its development or progression.

**Methods:** This is a retrospective study includes 312 patients underwent kidney biopsy at Minia university hospital between 2014 to 2019. The aim of this study was to highlight the histopathological patterns of glomerular disease in Minia governorate.

**Results:** A total of 312 biopsy-proven glomerular diseases were reported. The mean age was 31.65±13.77 years, 61.5% were females Table (1). The most common clinical presentation was nephrotic Syndrome (39.4%). Lupus Nephritis contributed 27.9%, followed by Membranoproliferative glomerulonephritis (15.4%) Focal segmental glomerulosclerosis (13.5%), IgA nephropathy (11.5%), amyloidosis (7.7%), Crescentic glomerulonephritis (5.8%), Thrombotic microangiopathy (4.8%), Vascular nephropathies (3.8%), Minimal change disease (3.8%), Membranous nephropathy (2.9%), Postinfectious glomerulonephritis (1.9%) and Diabetic nephropathy (0.96%). Table (2). Eighteen patients (62.1%) of lupus nephritis belonged to FSGS/RPG class IV, seven patients belonged to class III, and four patients belonged to class V.

**Conclusions:** Histopathological patterns of glomerular disease may indicate regional and ethnic variations that could point towards genetic or environmental influence. This might help in effectively managing this disease by identifying the predisposing factors.

**Results:**

<table>
<thead>
<tr>
<th>Glomerular Disease</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal change disease (MCD)</td>
<td>34</td>
<td>10.9%</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis (FSGS)</td>
<td>36</td>
<td>11.5%</td>
</tr>
<tr>
<td>Membranous nephropathy (MN)</td>
<td>21</td>
<td>6.7%</td>
</tr>
<tr>
<td>Lupus nephritis (LN)</td>
<td>23</td>
<td>7.4%</td>
</tr>
<tr>
<td>Membranoproliferative glomerulopathy (MPGN)</td>
<td>9</td>
<td>2.9%</td>
</tr>
<tr>
<td>Crescentic glomerulonephritis (CGN)</td>
<td>7</td>
<td>2.2%</td>
</tr>
<tr>
<td>Amyloid</td>
<td>6</td>
<td>1.9%</td>
</tr>
<tr>
<td>Diabetic nephropathy (DN)</td>
<td>5</td>
<td>1.6%</td>
</tr>
<tr>
<td>Vascular nephropathy (VN)</td>
<td>4</td>
<td>1.3%</td>
</tr>
<tr>
<td>IgA</td>
<td>3</td>
<td>0.9%</td>
</tr>
<tr>
<td>Thrombotic microangiopathy (TM)</td>
<td>3</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

**Conclusions:**

The most common glomerular disease was minimal change disease (10.9%), followed by focal segmental glomerulosclerosis (11.5%), membranous nephropathy (6.7%), lupus nephritis (7.4%), and membranoproliferative glomerulopathy (2.9%). Other less common diseases included crescentic glomerulonephritis (2.2%), amyloidosis (1.9%), diabetic nephropathy (1.6%), and vascular nephropathy (1.3%).

**Discussion:**

The epidemiology of glomerular diseases in Minia governorate shows a predominance of mesangial and membranous diseases, with minimal change disease being the most common. These findings highlight the need for targeted interventions to prevent and manage these conditions effectively.
**A for Amyloidosis**

Muhammad Y. Jan, Simit Doshi. Indiana University School of Medicine, Indianapolis, IN.

**Introduction:** We present a case of amyloidosis related amyloidosis presenting as acute injury (AHUS) with nephritic range proteinuria.

**Case Description:** A 62 years old man with type 2 diabetes mellitus and hepatitis C (transplant) was admitted with complaints of bilateral foot pain of 3 weeks duration leading to inability to ambulate. Work up revealed pedal wounds with drainage and imaging was consistent with amyloidosis. Blood cultures were positive for methicillin sensitive staphylococcus aureus (MSSA) which was treated with IV antibiotics. Baseline serum creatinine (SCr) was 2.0 mg/dL and SCr on admission was 3.85 mg/dL, which was thought to be from acute tubular necrosis related to sepsis from amyloidosis. Work up of AKI revealed nephrotic range proteinuria of 4.7g, hematuria without dysmorphic red blood cells and monoclonal kappa IgM spike on serum protein electrophoresis. Kappa/Lambda ratio was 8.6g/dl with serum albumin of 1.9g/dl. Hemoglobin A1c level was 4.6%. Left below knee amputation was performed and patient was transitioned to 4 weeks of oral cephalixin. SCr on discharge was 2.9 On clinic follow up, repeat labs showed non-resolution of AKI as well as nephrotic range proteinuria of 6.8g and a kidney biopsy was obtained. His wound was healing slowly and antibiotic duration was extended.

Kidney biopsy showed no glomerular obsolescence or hypercellularity. Mesangial and glomerular capillary walls showed Congo Red Positive deposits. Thickening of glomeruli was noted with segmental duplication. Tubular atrophy and interstitial fibrosis was 20%. Staining was positive for serum amyloid A (AA) in glomeruli, arterioles, and tubular basolateral membranes. Immunofluorescent staining was negative. Electron microscopy showed mesangial expansion with randomly arrayed extracellular fibrils with solid cores and a mean diameter of 9.8 nanometer.

**Discussion:** Patient completed extended oral antibiotic therapy for osteomyelitis with resolution of M spike on SPEP and improvement of creatinine to baseline. Deposition of serum amyloid A (SAA) protein, an acute phase reactant is a potential complication of therapy. Causes can be sometimes chosen, and results from multiple prospective multicentered studies have been reported for its clinical usefulness. However, the treatment selection criteria has not been cleared. We retrospectively analyzed the patients who underwent TSP therapy in our facility and investigated the factors associated with efficacy of this therapy.

**Methods:** Subjects are 63 patients with IgAN who underwent TSP in our hospital (treated) was admitted with complaints of bilateral foot pain of 3 weeks duration leading to inability to ambulate. Work up revealed pedal wounds with drainage and imaging was consistent with amyloidosis. Blood cultures were positive for methicillin sensitive staphylococcus aureus (MSSA) which was treated with IV antibiotics. Baseline serum creatinine (SCr) was 2.0 mg/dL and SCr on admission was 3.85 mg/dL, which was thought to be from acute tubular necrosis related to sepsis from amyloidosis. Work up of AKI revealed nephrotic range proteinuria of 4.7g, hematuria without dysmorphic red blood cells and monoclonal kappa IgM spike on serum protein electrophoresis. Kappa/Lambda ratio was 8.6g/dl with serum albumin of 1.9g/dl. Hemoglobin A1c level was 4.6%. Left below knee amputation was performed and patient was transitioned to 4 weeks of oral cephalixin. SCr on discharge was 2.9 On clinic follow up, repeat labs showed non-resolution of AKI as well as nephrotic range proteinuria of 6.8g and a kidney biopsy was obtained. His wound was healing slowly and antibiotic duration was extended.

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Sudden Explosive Onset of Collapsing FSGS in the Setting of Influenza: An Unusual Presentation

Amaresh R. Vanga, Varun Malhotra. Eastern Virginia Medical School, Norfolk, VA.

Introduction: Collapsing FSGS (Focal Segmental Glomerulosclerosis) is often seen in the setting of HIV, parvovirus infection, and parvovirus infections. Here we present a case that was explosive in onset and was associated with influenza.

Case Description: An 68-year-old African American male presented with three weeks of dysphagia secondary to esophageal rings with dilations in the past, acute myeloid leukemia s/p allogetic stem cell transplant and deep vein thrombosis. His stem cell transplant was a year prior to presentation, and he was tapered off MMF and to a lower dose of tacrolimus with prednisone. On physical exam, he had gross anasarca. His labs were notable for a serum creatinine of 1.5 mg/dL from a prior baseline of 1.3 mg/dL. His albumin was 1.2 g/dL with a spot urine protein to creatinine ratio of 3.12 and a LDL of 292. Serologies for hepatitis and lupus were negative. Complement levels were indicated corrected calcium of 11, potassium of 5.9, Co2 of 18, hemoglobin of 8 with 97%. Physical examination was benign. His creatinine was 6.9. His baseline creatinine was 1.8(for the past few years) and thought to be related to his hypertension. Other labs indicated corrected calcium of 11, potassium of 5.9, Co2 of 18, hemoglobin of 8 with normal platelets, and WBC. USG(Ultrasound) of kidneys revealed subepithelial Indigenous variant focal segmental glomerulosclerosis (FSGS), with diffuse fusion of foot processes, but no tubular epithelial changes. Lithium was discontinued, and the patient continued to improve to creatinine of 2.4 with improvement in urine output at which point he was discharged on ACE-I.

Discussion: Collapsing FSGS in probably related to complex interplay of multiple factors like infection, acute kidney injury due to other etiologies, genetic risk factors such as APOE1. Recent cases of COVID-19 related AKI point towards the possibility of collapsing FSGS as the etiological mechanism, especially with APO1 association. Though it is traditionally described in the setting of infections like parvovirus and HIV, there could underlyling common mechanisms for infections that may not be exclusive to these and may expand to other infectious etiologies like influenza, COVID.

Renal Response and Its Predictive Factors of Lupus Nephritis: A Two-Year Cohort of 77 Hospital-Based Patients

Zhiming Lin, Junmei Feng, Jun Zhang, Changlin Zhao, Zhen Wu. Department of Rheumatology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; Department of Nephrology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; Department of Vasculocardiology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

Background: To evaluate the renal response rates of lupus nephritis (LN) patients undergoing standard treatment during a two-year follow-up and investigate its predictive factors.

Methods: A prospective cohort study enrolled 77 clinically diagnosed LN patients was carried out. All patients underwent standard treatment according to Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations or American College of Rheumatology (ACR) guidelines for the management of LN. Regular visits were performed every 6 months until 2 years. Data on renal response and clinical characteristics were collected and analyzed.

Results: Among 77 patients, 41(53.2%) and 15(19.5%) patients achieved complete response (CR) and partial response (PR) at 6 months after induction therapy, respectively. With every 6-months visit, 53(68.8%) patients completed the whole 2-year follow-up. 38(71.7%) and 5(9.4%) patients developed CR and PR at 2 years. During follow-up, serum creatinine (SCr) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score showed a significant difference as compared to baseline data, while estimated glomerular filtration rate (eGFR) and C3 level gradually elevated. In multivariate regression model, immunological disorder (OR 4.73, 95%CI 1.00-22.40, p=0.05), eGFR (OR 1.04, 95%CI 1.02-1.07, p<0.001) and SLEDAI (OR 1.21, 95%CI 1.05-1.40, p=0.01) at baseline were found to be associated with CR/PR at 6 months as compared to non-responders.

Conclusions: Nearly 70% LN patients achieved renal response after 6-months standard induction therapy, and the renal response rates were higher after 2 years. Renal function and disease activity showed a significant improvement during follow-up. Besides, immunological disorder, higher baseline eGFR and SLEDAI were predictive factors for renal response.

Funding: Government Support - Non-U.S.

Hypoaalbuminemia Out of Proportion to Proteinuria in a Patient with Nephrotic Syndrome

Chidi Egwim, Javier Jaramillo Morales, Laura Binari, Gautam B. Bhave. Vanderbilt University Medical Center, Nashville, TN.

Introduction: Hypoaalbuminemia is a fundamental characteristic of nephrotic syndrome, with most of the albumin loss resulting from urinary excretion. As such, the degree of proteinuria in a glomerular process often mirrors the serum albumin. The differential and work-up changes when there is discordance between the two.

Case Description: A 68-year-old African American male presented with three weeks of a worsening cough, diarrhea, and progressive swelling. His past medical history was notable for dysphagia secondary to esophageal rings with dilations in the past, acute myeloid leukemia s/p allogetic stem cell transplant and deep vein thrombosis. His stem cell transplant was a year prior to presentation, and he was tapered off MMF and to a lower dose of tacrolimus with prednisone. On physical exam, he had gross anasarca. His labs were notable for a serum creatinine of 1.5 mg/dL from a prior baseline of 1.3 mg/dL. His albumin was 1.2 g/dL with a spot urine protein to creatinine ratio of 3.12 and a LDL of 292. Serologies for hepatitis and lupus were negative. Complement levels were indicated corrected calcium of 11, potassium of 5.9, Co2 of 18, hemoglobin of 8 with 97%. Physical examination was benign. His creatinine was 6.9. His baseline creatinine was 1.8(for the past few years) and thought to be related to his hypertension. Other labs indicated corrected calcium of 11, potassium of 5.9, Co2 of 18, hemoglobin of 8 with normal platelets, and WBC. USG(Ultrasound) of kidneys revealed obstructing 3mm left UVJ stone with hydronephroenephrosis. UA revealed 3 plus protein with moderate blood, 10-20 RBC per HPF, bacteria. He was started on antibiotics and a double JJ stent was placed. His stone disease is probably a manifestation of parathyroid adenoma. He was awaiting parathyroidectomy and was maintained on sensiparin in the interim. His creatinine continued to increase and peaked at 7.5 mg/dL. However repeat urinalysis revealed significant proteinuria and on quantification, it was 17g with albumin of 2.

Discussion: Though it is traditionally described in the setting of infections like parvovirus and HIV, secondary membranous nephropathy. Staining for PLA-2R was positive. He was started on basiliximab and continued treatment as an outpatient.

Discussion: Here we describe a case of nephrotic syndrome in which the degree of hypoaalbuminemia was not consistent with the amount of proteinuria. This discordance represents a defect in the homeostasis of albumin typically seen in nephrotic syndrome. At a steady state, albumin synthesis is balanced by albumin catabolism and urinary loss. In nephrotic syndrome, catabolism is decreased while synthesis and urinary loss increases.

The patient’s history of diabetes and dysphagia suggested that he had either increased catabolism from non-renal GI losses or decreased synthesis due to poor intake. This case highlights alternative laboratory findings in membranous nephropathy and a framework for understanding the differences.

An A-Tip-ical Side Effect of Lithium

Casie James, Randall Craver, Isa Ashoor. Louisiana State University Health Sciences Center, New Orleans, LA.

Introduction: Lithium is a mood stabilizer approved for bipolar disorder treatment in children as young as 12 years. Though effective in the pediatric population, lithium requires close monitoring for toxicity and adverse effects.

Case Description: An 18 year old male with Hashimoto’s thyroiditis, bipolar I disorder, and anxiety presented with 10 days of edema, weight gain, progressive abdominal pain, nausea, diarrhea, and decreased urine output with frothy urine. Medications included levothyroxine, Risperdal, and lithium. Creatinine was 1.2 mg/dL, up from baseline of 0.8 mg/dL. There was nephrotic-range proteinuria, with spot urine protein/creatinine ratio of 9. Serum lithium level was 2.5 mmol/L (therapeutic range 1-1.2 mmol/L). Renal biopsy showed tip variant focal segmental glomerulosclerosis (FSGS), with diffuse fusion of foot processes, but no tubular epithelial changes. Lithium was discontinued, and the patient underwent diuresis with Lasix/albumin infusions. Proteinuria resolved within two months, and he remains in remission. Bipolar disorder is now treated with Lamictal and Risperdal.

Discussion: Lithium has a wide side effect profile, requiring close monitoring. Lithium-induced nephrotic syndrome is a known, idiopathic side effect. Most renal biopsies show minimal change disease; however, FSGS has also been associated with lithium use. To our knowledge, this is the first documented case of tip variant FSGS in a teenager. While lithium may have induced nephrosis, the low effective circulating volume in nephrotic syndrome with subsequent decrease in glomerular filtration rate likely led to poor excretion of lithium, leading toxic levels and protracted recovery from adverse effects. Despite atypical histology, the patient followed a favorable course and remains in remission without immunosuppressive therapy.
AKI After Eculizumab Interruption in a Case of C3 Glomerulopathy
Mostafa F. Elshirbeny, Mohammed E. Hussain, Essa Abuhelaiqa, Awaïs Nauman. Hamad Medical Corporation, Doha, Qatar.

Introduction: C3 glomerulopathy (C3G) is a newly recognized rare disease characterized by predominantly glomerular deposition of complement C3. Treatment with the C5 complement inhibitor eculizumab may be a therapeutic option but due to rarity of the disease, predicting tools of the outcomes remain largely unknown.

Case Description: Here we report 25-year old female patient who was referred to nephrology clinic with renal impairment, hematuria, and proteinuria. Kidney biopsy results revealed membranoproliferative changes with predominant C3 deposits, suggestive of C3 glomerulopathy. Genetic testing revealed two unrelated mutation in C3 gene, likely not related to C3G. Patient was responding well to oral steroid and MMF with remission of proteinuria and normalized serum creatinine. She was relapsed again, 1 year later with hematuria and nephrotic proteinuria. Steroids and MMF were resumed with no response then started on eculizumab, after which she achieved partial remission with reduction in serum creatinine and urine protein. During next 2 years, patient missed eculizumab in 2 occasions. The first, when she missed one dose followed by mild rise in serum creatinine which improved after eculizumab resuming and few months later she missed two doses then presented with severe AKI requiring dialysis. Was started on steroids and eculizumab was resumed with no improvement in kidney function and patient still dialysis dependent.

Discussion: Despite looks like safe and valuable therapeutic option in patients with C3G but the response to eculizumab is heterogeneous and when to discontinue the therapy still unsolved problem as transient interruption of the therapy sometimes complicated with AKI which may be severe enough to end with ESRD like this case.

Serum creatinine results during 40 months of follow up
remission rate of hematuria in TSP group (100%) was much higher than that in CT group (48%). Moreover, immunosuppression therapy was effective to prevent significant decline in kidney function.

Conclusions: We clarified that more than half of patients with isolated hematuria showed crescend or endocapillary proliferation in present study. Immunosuppression therapy is effective for those lesions. Thus, even in the patients with isolated hematuria, conservative treatment can be a risk for deterioration of renal function.

PUB184

Indolent Pauci-Immune Crescentic Glomerulonephritis
Elizabeth Pepper1, Jalal E. Hakem1,2 Edward Via College of Osteopathic Medicine - Carolinas Campus, Spartanburg, SC; 3Palmetto Nephrology, Orangeburg, SC.

Introduction: Pauci-immune glomerulonephritis (PIGN) is most commonly associated with a rapidly progressive course towards renal failure, although rarely, an indolent course may be observed. PIGN has a frequent association with either MPO- or PR3-antibodies and is associated with extra-renal manifestations. We report a patient with slowly decreasing renal function over the course of two years that had a renal-limited MPO-antibody associated pauci-immune glomerulonephritis.

Case Description: A 61 year old Caucasian female with controlled hypertension, hypercholesterolemia, and prediabetes without complaints was noted by her PCP to have a slowly rising creatinine over two years. A nephrology referral was made with new onset 1+ pitting edema in the bilateral, distal lower extremities and a creatinine of 1.7mg/dL. Urinalysis at this point showed a sediment and 2g/g of protein to creatinine. A renal ultrasound showed structurally sound kidneys. Common infectious causes of renal disease were ruled out. C and HIV were negative and ANA, PR-3, and C4 were sent to see if there was an autoimmune cause. A positive MPO prompted a renal biopsy which yielded a sample of 50 glomeruli with 15 completely sclerosed, 4 with crescent formation, and moderate to severe interstitial fibrosis and tubular atrophy. This confirmed the diagnosis of MPO- associated PIGN. Immunosuppression was begun with a rituximab based therapy, but the second dose of rituximab was interrupted due to severe back pain combined with nausea and vomiting. Creatinine was elevated at 3.6mg/dL from 2.2mg/dL the day before. Methylprednisolone was tapered and further infusions were not pursued due to development of deranged liver function tests, hospitalization for diverticulitis, development of uncontrolled DM, and severe psychological symptoms. Over the following two months, the patient’s creatinine has trended down to 1.5 mg/dL.

Discussion: Her consistently rising creatinine was the main driver to begin immunosuppressive therapy despite having moderate to severe interstitial fibrosis and tubular atrophy. Rituximab-based therapy was shown in the RAVE trial to be non-inferior to cyclophosphamide for induction of remission in ANCA associated disease. This combination may also have superior relapse rates and a better safety profile in comparison with cyclophosphamide. Her improving creatinine suggests that even an incomplete regimen might have conferred some benefit.

PUB185

IgG4-Related Disease Presenting with Membranous Nephropathy
Elena Zakhareva1,2 City Clinical Hospital n.a. S.P. Botkin, Moscow, Russian Federation.

Introduction: Immunoglobulin G4-related disease (IgG4-RD) is a condition, affecting multiple organs. Retroperitoneal fibrosis with obstructive nephropathy and interstitial nephritis are most typical kidney damage. Rare cases of glomerular disease, including membranous nephropathy (MN), had been described. Search for IgG4-RD in the database of our nephrology unit showed 11 patients, in three cases kidney biopsy was performed, and we present one of them.

Case Description: 73 years old Caucasian female with a history of arterial hypertension, diabetes, skin patchy hyperpigmentation, asthma and nasal polypsym at the time of presentation. In 2016 with the weight loss and skin rash. 9 months later, at admission, she was undernourished, with multiple skin scratches, pedal edema, and otherwise unremarkable physical exam; her blood pressure was 150/90 mm Hg, vital signs were normal. Work up demonstrated nephrotic syndrome and marked eosinophilia (32.6% vs 2.6%-10^9/L). Her blood chemistry tests, serum and urine immunocomplex, p and C ANCA, PR3, MPO, and anti-CEP-PR3 antibodies were negative. Kidney biopsy showed MN with IgG, C3, kappa and lambda fine granular deposits on the capillary loops periphery. Her anti-PR3 antibodies titer was <1:10; kidneys, abdomen, neck and pelvis ultrasound, chest CT, gastroscopy and colonoscopy were unremarkable. Tests for parasitic infections and mycofus hypersusnicosis syndrome markers (FPII1/ PDGF-Rα and ETV6-PDGFβ) were negative. IgG4 level was 1.9g/l (0.8-1.4) – 29.2% (4.0-5.0). We diagnosed IgG4-RD and started her on oral prednisone 40 mg daily. Her skin rash resolved immediately, in a month her eosinophil count became normal, two months later complete remission of nephrotic syndrome. We added cyclosporin A and slowly tapered prednisone. At the latest follow-up visit January 2020, she was doing well, with the complete remission of nephrotic syndrome, preserved kidney function and normal IgG4 level.

Discussion: Clinical presentation was suggestive for ANCA-associated vasculitis or systemic sclerosis, not confirmed by serology and kidney pathology findings. The search for the hypersusnicosis syndrome causes was negative, and only IgG4 testing gave a clue to the diagnosis. Steroids allowed controlling hypersusnicosis symptoms, but not kidney disease, which was in favor of IgG4-RD. We conclude that IgG4-RD should be considered in differential diagnostics of membranous nephropathy.

PUB186

Role of Therapeutic Plasmapheresis in ANCA-Associated Vasculitis: A Single-Center Study
Aglaia Chalkia1, Alexandros G. Panagiotopoulos1, Panagioti E. Giannou, Dimitris Kourniotis1, Athanasia Kapota1, Margarita Mpora1, Dimitrios Vassilopoulos2, Dimitrios I. Petras1, Nephrology Department, Hippokration General Hospital, Athens, Greece; 2Joint Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine - Clinical Immunology - Rheumatology Unit, 2nd Department of Medicine, Athens, Greece.

Background: Recently Pexivas trial showed no benefit of plasmapheresis (PEX) in ANCA-associated vasculitis (AAV), even in patients with alveolar hemorrhage, but is this the end of PEX in AAV? The aim of this study is to describe the indications, method and complications of PEX, as well as whether PEX is associated with improvement in renal function and survival at 12 months.

Methods: Retrospective study of 28 patients with severe manifestations of AAV, who had received PEX adjunctive to conventional therapy for the first episode of AAV or in relapse.

Results: We recorded twelve patients receiving PEX. This group (n=12) had an average age at diagnosis 79 years and was followed for a median period of 20 months. In 75% of the patients MPO-ANCA was positive, in 17% ANCA negative and in 8% double positive anti-GBM/ANCA. On admission, all patients had abnormal renal function with average creatinine 5mg/dL±2.12 and the majority of patients (9/12) were dialysis dependent. Indications for plasmapheresis were: alveolar hemorrhage in 33%, renal impairment in 25% and combination of the two above in 42%. Plasmapheresis was performed using filtration and fresh frozen plasma as replacement fluid. The mean number of plasmapheresis treatment was 8 (1-19 days) and the average internal time between admission and first plasmapheresis treatment was 3 days. No episodes of severe infection or death were recorded during plasmapheresis. All patients received concomitant therapy with Cyclophosphamide and corticosteroids while Rituximab was added in 3 patients. Hbpation was reduced for patients with alveolar hematoma. The study included all patients (100%). After one year, 75% of the patients had renal recovery (cre±5mg/dL±2.12 vs cre±2.6mg/dL±1.6, p=0.06) and 67% of the patients who received hemodialysis at the time of diagnosis, during the first year became independent of dialysis (75% vs 33%, p=0.5). Finally, survival rate at the end of the first year was 83%.

Conclusions: Plasmapheresis is quite often used in daily clinical practice with remarkable results in dialysis independence and survival, without serious complications.

PUB187

Retrospective Analysis of Five Cases of Proliferative Glomerulonephritis with Monoclonal IgG Deposition Regarding Their Clinical Course and Responses to Therapy
Takatsugu Iwashita1, Minoru Hatano, Koki Ogawa, Ryo Yamamoto, Yuta Kogure, Hajime Hasegawa. Saiitama Medical Center, Saiitama Medical University, Kawagoe, Japan.

Introduction: At present, limited knowledge is obtained regarding pathophysiology and clinical course of proliferative glomerulonephritis with monoclonal IgG deposition (PGNMID). It is rarely diagnosed by renal biopsy, and there is no established therapeutic strategy for this disease. We report clinical course and responses to the therapy of 5 cases diagnosed as PGNMID in our facility.

Case Description: Method Five cases (3 males and 2 females, median age 62 years) with renal biopsies and diagnosed as PGNMID between January 2016 and December 2019 were retrospectively analyzed regarding the transition of eGFR and urine protein level by the treatment. Three of 5 cases were treated by steroid alone in combination with intravenous methyl prednisolone (PSL) 500 mg/day for 3 days and oral PSL 30 mg/day. Remaining 2 cases were treated with intravenous methyl PSL and oral PSL followed by Cyclophosphamide intravenously (750 mg/day, twice) or orally (100 mg/day, daily) administration and Rituximab (500 mg/bottle, twice) administration. Results Light microscopic findings were MPGN type in all cases, and immunofluorescent staining showed 4 cases were IgG3-kappa and only 1 case was IgG3-lambda. Three cases in the first month of the treatment had partial remission (KDIGO diagnostic criteria, defined as a urinary protein level of < 0.3-3.5 g/day and a reduction of ≥ 50% from baseline), and all had partial remission at 6 months. Hemataria was observed at the start of treatment in three cases and disappeared in only one case by the treatment. And, the remarkable deterioration of renal function was not observed during the clinical course. However, two cases showed the increase of urine protein after about one year from mPSL administration, and IVCY and RTX were administered, but urine protein and hemataria were not decreased, and mPSL was administered again. In one case, the improvement of the urinary finding was scarce even after the increase in the administered steroid.

Discussion: Conclusion Our results suggest that the treatment responsiveness to IVCY and RTX is poor, that steroids are more responsive to initial therapy, that disease activity increases with dose reduction (a steroid-dependent condition), and that treatment responsiveness to steroids may decrease after relapse.
AA Amyloidosis and CKD in a Patient with Coexisting Hepatitis C Infection and Crohn Disease

Introduction: AA amyloidosis is in the differential diagnosis of patients with proteinuria and may lead to chronic kidney disease (CKD). It is usually associated with chronic inflammatory conditions like rheumatoid arthritis which is implicated in 40% of cases. Crohn’s disease (CD) is also recognized as an underlying etiology. We present a patient with chronic Hepatitis C infection (HCV) and CD who developed proteinuria and CKD in a relatively short period of time.

Case Description: 33-year-old man with a past medical history of CD, HCV, and cocaine/heroin abuse with frequent IV drug use presented to the ED with complaints of bilateral lower extremity swelling and tenderness. Initial laboratory studies were significant for a creatinine of 4.56 and nephrotic range proteinuria. On review, his creatinine had been trending up from 0.75 mg/dl to 4.09 mg/dl in the last year. Secondary work-up for proteinuria including: ANA, RPR, RF, ANCA, C3, C4, Cryoglobulin with reflex, ds DNA Ab, UPEP, and SPEP w/ immunofixation screenings all yielded negative results. S. cerevisiae Ab IgA was 51.5, a positive confirmation of patient’s CD. HCV antibody test was positive with a positive HCV RNA. Renal biopsy was performed and revealed AA amyloidosis with severe interstitial fibrosis and tubular atrophy.

Discussion: AA amyloidosis is a disorder characterized by the overproduction of extracellular proteins that deposit and subsequently cause organ and tissue impairment. It is often attributed to chronic inflammatory/infectious diseases. Though literature about the incidence of AA amyloidosis in people afflicted with HCV is limited, incidence in individuals afflicted with CD has been reported to be between 0.5%-8%. AA amyloidosis has also been found to be a major cause of CKD in IV drug users. One UK study found that up to 55% of these patients have associated HCV. There are reports of increased CD “flares” in patients undergoing treatment for chronic HCV, which may suggest that the coexistence of both diseases may lead to worse morbidity. Our case is unique due to the coexistence of two chronic diseases that lead to inflammatory/infections processes known to be involved in the pathophysiology of AA amyloidosis. This co-existence may lead to a faster progression of CKD and overall worsening outcomes.

Awareness of Association of ANCA Vasculitis and Aortic Aneurysm Can Improve Survival
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Introduction: ANCA vasculitis is a small-medium vessel vasculitis which is characterized by systemic necrotizing inflammation of blood vessels. Aortic aneurysm is a very rare complication of ANCA vasculitis. We describe a case of such association and highlight the need for guidelines for its screening in patients diagnosed with ANCA vasculitis.

Case Description: 40 year old man with no known medical history presented with renal failure and was started on dialysis. Kidney biopsy showed pauci immune crescentic glomerulonephritis. As per KDIGO guidelines, he was treated with steroids, cyclophosphamide and plasmapheresis after which he recovered from dialysis. 3 months later, he presented with hematemesis and shock. Due to worsening hematemesis and shock, upper endoscopy was done which revealed aorto-esophageal fistula and patient died of shock with no time for surgical intervention. On retrospective analysis, we found that unfolding of aorta seen on chest xray 3 months ago was likely aortic aneurysm which had increased in size and ruptured.

Discussion: To the best of our knowledge, this is the first case reported from India. The reason we think ANCA vasculitis is associated with aortic aneurysm is because it has been proven by biopsy in case reports in the past and in few of them, aneurysm had even decreased in size with chemotherapy. Also, it is surprising that such degenerative condition would occur without any risk factor like smoking, atherosclerosis, history of hypertension, or family history of connective tissue disorders in such a young patient. Since both ANCA vasculitis and aortic aneurysm are rare pathologies, it is reasonable to consider that they are related when occurring together. Again, its rapid expansion and rupture within a span of 3 months favors an underlying association. This case highlights that nephrologists should be aware of such association, screen the patient on presentation and then at intervals likely earlier than recommended for aortic aneurysm of other etiologies.
Kidney Crimes: Stop That Drug!
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Introduction: Drug associated antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (DAV) with rapidly progressive glomerulonephritis (RPGN) is rare. Historically linked to antithyroid drugs, new evidence implicates almost every pharmacological class. Untreated, it is catastrophic. Prompt diagnosis & cessation of the offending agent is paramount. This is a case of DAV-RPGN secondary to diltiazem.

Case Description: 76-year-old male with T2DM, cirrhosis, HTN & MM in remission, on diltiazem, propranolol, insulin, presented to an outside hospital with 10- days of weakness, reduced appetite & leg swelling. On exam BP 191/79, T 97° F & anasarca. He had an upper respiratory infection and dental pain for which he took 1g of ibuprofen daily. Labs showed Na128, K 5.3, Cl100, HCO3 19, BUN 79, creatinine (Cr) 16.9mg/dL, and urine protein to creatinine ratio of 5.85. Renal ultrasound showed no hydronephrosis. Abdominal CT showed diffuse colitis. Dialysis was initiated for uremic colitis. Workup for ARF was negative for hepatitis, HIV, and autoimmune markers. Kidney biopsy revealed podocyte effacement and nonspecific minimal deposits with severe ATN. Immunofluorescence showed nonspecific mild granular tubular and glomerular IgG deposition. Electron microscopy noted widespread podocyte effacement consistent with MCD. Prednisone 60 mg daily was started. Within 48 hours oliguria resolved and dialysis was discontinued. Cr at discharge was 3.6. After a slow taper of steroids, he had a full recovery.

Discussion: Although NSAID-induced ATN is well understood, it is unusual to see ATN causing ARF with oliguria in a young patient with no comorbidities. Nephrotic syndrome induced ATN has been specifically documented in association with MCD. This is likely the mechanism of ATN development in our patient with drug-induced MCD. MCD is the most common cause of nephrotic syndrome in children but accounts for only 10-15% of adult cases. Data evaluating drug-induced MCD in adults is limited to a few case series and retrospective studies associating NSAIDs with acute interstitial nephritis, rather than ATN, as the cause of MCD. Contrary to our case, NSAIDs have shown to reduce proteinuria in idiopathic nephrotic syndrome. Corticosteroids are the first-line therapy, and adults with MCD require prolonged therapy with a slow taper. The majority of ARF induced by MCD is reversible, with complete recovery of renal function.

Kidney Aging and Estimation Equations for GFR in Beijing
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Background: When evaluating renal function, eGFR data show significant variation across different equations, particularly in elderly patients. Here, we investigated how age affected renal function in healthy subjects in Beijing and compared different eGFR equations for the evaluation of renal function.

Methods: We recruited all patients undergoing routine assessment in our hospital between January 2012 and December 2014. For each patient, we recorded age, gender, and Cr. Kidney function was evaluated by five equations: CKD-EPI, MDRD, MDRDc, FAS and BIS.

Results: A total of 46,713 subjects were enrolled. Subjects were 16 - 100 years-of-age and were followed-up for 3 years. All subjects showed an increase in Cr and decrease in eGFR with increasing age. For males, there was a more obvious and significant reduction of eGFR in the elderly; but in older females, eGFR did not tend to change. Different equations showed good consistency [the intraclass correlation coefficients (ICC) was 0.849 for males, and 0.817 for females]. The CKD-EPI equation yielded higher eGFR for older populations, with a slight overestimation of the more advanced CKD-according-to-sCr levels. There was no obvious trend for age-related change in the 3-year mean rate of GFR change when compared across age groups. For subjects aged over 70 years, the MDRD and MDRDc equations yielded significantly higher eGFR data and the BIS produced the lowest eGFR values.

Conclusions: The annual rate of GFR change was not associated with age. Different eGFR equations yielded data that varied across different populations of patients and sCr levels. We were unable to identify a specific equation for use in the elderly Chinese population.

A comparison of different GFR equations across all age groups. (A) Male. (B) Female.

Comparison of eGFR equations for different serum creatinine levels. (A) Male. (B) Female.
A Workplace Wellness Program Results in Improvements in Physical Activity and Blood Pressure in the Staff of a Hemodialysis Clinic
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Background: Evidence indicates that health and wellness programs in the workplace provide numerous benefits with respect to altering indices of health. The purpose of this study was to assess the feasibility of a workplace wellness program (WOW) as a means of improving blood pressure by participation in habitual physical activity (PA) and improving dietary choices among the staff at a hemodialysis clinic.

Methods: 26 staff members (age 46.5 ± 12.2; BMI: 28.7 ± 5.6 kg/m²) from a hemodialysis clinic (nurses, technicians, social workers, dietitians, and administrative staff) participated in the 12-week WOW program that consisted of weekly counseling sessions, the provision of educational resources, PA incentive challenges, and healthy dietary choices challenges. Body weight (kg), height (cm), blood pressure, BMI, 24-hr dietary recalls, PA behaviors (IPAQ), and waist/hip circumference were collected at weeks 0 (baseline), 6, and 12 following the conclusion of the intervention. Statistical analysis was performed using SPSS24. All primary and secondary outcomes were assessed by one-way Analysis of Variance (ANOVA) comparing values at the different testing time points, with significance at (p<0.05). Paired sample t-test was used to test the questionnaire (IPAQ) data that was collected at baseline and post intervention.

Results: The program also resulted in improvements in several health related metrics. This included reductions in body weight (1.07 kg ± 21.4; p<0.05), body mass index (p<0.005), waist circumference (cm 96.9 ± 14.8; p<0.005), and hip circumference (cm 111.7 ± 13.6; p<0.05). Systolic blood pressure change was non-significant but trending toward significance (p=0.08), while diastolic blood pressure was reduced (p<0.05). There were significant changes in PA behavior, specifically walking behavior (p<0.05), as indicated by the IPAQ.

Conclusions: The WOW program demonstrated increased measures in the staffs PA. As a result, this led to the improved health outcomes which included body weight reductions, BMI improvements, lowered hip and waist circumference, and improved diastolic blood pressures values. The study suggests that a workplace wellness program has the potential to improve health indices of the staff of hemodialysis clinics and may positively impact the health behaviors in the hemodialysis patients under their care.

Frailty Changes in Patients on Hemodialysis After an 8-Week Exercise Intervention
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Background: The Fried frailty phenotype defines frailty as having at least 3 of the following: unintentional weight loss, decreased grip strength, slow gait speed, exhaustion, and decreased physical activity. The vulnerability inherent in frailty is exacerbated in people with end-stage renal disease, but frailty assessments are typically not used. Exercise during dialysis has been shown to have positive effects on functional outcome and physiologic measures, but are not standard clinical care. The purpose of this study was to investigate the effects of an 8-week, supervised resistance and cycling program on frailty and function measures of patients undergoing dialysis.

Methods: 11 patients from the Wise Health System Dialysis Center in Decatur, TX (6 in the experimental group, 5 in the control group). The experimental group received a supervised elastic band resistance and cycling ergometer program 3 days per week for 8 weeks during dialysis. The resistance component included: ankle dorsiflexion and plantarflexion, knee flexion and extension, and hip abduction. A repeated measures 2-way ANOVA was conducted on the dependent variables of: frailty scores, gait speed, grip strength, 2-Minute Step Test, exhaustion, Timed Up and Go, and 30-second Sit to Stand Test.

Results: There was a significant difference in pre- to post-test frailty scores [F(1, 9) = 6.14, p = 0.035, \( \eta^2 = 0.41 \)]. Specifically, the exercise group’s frailty score dropped from 3.67 to 2.67 while the control group’s score did not change. This change in frailty scores was influenced by the change in the exhaustion component of the frailty score from a mean of 1.00 to 0.17 [F(1, 9) = 16.05, p = 0.003, \( \eta^2 = 0.64 \)]. There were no significant differences found in the other dependent variables. There were no adverse reactions to the exercise intervention.

Conclusions: The results of this feasibility study support the hypothesis that an exercise program during dialysis can change frailty scores in people with ESRD, as the exercise group decreased their frailty classification from frail to pre-frail. It is not clear if the benefit would persist after this time or if results would change based on the length of the program, which provides support for additional longitudinal research designs. In conclusion, it appears that a resistance and cycling exercise intervention can mitigate frailty effects in persons with ESRD.

Relation Between Anxiety, Depression, and Frailty in Maintenance Hemodialysis Patients
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Background: Both psychological disorders and frailty are prevalent and burdensome in MHD patient. However, the relationships between these entities are unclear. The aim of this study was to investigate the prevalence and associations between frailty and psychological disorders in Southern Chinese MHD patients.

Methods: This was a multicenter, cross-sectional and observational investigation conducted at 4 institutions. Frailty was evaluated with the Tilburg Frailty Indicator (TFI) and it was used as the self-reported questionnaire. Anxiety symptoms was assessed by the Self-Rating Anxiety Scale (SAS), depressive symptoms was assessed by the Self-Rating Depressive Scale (SDS). We collect sociodemographic and clinical characteristics the patients who complete the scale. Statistical analysis was performed using SPSS20.0 for Windows.

Results: Of the 623 patients visiting each institution, 300 were enrolled in this study. The mean age was 61.9 ± 13.64 years, with mean duration of HD 30.7 ± (34.3±26.3) months. 116 patients (38.7%) were female and 133 (44.3%) had diabetic kidney disease. In total, there were 225 patients (73%) were evaluated as frail. The prevalence of frailty increased steadily with age and was more prevalent in the diabetes mellitus patients. A multivariate logistic regression analysis revealed that the factors independently associated with frailty were the following: age, Charlson comorbidity index, DMSAS, SDS. There was no relationship between the duration of HD and frailty status. Anxiety and depression symptoms by SAS and SDS were identified in 52.6% and 72.0% of MHD patients. MHD patients with both anxiety and depression generally had higher frailty score. The coexisting frailty and psychological disorder were present in 45.0% patients. There was an additive effect of psychological disorder and frailty on nutritional status. For the groups with frail and psychological conditions and no frail and no psychological conditions, both serum albumin and creatinine decreased.

Conclusions: This study demonstrated that anxiety and depressive symptoms are associated with prevalent frailty in Southern Chinese MHD patients. Older age, diabetes mellitus, CCI and lower serum albumin were associated with frailty among patients on MHD. Anxiety and depressive symptoms are independent risk factors of frailty.

Potassium Binders for Treatment of Hyperkalemia: Patient Survey Examining Side Effects, Tolerability, Palatability, and Interference with Daily Activity
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Background: Even mild hyperkalemia is associated with increased mortality. There are three FDA-approved oral potassium binders for outpatient treatment of non-life-threatening hyperkalemia: sodium polystyrene sulfonate (SPS), patiromer, and sodium zirconium cyclosilicate (ZS-9). Specific studies of patient experience, satisfaction, and adherence have not been conducted for any of the three agents. We surveyed outpatients regarding their experience with these medications, including taste, texture, tolerability, and interference with daily activity.

Methods: An online, anonymous survey of outpatients a 18 years old who were dispensed SPS, patiromer, and/or ZS-9 from September 2017 to August 2019 at military treatment facilities in the National Capital Region was conducted over 8 weeks. Respondents were invited by letter including the survey url (with a reminder at 4 weeks). Survey questions included queries about demographics, medical diagnoses, medications associated with hyperkalemia, side effects, taste, palatability, and daily activity interference.

Results: 212 qualifying individuals were invited to participate. Response rate was 16% (34/212). All respondents were a51 years old. 36% were on RAASI. 28 respondents had used SPS, 6 had used patiromer, and 1 had used ZS-9. 18% of respondents treated with SPS vs. 0% treated with patiromer reported side effects. 1 reported discontinued SPS without informing their physician due to side effects. 48% reported diarrhea with SPS, 50% reported constipation with patiromer. Respondents favored taste and texture of patiromer vs. SPS (72 vs. 56 for taste, and 70 vs. 50 for texture, with a scale rating of 100 being best), and reported more difficulty swallowing SPS vs. patiromer (3% vs. 0%). Side effect severity and interference with daily activity were the same (2 and 3 respectively for both SPS and patiromer, scale of 0-10, 10 being worst).

Conclusions: Respondents who used patiromer reported better palatability and fewer side effects than those who took SPS. However, side effect severity and daily activity interference were equivalent between SPS and patiromer. Disclaimer: The views expressed are those of the authors and do not necessarily reflect the official policy or position of the Department of the Army/Navy/AFire Force, the Department of Defense, nor the US Government.
Evaluation of the Establishment of a Nutrition Care Process in a Group of Spanish Haemodialysis Patients


Background: Keeping a good nutritional status during hemodialysis must be a priority goal of the treatment to prevent complications and mortality, as well as, to improve patients quality of life. The main objective of this survey will be to evaluate if the establishment of a nutritional care process adapted to the chronic kidney disease, could improve anthropometrics and biochemical parameters in a hemodialysis hospital group of patients. We will also try to assess if the compiled results of the questionnaire about malnutrition and inflammation are correlated to the biochemical results obtained.

Methods: Information about sex, gender, dry weight, IMC, albumin status, PCR and Malnutrition Inflammation Score were collected during the months of July 2019 and March 2020. 38 haemodialysis patients participated in this study. A descriptive and frequency analysis has been carried out with all the parameters obtained. The T of Student for a related sample test was used due to the normality of the data and the participants condition of intervention - control.

Results: The results indicate that since the month of July 2019 until March 2020, 81.7% of the patients stayed on the hemodialysis program, 13.1% of the patients died, 2.6% changed malnutrition to hemodialysis, and 2.6% were transplanted. 42.1% of the total number of patients decreased their dry weight, 13.2% maintained it, and 26.3% increased it. The median values obtained in July and March respectively were: dry weight (70.2 ± 14.4 kg vs 68.9 ± 14.4 kg), IMC (20.6 ± 5.6 vs 20.6 ± 5.6 kg/m²), albumin (3.6 ± 0.3 vs 3.6 ± 0.3 g/dL), PCR (0.8 ± 1.8 vs 0.8 ± 1.8 g/L), and MIS (6.1 ± 2.8 vs 6.1 ± 2.8). No statistical significance in any of the values has been found, being dry weight and IMC (p = 0.08) the closer parameters to get this condition.

Conclusions: The establishment of a nutritional care process seems to be a helpful and efficient method to improve anthropometrics and biochemical parameters in hemodialysis patients. Likewise, the use of malnutrition inflammation questionnaire as a tool to evaluate the nutrition status, seems to be effective when correlating with better biochemical nutritional parameters in hemodialysis patients.

Scope and Consistency of Physical Fitness Outcome Measures in CKD: A Systematic Review

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Background: Impaired physical fitness is prevalent in people with chronic kidney disease (CKD), associating with an increased risk of mortality, falls and hospitalization. A plethora of physical fitness outcomes have been reported in randomized trials. This study aimed to assess the scope and consistency of physical fitness outcomes and outcome measures reported in trials in CKD.

Methods: A systematic review of randomized trials reporting physical fitness outcomes in adults with CKD (not requiring kidney replacement therapy), receiving hemodialysis, peritoneal dialysis, and kidney transplant recipients was conducted. Studies were identified from MEDLINE, Embase and the Cochrane Library from 2000 to 2019. The scope, frequency and characteristics of outcome measures were categorized and analyzed.

Results: From 112 trials and 6,047 participants, 87 tests/measurements were used to evaluate 30 outcomes measures that reported on 23 outcomes, categorized into five domains (i.e. fitness (30%), physiological-metabolic (49%), body composition (36%) and cardiorespiratory fitness (30%). Neuromuscular fitness was examined by 37 tests/measurements including 335.6 vs 1367.9 kcal/day (p<0.05), 0.39 vs 0.85 mg/dL (p<0.05) and ate more cholesterol (411.6±65.2 vs 287.3±61.0, p=0.034), fatty acids (1.1±0.54 vs 0.7±0.61, p=0.034) and more protein (1.5±0.27 vs 0.42±0.16, p=0.048) and drank more fluid (2499.0±335.6 vs 1367.9±167.1, p=0.005) than FM pts, but fruit/veg intake was poor. PBE-score did not correlate with dietary intake of any nutrient in either group.

Conclusions: In our populations 1. Pts with CKD had a more positive attitude towards plant-based eating. 2. CKD pts ate more cholesterol with higher intake of eggs and fatty food. 3. Despite difference in attitude there was no difference in actual vegetable intake between groups. 4. The positive attitude of CKD pts towards PBE suggests that education will be successful in this group, especially as they appear to be following the recommendation to increase fluid intake. The poorer attitude in FM patients should be addressed as the population as a whole has a high prevalence of hypertension, obesity and diabetes and all patients could benefit from PBE.

Diabetes and Influenza Vaccination Rates and Patient Misconceptions in Inner-City CKD and Kidney Transplant (KTR) Patients

Takisha Morancy, Iqra Nadeem, Kingsley Cruickshank, Ahmad Saleh, Mariana Markell. SUNY Downstate Health Sciences University, Brooklyn, NY.

Background: Pts refuse vaccination for unclear reasons. Vaccination rates and attitudes towards vaccination were studied in an inner-city population of CKD pts and KTRs.

Methods: A face-to-face survey was conducted in a random convenience sample of pts with kidney disease attending CKD (30) and Transplant clinic (45). Pts were asked if they refused or accepted the influenza vaccine and associations between beliefs about vaccines and cause of vaccine refusal examined.

Results: There were 37 (49.3%) women and 38 (50.7%) men with 66 black (80%). 40 (40%) did not attend any college. 17 (22.7%) were employed. Mean age was 56.8±1.4 yrs. 34/65 pts (45.3%) reported having had influenza with more TTP pts (63% vs 31%, p=0.009) and more men (62% vs 37%, p=0.035) in the group by Chi-square. 18.36% (50%) of pts reported a family history of influenza. 68.76% believed prevention was easy, 17.24% believed vaccines were not needed, 14.39% believed vaccines caused side effects, 33%, feared related to 3rd party information (22%) and other. Pts who did not think influenza prevented by vaccines were severely agreed they should question shots (r=0.58, p<0.0001), felt knowledgeable about vaccines (r=0.36, p=0.012), trusted information they received (r=0.55, p<0.0001) and felt they could discuss concerns with their doctor (r=0.58, p<0.0001). They were more likely to receive information from friends and family (r=0.58, p<0.0001). Pts who were concerned about side effects were concerned with vaccine safety (r=0.77, p<0.0001) and felt vaccines may be ineffective (r=0.76, p<0.0001) but they did not feel knowledgeable about how vaccines work (r=0.372, p=0.01).

Conclusions: In our population 1. Influenza vaccination rates are low and prevalence of self-reported influenza high. 2. Patients who refuse vaccines believe they are low vaccine safety, and have a high prevalence of preventable illnesses. Pts who believed preventable illnesses were not severe were more likely to receive information from friends and family, felt knowledgeable but did feel comfortable discussing concerns with their doctor. 4. Pts who were concerned about vaccine safety did admit to lack of knowledge. 5. Effective education regarding how vaccines work as well as efficacy and side effect profiles may help improve vaccination rates in this high risk population.

Diet Composition and Understanding of Plant-Based Eating (PBE) in an Inner-City Population of CKD Compared with Family Medicine Patients

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Background: Patients with CKD may benefit from PBE but dietary restrictions may create confusion regarding implementation. We compared attitudes toward plant-based eating and dietary components in an indigent, immigrant population of patients with CKD and those attending Family Medicine clinic (FM).

Results: A total of 15 studies with 82,706 participants were included, of which 5 were validated in a HF cohort different from the model derivation cohort. They consisted of

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
A variety of HF populations (e.g., acute, chronic, carrying mechanical circulatory device) and the median number of included parameters was 7. There was substantial variation across models in the reporting of the kidney related parameters as well as the studied outcomes. While no study included eGFR, serum creatinine and BUN were included in only 6 and 4 studies respectively. Interestingly, serum chloride level was included in none of the included models, while still contain data serum potassium level.

Conclusions: The emerging clinical evidence on the paramount prognostic value of hypochloremia for adverse outcomes in HF is in keeping with distinctive physiologic mechanisms relating it to renin secretion and modulation of renal tubular sodium transport. However, we found that there is still a lag in its integration into contemporary predictive models of HF. This observation highlights the need for revisiting these models in backdrop of emerging data and explore whether incorporation of hypochloremia, or replacing hyponatremia by hypochloremia, would add to their predictive value.

PUB204
Long-Term Ambient PM2.5 Exposure Associated with Major Cardiovascular Risk Factors in a Large Chinese Population-Based Study
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Background: The association between long-term exposure to ambient air pollution and hyperlipidemia or overweight is still controversial. We aimed to investigate the relationship between long-term exposure of PM2.5 and cardiovascular risk factors in a large multi-provincial and multi-ethnic Chinese adult sample.

Methods: We recruited 19,236 adult participants from 2007 to 2010 in 6 provinces of China (Chinese Physiological Constant and Health Condition Study, CPHCS). A questionnaire, physical examination, and biochemical tests were performed. The PM2.5 data used were derived from aerosol optical depth with the GWR model and GEOSChem method.

Results: The average age of the participants 42.7±16.12 years and nearly half were male (47.0%). Annual average PM2.5 exposure 1-year before the CPHCS study was 33.4±18.3 μg/m³. Multiple linear regression showed that each 10 μg/m³ increment of PM2.5 was associated with 0.025% (95% CI: 0.011%, 0.040%) decrease of cholesterol and 0.098% (95% CI: 0.083%, 0.113%) decline of BMI. Adjusted by age, sex, education, ethnicity, physical activity, and smoking, logistic regression indicated that PM2.5 exposure still associated with the prevalence of hyperlipidemia (OR = 0.958, 95% CI: 0.942, 0.974) and overweight (OR = 0.925, 95% CI: 0.911, 0.939). PM2.5 exposure was also corresponded to elevated SSBP (0.048%), 95% CI: 0.034%, 0.063%) and an increased prevalence of hypertension (OR = 1.020, 95% CI: 1.001, 1.039).

Conclusions: Long-term PM2.5 exposure was associated with an increased prevalence of hypertension, decreased prevalence of hyperlipidemia and overweight.

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PUB205
Predictive Models for Prognosis of Cardiovascular Events (in 5 Years) in Asian Patients with CKD
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Background: Chronic kidney disease (CKD) is viewed as a major health problem worldwide. However, independent influencing factors related to the prognosis of CKD patients (especially in cardiovascular events) is still potential to be exploited, and few researches on predictive models for individualized prognosis in CKD patients were published, especially in Asian area. Therefore, we are willing to evaluate independent influencing factors in regard to prognosis of CKD patients and build predictive models for individualized prognosis in CKD patients.

Methods: 1246 participants were included in this cross-sectional study. All data were used in univariate Cox proportional hazards regression models and multivariable Cox regression analyses (P<0.05). Then, 1246 participant were divided into two cohort (development cohort and validation cohort). We will establish one best predictive model by the means of CINDEX, AIC, NRI, IDI.

Results: In the Cox regression analysis of cardiovascular events, we found that HGB, K, Pre-albumin, APOB, Heart failure, CKD progression are independent risk factors. In the development cohorts, we found that the model (K, pre-albumin, HGB, HF, CKD) the best prediction model of cardiovascular events (P=0.088e^1.93584*APOB + 0.00356*pre-albumin + 0.00679*HGB + 1.11488*Heart failure - 0.22131*K - 0.10215*CKD progression) was the best prediction model of cardiovascular events.

Conclusions: Lower HGB is independent protecting factor of cardiovascular events, and higher K, Pre-albumin, APOB, Heart failure, CKD progression are independent risk factors. And we establish the best prediction model (P=0.088e^1.93584*APOB + 0.00356*pre-albumin + 0.00679*HGB + 1.11488*Heart failure - 0.22131*K - 0.10215*CKD progression) of cardiovascular events (in 5 years).

PUB206
Epidemiology of Cardiovascular Risk Factors in Hemodialysis Patients in a Tertiary Care Hospital
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Background: Cardiovascular events remains the leading cause of mortality in patients with end stage renal disease (ESRD) and the risk of cardiovascular events is 10 to 20 times higher in ESRD as compared to general population. The main objective of this study was to evaluate the prevalence of traditional cardiovascular risk factors in the population of ESRD outpatients on chronic hemodialysis in a tertiary care center in Kolhapur city of Western India.

Methods: All patients undergoing regular hemodialysis for ESRD in the tertiary care center of CPR Hospital were considered for inclusion in the retrospective study. Clinical and demographic data were obtained from the medical records, whereas laboratory records were obtained as the most recent result in the six preceding months. Adequate statistical tests were carried out and for all tests, a p-value <0.05 was considered statistically significant.

Results: A total of 1937 patients were included from the data of 2 years from May 2018 to April 2020 at our institute. Their average age was 61.3 years old, 69.3% were males. The prevalence of cardiovascular risk factors observed was 89.3% for hypertension, 83.9% for dyslipidemia, 75.3% for sedentary lifestyle, 49.7% for tobacco use, and 43.5% for diabetes. In a multivariate adjusted analysis, we found that sedentary lifestyle (p = 0.041, PR 1.15 – 95% CI: 1.09 - 1.17), diabetes (p = 0.021, PR 1.05 – 95% CI: 1.01 - 1.11), and obesity (p < 0.0001, PR 1.88 – 95% CI: 1.59 - 2.95) were more frequent in women; and hypertension (p = 0.019, PR 1.03 – 95% CI: 1.01-1.17) and tobacco use (p = 0.009, PR 1.31 – 95% CI: 1.97 - 4.67) were more often found among patients under 65 years old. Sedentary lifestyle was independently associated with time in dialysis less than 12 months (p < 0.001, PR 1.33 – 95% CI: 1.19 – 1.43).

Conclusions: The population in chronic hemodialysis in the city of Kolhapur presents a high prevalence of cardiovascular risk factors. These findings confirm the high-risk cardiovascular profile of hemodialysis patients. Prospective studies and clinical trials are needed to further clarify interventions that can be transformed in public health strategies to prevent cardiovascular death in hemodialysis patients.

PUB207
Prevalence and Associated Risk Factors of Pre-Hypertension and Hypertension Among University Students in Bahrain
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Background: The increase of hypertension in the developing countries may be connected with the economic transition within those countries. This study aimed to assess the prevalence of prehypertension and hypertension among university students and their associated risk factors.

Methods: The study used a cross-sectional design. Data were collected from February 2019 to May 2019 at the Arabian Gulf University Campus in Bahrain. A total of 411, randomly selected students aged 17 to 24 years (196 males, 215 females) were included in the study. The data were obtained through a self-completed structured questionnaire, which included data about nutritional lifestyle, sleep, exercises, family history and smoking pattern. In addition, blood pressure and body mass index were measured. Systolic and diastolic blood pressure measurements were taken by trained personnel.

Results: The mean age was 19 ± 1.9 years. Normotensive cases constituted 61.3% (n = 252), prehypertensives formed 30.7% (n = 126), and hypertensive students comprised of 8% (n = 33). The overall proportions of hypertension and prehypertension were higher among male students (81.8 and 69.8%) than female students (18.2 and 30.2%), respectively.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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Higher body mass index was associated with significantly higher prevalence of hypertension (37.3%), overweight (33.3%), and obesity (39.8%) but not with pre-hypertension (normal weight 47.6%, overweight 32.5%, and obesity 17.5%). The Univariate analysis showed an association between hypertension and age, sex, body mass index (BMI), nutritional lifestyle, sleep duration, physical activity, smoking pattern and family history of hypertension (p < 0.05). Multivariate logistic regression analysis revealed a significant association between hypertension and the above stated factors.

Conclusions: The findings of this present study highlighted the prevalence of hypertension (8%) and prehypertension (30.7%) among university students in Bahrain. This outcome is consistent with associated risk factors (age, sex, body mass index, smoking, sleep duration, physical activity and family history of hypertension). The results of this study recommended that periodic screening and monitoring of students for hypertension should be done to the university students.

PUB208
A Combined Effect of Sacubitril/Valsalter and Evolocumab on Chronic Heart Failure in an ESRD Patient
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Introduction: End-stage renal disease (ESRD) patients generally have underlying risk factors for coronary artery disease and heart failure (HF) such as hypertension and diabetes mellitus. In fact, chronic HF is highly prevalent and is one of the leading causes of death in these patients. We report a combined effect of sacubitril/valsalter and evolocumab on chronic HF in an ESRD patient.

Case Description: A 63-year-old man with a history of chronic HF for 3 years, along with hypertension, diabetes mellitus, hypercholesterolemia, coronary artery disease, status post coronary artery bypass graft with multiple stents, and ESRD on hemodialysis, presented with worsening dyspnea over 2 months (NYHA Class IV). His medication list included cardiotoxic chemotherapy, carfilzomib, carmustine, clopidogrel, hydralazine, ibuprofen, indomethacin, loratadine, mononitrate, ranolazine, aspirin, warfarin, amiodarone, erythropoietin, rosvastatin, sevelamer, linaglaptin, and insulin. An echocardiogram revealed an ejection fraction (EF) of 15%. He was placed on a cardiac transplant waiting list after receiving an implantable cardioverter defibrillator. Meanwhile, enapril and valsartan were replaced by sacubitril/valsalter for chronic HF, and evolocumab was added to reduce the risk of myocardial infarction. During an initial follow-up for 10 months, his dyspneic symptoms improved significantly to NYHA Class I. An echocardiogram later revealed an EF of 60%. He was followed for 4 years during his hospitalizations, worsening of HF, or side effects of the medications such as hypertension, hyperkalemia, and nasopharyngitis.

Discussion: Sacubitril/valsalter, an angiotensin receptor-neprilysin inhibitor, has multiple mechanisms of action and is known to reduce the risk of cardiovascular death and HF hospitalization in patients with chronic HF with reduced EF. Besides evolocumab, a PCSK9-inhibitor antibody, is known to promote plaque regression and stabilization. The combined use of sacubitril/valsalter and evolocumab in our patient for 10 months resulted in an improvement of his EF from 15% to 60%, most likely due to a significant improvement of coronary blood flow with a recovery of hibernating ischemic myocardium. Therefore, additional studies are highly recommended to explore the beneficial effect of these medications used in combination.

PUB209
Fanconi Syndrome and Acute Interstitial Nephritis: A Toxic Combina- tion Associated with Ifosfamide
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Introduction: Ifosfamide is an alkylating chemotherapeutic agent used in the treatment of various soft tissue tumors. Nephrotoxicity associated with ifosfamide is less consistent with ifosfamide associated renal toxicity which often results in irreversible damage. Therefore, the results of this study recommended that periodic screening and monitoring of students for hypertension should be done to the university students.

Case Description: 33-year-old female with chest wall Ewing Sarcoma presented to our institution with leukocytosis, rash, and fever. She was diagnosed with plasma cell leukemia. Renal biopsy revealed findings consistent with membranous glomerulopathy. She was treated aggressively with hemodialysis and immediate chemotherapy. The fairly recent development of the free light chain assay provides a tool to screen for MM and was treated with CyBorD therapy.

Discussion: Fanconi syndrome is a rare complication of ifosfamide administration during chemotherapy for solid tumors, particularly Ewing sarcoma. The pathogenesis of Fanconi syndrome following ifosfamide administration is not well understood. The mechanism of Fanconi syndrome associated with ifosfamide administration is likely multifactorial and includes a direct toxic effect on proximal tubular cells, tubular interstitial nephritis, and acute interstitial nephritis. Renal injury is a common presentation of underlying Multiple Myeloma. In a recently published study, considered the largest analysis to date between free light chains (FLC) and biopsy proven nephropathy confirmed McN (myeloma cast nephropathy). Median lambda light chain at diagnosis was 426.7mg/dL. Here, we present a case of a patient presenting in stage III acute renal failure with Lambda light chains measured at a level almost 9 fold greater at 3684mg/dL.

Conclusion: A 78 year old female with past medical history significant for breast cancer 20 years ago is electedly admitted from her primary care doctor’s appointment after having symptomatic anemia with a measured hemoglobin (hgb) of 6.3 g/dL. She was feeling weak, with weight loss of 30 pounds in 2 years as well as persistent proteinuria. She was treated with hemodialysis therapy with the intent of improving his EF from 15% to 60%, most likely due to a significant improvement of coronary blood flow with a recovery of hibernating ischemic myocardium. Therefore, additional studies are highly recommended to explore the beneficial effect of these medications used in combination.

PUB211
Biopsy-Proven Cast Nephropathy from Lambda Light Chain Measured at 3684 mg/dL in a Multiple Myeloma Patient
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Introduction: Kidney injury is a common presentation of underlying Multiple Myeloma. In a recently published study, considered the largest analysis to date between free light chains (FLC) and biopsy proven nephropathy confirmed McN (myeloma cast nephropathy). Median lambda light chain at diagnosis was 426.7mg/dL. Here, we present a case of a patient presenting in stage III acute renal failure with Lambda light chains measured at a level almost 9 fold greater at 3684mg/dL.

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**PUB212**

AKI Associated with Immune-Checkpoint Inhibitors: Management Challenges and Dilemmas Without Renal Biopsy

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**Introduction:** There is much to be learnt about renal lesions seen in patients with acute kidney injury (AKI) associated with the use of immune-checkpoint inhibitors (ICI). Acute tubulo-interstitial nephritis is the most common, with glomerulonephritis (GN) being increasingly recognized.

**Case Description:** A 61 Chinese male presented with generalised arthralgia and AKI with nephritic-nephrotic syndrome on a background of Stage IV metastatic clear cell RCC and left renal nephrectomy. At presentation, he was on treatment with pembrolizumab (PD-1 inhibitor) and axitinib (VEGF receptor TKI). Investigations revealed 24-hour TUP of 8.26g/day and peak serum creatinine (SCr) of 605 μmol/L (CTCAE G3; baseline Scr 117 μmol/L). Autoimmune markers and complements were negative. Patient was counselled for but refused a high-risk renal biopsy. Pembrolizumab was discontinued. High dose prednisolone was initiated for renal and rheumatological IRAE. SCr improved to 224 μmol/L at 3 months but his nephritic-nephrotic state persisted. Risks and benefits of empiric mycophenolate mofetil were discussed extensively and patient opted to continue with corticosteroid (CS) monotherapy. His subsequent clinical course was complicated by community acquired pneumonia and herpes simplex viral oral mucositis, before eventually succumbing to polymicrobial sepsis from acute cholecystitis despite optimal management.

**Discussion:** The clinical presentation of our patient is highly suggestive of an underlying GN. In view of concurrent rheumatological IRAE, we postulated that his AKI was related to ICI use. Empiric use of high-dose CS resulted in partial improvement in renal function but persistence of nephritic-nephrotic state, suggesting that CS monotherapy is suboptimal. Without histological data, directed therapy was not possible. However, given the rarity and heterogeneity of ICI associated GN, success of previously tried agents was limited to case reports and optimal treatment remains unknown. In view of this uncertainty, hesitancy with the empiric use of immunosuppressants beyond CS is understandable. While we await further research, in-depth discussion of treatment risk and benefits, especially infective complications, during shared decision-making remains a key element in the optimal care of this unique population with advanced malignancies and often, limited life expectancy.

**PUB213**

Abiraterone-Induced Rhabdomyolysis as an Unusual Cause of AKI Requiring Hemodialysis

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**Introduction:** A 86-year-old male diagnosed with metastatic, castration-resistant prostate cancer (mCRPC) treated with abiraterone (Zitaiga) for 3 months was admitted to the emergency department due to hypoxemia, worsening fatigue and lethargy.

**Case Description:** After being diagnosed with prostate cancer, the patient had been subject to a radical prostatectomy 10 years prior to admission; 12 months prior to admission he developed deep-vein thrombosis that required endovascular treatment. The patient was prescribed daily 10mg rivaroxaban and 5mg prednisone for 1 year. For over 4 years, the patient had an irregular consumption of esomeprazole, atorvastatin, and risperidone.

Upon admission to the emergency department laboratory analysis revealed a dialytic emergency: serum creatinine of 6.1mg/dL, urea 295 mg/dL, BUN 138mg/dL and potassium of 7.3mEq/L. The patient refused renal replacement therapy. Agressive hydration and treatment with calcium gluconate, IV insulin and beta-agonist was initiated for renal and rheumatological IRAE. He was resuscitated with isotonic IV fluids, with resolution of perinephric hematoma and rectus abdominis hematoma. Urology recommended no surgical intervention. He was resuscitated with isotonic IV fluids, with resolution of shock. Subsequent MRA showed no evidence of enhancing left nephric hernia but multiple rounded hypo enhancing lesions in the renal parenchyma bilaterally. He remained with persistent anion gap metabolic acidosis with increasing lactic acid up to 14.5. A kidney biopsy was planned but aborted as patient became hypotensive and confused with a drop-in hemoglobin to 5.6. Patient endorsed dark stools so, when hemodynamically stable, EGD was performed and gastric biopsies showed aggressive Burkitt’s lymphoma.

**Discussion:** Lactic acidosis (LA) can occur in the presence or absence of tissue hypoxia (type A and type B LA respectively). Persistent LA without identifiable causes of tissue hypoxia should prompt clinicians to suspect non-hyptoxic etiologies, including occult high-grade malignancies. Hematological malignancies constitute and uncommon cause of type-B LA, carrying a poor prognosis.

**PUB215**

Bilateral Renal Burkitt Lymphoma Presenting with Persistent Lactic Acidosis in an HIV-Negative Patient

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**Introduction:** Burkitt lymphoma is an uncommon and aggressive B-Cell lymphoma accounting for <1% of adult Non-Hodgkin Lymphomas. The ileocelecal region is the most common affected area, but it can involve extra nodal sites including the kidney. Renal involvement is usually asymptomatic and requires a high degree of suspicion to prevent early complications.

**Case Description:** 63 years old non-smoker, HIV negative male with a history of an incidentally found left medial upper pole exophytic perinephric hemihyphoma on CT 2 months prior to presentation, presented to the ED complaining of acute on chronic lumbar back pain. Noted afebrile, BP 86/52 mmHg with orthostatic changes, HR 92bpm, RR 20rpm and SO2 96% on RA somnolent but arousable, pale, no abdominal, or costovertebral tenderness. Laboratories showed Hb 8.2 (14.7 a month prior), WBC 17,000, Na 126, Sodium bicarbonate 16, Anion gap of 22, Lactic acid 5.0 and SrC 1.5 (base 0.8). UA unremarkable. CT-CAP w/o contrast with interval increase of perinephric hemihyphoma and rectus abdominis hemihyphoma. Urology recommended no surgical intervention. He was resuscitated with isotonic IV fluids, with resolution of shock. Subsequent MRA showed no evidence of enhancing left nephric hernia but multiple rounded hypo enhancing lesions in the renal parenchyma bilaterally. He remained with persistent anion gap metabolic acidosis with increasing lactic acid up to 14.5. A kidney biopsy was planned but aborted as patient became hypotensive and confused with a drop-in hemoglobin to 5.6. Patient endorsed dark stools so, when hemodynamically stable, EGD was performed and gastric biopsies showed aggressive Burkitt’s lymphoma.

**Discussion:** Lactic acidosis (LA) can occur in the presence or absence of tissue hypoxia (type A and type B LA respectively). Persistent LA without identifiable causes of tissue hypoxia should prompt clinicians to suspect non-hyptoxic etiologies, including occult high-grade malignancies. Hematological malignancies constitute and uncommon cause of type-B LA, carrying a poor prognosis.

**PUB216**

Oxaliplatin-Induced Hypomagnesemia

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**Introduction:** Platinum based chemotherapy is used in the treatment of several malignancies including lung, colorectal, ovarian, breast, head/neck, bladder and testicular cancers. We present a case of profound electrolyte disturbances in the setting of oxaliplatin therapy.

**Case Description:** 78-year-old Caucasian male diagnosed with pancreatic cancer three months prior to admission, on oxaliplatin therapy, presented to emergency room with new onset atrial fibrillation. He was afebrile, hemodynamically stable, and without respiratory distress. He endorsed a history of chronic diarrhea since beginning chemotherapy, however he began to have weakness and dizziness three days prior to...
as its prompt diagnosis and treatment can prevent the associated complications. However, case reports of oxaliplatin associated magnesium wasting are limited. This can be partially explained by the fact that oxaliplatin is protein bound and cannot readily accumulate in the kidney tubules to mediate nephrotoxicity, as is the case with carboplatin which is not protein bound. Magnesium deficiency is an under recognized entity, however it can precipitate potentially fatal cardiovascular dysfunction. Clinicians need to be aware of this potential adverse effect related to oxaliplatin therapy, as its prompt diagnosis and treatment can prevent the associated complications.

**Introduction:** Immune related adverse events (irAEs) associated with immune checkpoint inhibitors (ICI) are increasingly recognized as a side effect of treatment. This case report describes a side effect following the patient receiving this therapy. Sarcoïd-like / granulomatous lesions from ICI are reported to be as high as 5% based on case series and registries. In all reported cases, patients presented with lymph node, skin, or lung involvement. We present the first case of sarcoid in lesions in the heart in a patient being treated with immune checkpoint therapy.

**Case Description:** A 62-year-old male with stage IV metastatic melanoma received two cycles of pembrolizumab in November 2019 followed by three cycles of with ipilimumab and nivolumab. In March 2020 he was admitted with acute kidney injury, creatinine peaked at 2.85 mg/dL (baseline 0.80-0.94 mg/dL). Urinalysis and serologies were unremarkable. A kidney biopsy was obtained and revealed granulomatosis tubulointerstitial nephritis with focal necrotizing granuloma. Acid-Fast Bacilli (AFB) and Grocott methenamine silver (GMS) stains were negative. Initially, the patient was noted to have increased shortness of breath. Echo revealed new-onset cardiomyopathy with ejection fraction (EF) of 22% and SVT. Cardiac catherization was negative for coronary artery disease, but endomyocardial biopsy revealed lymphohistiocytic infiltrate with granulomatous myocarditis consistent with cardiac sarcoidosis. He was initiated on pulse IV steroids with improvement of both his cardiac and renal function. EF improved to 46% and creatinine improved to 1.0 mg/dL. Follow-up PET/CT imaging showed small ingunal nodes that could be sarcoïdosis otherwise no indication of melanoma.

**Discussion:** Use of ICI has dramatically improved patient survival; however, there is a growing appreciation for adverse events that can be associated with increased morbidity. To our knowledge, this is the first case of sarcoid involvement in both the kidney and heart. Our case highlights the need for aggressive approach to ICI toxicity when clinical work-up is unrevealing. The timely manner that both kidney and heart biopsies were obtained and treated with immune checkpoint therapy. Further follow-up is needed to determine long-term outcomes of both irAEs and cancer status.

**Discussion:** The nephrotoxicity associated with Gemcitabine can occur weeks to months after the drug is initiated. The mechanism of injury is driven by antibody formation to the drug resulting in drug-induced deposition of immune complexes and immune complex precipitation within the glomeruli. Treatment consists of discontinuation of this drug. Neither steroids nor plasma exchange have been reported as beneficial. AKI from this drug is reversible with supportive care.

**Introduction:** Thrombotic microangiopathies (TMA) are potentially life-threatening conditions caused by small- vessel platelet microthrombi and are characterized by microangiopathic hemolytic anemia, kidney injury, and thrombocytopenia. TMA secondary to gemcitabine therapy (GiTMA) is extremely rare and is associated with a poor prognosis, with nearly 50% of cases progressing to end stage kidney disease. The mainstay of management is withdrawal of the offending drug and supportive care. A 65-year-old Black female with a history of metastatic invasive ductal breast cancer on gemcitabine therapy, well-controlled hypertension, well-controlled type 2 diabetes mellitus without proteinuria, and normal baseline kidney function presented with a 1 month history of poor oral intake, worsening hypertension, and progressive decline in kidney function. She was receiving 1250 mg/m²/week of gemcitabine for 3 weeks/months for 11 cycles over 1 year. She presented with acute presentation with 20% intravascular volume depletion, 14 x 20 x 16 cm in mid- abdominal region, pushing all the adjacent abdominal viscera to the anterior abdominal wall. Patient refused enucleation procedure. Later, aspiration was used chemotherapeutic agent for cancers of the pancreas, breast, lung, and ovaries. GiTMA is a very rare and highly fatal condition with mortality rates ranging from 50 to 70%. It is thought to be immune and non-immune mediated. Physicians should have a high index of suspicion to diagnose GiTMA early in the course of the disease. Mainstay of management is discontinuation of gemcitabine therapy, supportive care, and treatment of kidney injury with dialysis if necessary.}

**Discussion:** The nephrotoxicity associated with Gemcitabine can occur weeks to months after the drug is initiated. The mechanism of injury is driven by antibody formation to the drug resulting in drug-induced deposition of immune complexes and immune complex precipitation within the glomeruli. Treatment consists of discontinuation of this drug. Neither steroids nor plasma exchange have been reported as beneficial. AKI from this drug is reversible with supportive care.

**Introduction:** Immune checkpoint inhibitor-induced renal and cardiac sarcoidosis

**Introduction:** Recurrent Mesenteric Cyst in an ESRD Patient on Maintenance Hemodialysis

**Discussion:** We chronicle a case of 47 years old male on hemodialysis for last 15 years with an unknown primary cause of end stage renal disease (ESRD). He never underwent peritoneal dialysis and had no prior history of abdominal surgery. He presented with gradual onset of abdominal pain and altered bowel habits. CT scan of abdomen and pelvis revealed encysted fluid in mesentery, measuring 10 x 5 cm, located behind the anterior abdominal wall. Patient refused enucleation procedure. Later, aspiration was done, which drained three liters transudative fluid. Cytology was negative for malignant cells, Histopathology demonstrated cuboidal epithelial cells of enteric origin and was not suggestive of cells of mesothelial origin. One month after first aspiration, patient presented with re-accumulation of cystic fluid and underwent second session of aspiration. Patient presented with worsening symptoms of abdominal distension and pain within two months of last aspiration. Repeat CT scan showed large intra-abdominal cystic lesion measuring 10 x 16 x 20 cm in mid-abdominal region, pushing all the adjacent abdominal viscera to the left side. At this time, cystic mass was surgically removed. Abdominal ultrasound and CT scan were negative for cirrhosis or Budd chiari malformation. Hepatobiliary system was also unremarkable. It re-demonstrated large mesenteric cyst 13 x 10.3 x 14.1 cm, located in the small bowel mesentery around the ligament of Treitz, extending down and exerting mass effects on the adjacent bowel loops. The extensive workup for causes of ascites, including liver disease, hepatatis panel, Tuberculosis, Brucellosis, Hydatid cyst and malignancy screening with markers namely CEA, CA 125, CA 19-9, CA-153, were all unremarkable. Erythrocyte Sedimentation Rate (ESR) was mildly elevated at 35 mm/ hour.

**Discussion:** This is the first reported case of recurrent mesenteric cyst in ESRD patient from KSA. Recurrent mesenteric cysts are extremely rare and are very difficult to manage. Enucleation and aspiration, both are ineffective modalities for such cysts.
Urinothorax: A Rare Cause of Pleural Effusion

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Introduction: Urinothorax [UT], the accumulation of urine in the pleural space, is an uncommon cause of pleural effusions resulting from trauma, obstruction, or iatrogenic causes. Thoracentesis with pleural fluid analysis and evaluation of biochemical characteristics, such as pleural fluid creatinine (PcCR) to serum creatinine (Scr) ratio, is necessary to diagnosis.

Case Description: A 93-year-old man with a history of chronic kidney disease, right kidney transitional cell carcinoma with hydronephrosis, adenocarcinoma of the prostate status post brachytherapy complicated by proctosis and urinary obstruction was hospitalized for worsening hematuria and suprapubic pain. CXR showed a large right pleural effusion. CT of the abdomen and pelvis illustrated severe right-sided hydronephrosis and hydrourereter with a heterogeneous density in the right renal pelvis and diffuse mural thickening in the posterior and right lateral bladder walls. An ultrasound guided thoracentesis was performed with the removal of 2L clear yellow fluid and analysis resulted: pH 7.423, LDH 48 IU/L, glucose 164 mg/dL, and Pcr 2.5 mg/dL. Cytology was negative for malignancy. Scr was 2.59 mg/dL and thus Pcr to Scr ratio of 0.96. A repeat thoracentesis was performed removing 1.85L clear yellow fluid. Pcr and Scr were 4.1 mg/dL and 3.94 mg/dL respectively. Again, this confirmed the diagnosis of UT with a Pcr to Scr ratio of 1.04. Bilateral retrograde ureteropyelograms with right ureteral stent placement failed to correct and an indwelling pleural catheter was placed.

Discussion: UT is a rare cause of transudative pleural effusion due to the mismatch of the rate of accumulation of pleural fluid and rate of reabsorption via pleural lymphatics. The most common etiologies resulting in UT include trauma and obstructive uropathy. Diagnosis requires pleural fluid analysis and is associated with a paucicellular, transudative effusion with an ammonia level, acidic pH less than 7.4, and a Pcr to Scr ratio greater than 1.0. Management is dependent on correcting the underlying pathology, such as repairing traumatic GU injury or obstruction.

PlACR-Positive Membranous Nephropathy in a Patient with Rectal Cancer

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Introduction: Malignancy associated Membranous Nephropathy(MA-MN) is well-recognized as a common paraneoplastic glomerulopathy, especially in solid tumors. Prevalence is around 10% of all membranous nephropathy(MN) cases. Anti M-type Phospholipase A2 receptor antibodies(Anti PL A-R) are seen in 70-80% of Primary MN but also present in around 30% of MA-MN cases. Further immunofluorescence studies on 1 domain-containing protein 7A(THSD7A) antibodies in MA-MN also exist. Pathological features of MA-MN usually resolve with successful medical or surgical treatment of the malignancy, or even emerge spontaneous remission. However, proteinuria may persist for months after remission of the primary disease. We report a unique case of MA-MN that did not resolve despite successful treatment of the primary disease.

Case Description: A 48 year old man with no known co-morbidities presented for evaluation of nephrotic syndrome. He had a urine protein creatinine ratio(UPCR) of 6.8 g/day; albumin 3.6 g/dL; and creatinine 1.3 mg/dL. His last anti PL A-R titre was negative. Anti PL A- R antibodies were positive at 1:400 (0.41 IU/mL). Renal biopsy showed membranous nephropathy stage III/IV, 1+ PL A-R staining. IF showed granular 4+ IgG subtype, 3+ kappa, 3+ lambda. Lambda Workup revealed adenocarcinoma of the rectum and was started on a 5-week combination chemoradiotherapy protocol. Low dose aspirin was started. Following diagnosis, he was referred to us for MA-MN. During follow-up for MA-MN for 12 months, he continued to be nephrotic with UPCR of 4.6 g/day and albumin 2.9 mg/dL. Thus, he was treated with tacrolimus initially and then rituximab. Currently, he is in remission from malignancy and nephrotic syndrome with a UPCR of 0.3 g/day and albumin 4.1 g/dL. Last anti PL A-R titre was negative.

Discussion: Our case highlights a rare clinical course different from the known natural progression of the disease and established therapeutic guidelines. Typically, MA-MN either resolves spontaneously or with management of the primary cancer without additional immunosuppressive therapy. If nephrotic syndrome persists despite cancer therapy, it is imperative for our patient, and the patient’s health care team, to continue to closely follow the patient for possible recurrence of underlying cancer. Additionally, age-appropriate cancer screening for all newly diagnosed MN cases is essential. We hope this report shall serve as a means for further discussion and research in onco-nephrology.

An Unusual Presentation of Atypical Hemolytic Uremic Syndrome in a Patient with Skin Ulcerations

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Introduction: Atypical hemolytic uremic syndrome (aHUS), characterized by microangiopathic anemia and acute kidney injury (AKI), is a rare and debilitating disease, but its diagnosis can be difficult because of potential overlap with several other autoimmune conditions. We present a case of aHUS-induced acute renal failure with skin ulcerations as initial presentation.

Case Description: A 61-year-old female presented with progressively worsening skin ulcerations on her hands after two cycles of rituximab and bendamustine for B-Cell chronic lymphocytic leukemia. She also reported cocaine use. On presentation, her physical exam was notable for bilateral ulcers on her knuckles and ankles. She was treated empirically for osteomyelitis without improvement. Skin biopsy was non-diagnostic. She was noted to have anemia, thrombocytopenia and AKI with nephrotic-range proteinuria. Other remarkable labs included a low haptoglobin and a high LDH. Urinalysis revealed dysmorphic red blood cells, and peripheral smear showed schistocytes. An autoimmune process was suggested; thus, pulse steroids was initiated. A renal biopsy was suggestive of thrombotic microangiopathy (TMA). A full immunological work-up eventually returned unremarkable. Plasmapheresis was initiated before her ADAMTS13 activity resulted at > 10%. She was then started on eculizumab. After one session of plasmapheresis and four doses of weekly eculizumab 900 mg, her platelet counts improved. However, she required initiation of renal replacement therapy. TMA panel and genetic testing showed a low factor H level and dysregulated complement cascade consistent with aHUS despite negative CFH-CFHR5 mutation. She had some improvement in urine output but continued to require hemodialysis on discharge. Biweekly eculizumab 1200 mg was continued with plan to closely monitor for renal recovery.

Discussion: Although a rare disease with features that may overlap with other autoimmune processes, aHUS can cause rapid decline in renal function, thus requiring early identification and treatment. Eculizumab mutation and the treatment of aHUS was initiated in 20% of the patients. In the presence of the dysregulated complement cascade, microangiopathic process and renal failure, early treatment with eculizumab is crucial in renal recovery, but the renal response to treatment can be delayed compared to the hemolytic response.

Renal Medullary Carcinoma Causing Obstructive Uropathy

Ramon A. Seneriz,2,1 Yanetsa Olivera Arencibia,2,1 Oscar A. Garcia Valencia,2,1 Juan D. Salcedo Betancourt,2,1 Oliver Lenz,2,1 University of Miami, Coral Gables, FL; 2Jackson Memorial Hospital, Miami, FL.

Introduction: Hypertrophy of the prostate (BPH) is a common cause of obstructive uropathy in older men. Here we present the case of a 62-year-old Hispanic man with BPH who was found to have an additional rare cause of hydronephrosis, namely renal medullary carcinoma (RMC).

Case Description: A 62-year-old Cuban male with a history of hypertension and BPH presented for urodynamic testing for worsening lower urinary tract symptoms. Further questioning revealed fever, chills, and 20-pound weight loss over 2 months. Laboratory data were remarkable for serum creatinine of 2.7 mg/dL. Urinalysis showed pyuria and bacteriuria but no casts. After placement of an indwelling urinary catheter and drainage of 500 mL of urine, a renal ultrasound showed increased kidney size (right: 10.8 cm x 5.2 cm and left: 15.2 cm) and moderate left-sided hydronephrosis for which a percutaneous nephrostomy was placed. A computed tomography revealed multiple nodular lesions in the liver, bones, right adrenal gland, and lungs, and tissue retrieved by liver biopsy was suspicious for PAIX-positive carcinoma. MR1 demonstrated findings concerning renal medullary carcinoma in the left kidney. A biopsy of the renal mass showed RMC. Percutaneous biopsy of the mass showed tissue positive for PAX-8, Pan-K, and CA-IX (focal) and negative for INI-1, confirming the diagnosis of RMC.
Effect of Gemfibrozil on Kynurenine Aminotransferases Activity and Kynurenic Acid Production in Rat Kidney

Rachana Marathi,1 Swetha Rani Kanduri, Karthik Kovvuru, Pradeep Vaitla. University of Mississippi Medical Center, Jackson, MS.

Introduction: Estimation of glomerular filtration rate (GFR) is important in assessing kidney function. GFR is a product of muscle breakdown that is filtered through the kidneys and is related to a steady-state in people with normal kidney function.

Case Description: 31-year-old African American female with a history of systemic lupus erythematosus, polymyositis, chronic respiratory failure presented with sepsis & rash. She was admitted to the hospital with fever, weight 63 kg, height 62 inches. 3 days after admission she deteriorated with worsening septic shock, requiring multiple pressors. She became deeply sedated with worsening septic shock, requiring multiple pressors. She became anuric secondary to acute kidney injury from septic shock, however, they were able to resolve the urine creatinine (SCr) to 60 μM/l/min/1.73m2. Despite the patient’s lack of muscle mass, muscle biopsy was performed which showed “skeletal muscle was almost entirely replaced by fat and the few remaining fibers were mostly necrotic”. Although the patient’s SCr continued to rise compared to baseline, it was still well below or within normal limits with a peak of 0.54 μM/l/min/1.73m2 despite the patient being anuric and required renal replacement therapy for metabolic clearance and volume management.

Discussion: Acidosis is not directly related to muscle mass and muscle breakdown, it is not surprising that our patient with little to no muscle mass maintained an unusually low SCr despite deteriorating renal failure. SCr value of 0.06 μM/l in a normal weight adult is one of the lowest reported values in the medical literature. eGFR based on SCr is the most common method of estimating kidney function it is important to recognize that the eGFR based on SCr may not be an accurate representation of the renal function, especially in persons with low muscle mass.

Conclusion: GFR decreases KYN production in rat kidney in vitro through inhibition of KAT I and KAT II isoenzymes. Present results indicate a novel mechanism of gemfibrozil’s action in the kidney. Its potential role in nephrotoxicity needs verification in upcoming studies.
PUB230

**Influence of Biopsy Prognosis on Graft Survival**

Cristina Andrades Gómez, Jorge Calvillo-Arbizu, Miguel angel Pérez valdivia, Gabriel Bernal blanco, Jose Luis Rocha Castilla. Hospital Universitario Virgen del Rocio, Sevilla, Spain.

**Background:** Renal transplantation is the best alternative renal replacement option for patients with advanced chronic kidney disease. However, the supply of young donors is limited, and does not cover the demand of patients on the renal transplant waiting list. For this reason, older donors are being used, and a high discard rate of those organs exists based on pathological results (score) of the preimplant renal biopsy. There are several methods to evaluate the quality of the kidneys and the Kidney Donor Profile Index (KDPI) has acquired special relevance to decide the performance of preimplant renal biopsy. Based on the score, a preimplant renal biopsy is performed, which is decisive in certain cases. However, there is poor evidence to support this decision, which can be described as “conservative,” since there is not enough certainty that there is influence of the preimplant biopsy score influences graft survival.

**Methods:** 389 biopsies of kidney transplant donors of cadaver donors in brain death and asystole type III were included. Donors in asystole type II, combined and live, were excluded. Samples were examined by the same pathologist and in paraffin (no case by freezing). A graft survival analysis was performed based on the results of the renal biopsy (score). Likewise, a multivariate analysis of graft survival was carried out including, in addition to the results of the renal biopsy, results such as the age of the donor and recipient and the KDPI.

**Results:** Graft survival was compared between two transplant subpopulations in our hospital based on whether a preimplant biopsy was performed. According to the data used there are no significant differences in graft survival between transplants in which biopsy has been performed or not.

**Conclusions:** The preimplant biopsy score by itself and the evaluation of the different histological components in the biopsy have no influence on graft survival. We believe that predictive indices that combine donor and recipient histological and clinical variables should be implemented.

PUB231

**De Novo Post Kidney Transplantation Thrombotic Microangiopathy**

Janany J. Sabescumur,1 Jeremy G. Taylor,1 Rauf Shahbazov,2 David M. Dewolfe.1 1University of Rochester, Rochester, NY; 2State University of New York Upstate Medical University, Syracuse, NY.

**Introduction:** De novo post kidney transplantation thrombotic microangiopathy (TMA) is rare. We present two cases of post kidney transplant TMA acquired from the donor kidney

**Case Description:** A 26 year old male with a significant past medical history of end-stage kidney disease secondary to hereditary focal segmental glomerulosclerosis (FSGS) requiring initially presented for deceased donor kidney transplantation. The kidney donation was from a brain death donor with no significant medical history. The preliminary kidney biopsy of the donor kidney revealed focal patchy acute tubular necrosis (ATN). Induction immunosuppression included a total dose of 5 mg/kg of thymoglobin and followed by initiation of tacrolimus for goal trough of 8 - 10 mg, prednisone 40 mg, and mycophenolate 1000 mg twice daily. The patient had delayed graft function with a creatinine initially at 18 mg/dL which only reduced to 17 mg/dL over the next couple of days. On postoperative day 5, the patient was dialyzed due to symptomatic ureemia. In addition, he was noted to have developed worsening anemia and thrombocytopenia with a platelet count dropping from 208 to 47 per microliter of blood. A renal biopsy was pursued and the pathology results revealed post-transplant thrombotic microangiopathy (TMA) due to hemolytic uremic syndrome. In addition, the final donor kidney biopsy had later revealed thrombotic microangiopathy within approximately 60% of the glomeruli. The patient who received the second kidney had a similar clinical course. Both recipients received one dose of eculizumab with improvement in allograft function. They were both discharged without hemodialysis with close follow up.

**Discussion:** TMA was acquired by the donor TMA which was likely caused by ATN. It wasn’t until later in the course that the final biopsy report of the donor kidney revealed TMA which confused the diagnosis of allograft kidney injury.

PUB232

**Hypercalcemia Secondary to Hyperthyroidism: A Unique Cause of Renal Failure in a Kidney Donor**


**Introduction:** Hyperthyroidism is associated with increased bone resorption resulting in hypercalcemia (HCA). Chronic HCA leads to defect in concentrating ability of kidneys by downregulation of aquaporin-2, calcium deposition in medulla, impairing osmotic gradient resulting in polyuria and persistent pre-renal state. HCA causes renal vasoconstriction leading to acute tubular injury (ATI) followed by atrophy and interstitial fibrosis (IFTA).

**Case Description:** We present a case of a 70 yr old female who donated a kidney 5 yrs ago with serum creatinine (Cr): 1.18mg/dL and Calcium (Ca): 10.2mg/dL at 2 yr fu. At routine 3 yr fu, Cr of 4.4mg/dL, BUN of 70 mg/dL, and Ca of 12.6mg/dL were noted. Kidney biopsy showed ATL severe IFTA, negative for any immune deposits (Figure 1A). Work up of HCA revealed; PTH: 5 (18.5-88 pg/ml), 25(OH)D: 55 ng/ml, 1-25(OH) D3: 70 ng/ml, angiotensin converting enzyme level: 42 (9-47 U/L), serum/urine protein electrophoresis: negative, PTHrp: <2 pmol/L, Vit A: 76 (22-69.5ug/dl) and detailed cancer work up was negative. CT scan revealed enlarged thyroid nodule (biopsy negative for cancer) and nuclear scan showed overactive thyroid nodule(Figure 1B). Thyroid studies [TSH: <0.005 (0.35-3.7 uIu/ml), FreeT4: 2.49 (0.76-1.46ng/dl)] were treated with radioactive iodine, methimazole and low dose steroids. After 9 months labs improved- TSH: 0.01 uIu/ml, FreeT4:0.93 ng/dL, Ca: 9 mg/dl and PTH: 42pg/ml. Unfortunately, Cr remained at 4.0mg/dL due to prolonged HCA leading to stage 5 CKD which eventually resulted in successful kidney transplant (KTx).

**Discussion:** To our knowledge we report the first case of irreversible renal failure in a kidney donor due to prolonged HCA from hyperthyroidism eventually requiring KTx. Progression of renal disease from prolonged HCA may be due to limited renal mass as a solitary kidney. Hence, prompt treatment and correction of hyperthyroidism and hypercalcemia may help in preventing progression of renal disease.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
Outcomes in Kidney Transplantation from Increased-Risk Donor Organs: A Single-Center Experience

Maria L. Safar-Bougeri,1,2 Jean M. Francis,2 Northwestern University Feinberg School of Medicine, Chicago, IL; 3Boston University, Boston, MA.

Background: Despite their lower Kidney Donor Profile Index (KDPI) score and demonstrated survival benefit of transplantation as compared with remain on dialysis, Public Health Service increased-risk donor (IRD) organs continue an underutilized source for transplantation.

Methods: This is a single-center retrospective cohort conducted at Boston Medical Center. Patients receiving IRD organs from 2016 and 2019 were evaluated. Baseline characteristics and outcomes one year after transplantation were described.

Results: We included 41 patients receiving IRD organs. Donors tended to be younger, with lower KDPI scores and good kidney function. Most common cause of death was anoxia from drug intoxication. Patients receiving IRD organs had stable kidney function at one year, with >70% having an estimated glomerular filtration rate (eGFR) of >60 mL/min (Table 1). None of the patients became positive for HBV, HCV or HIV.

Conclusions: Patients receiving IRD organs did not show a higher risk of infection or poor renal outcomes in this single-center population.

<table>
<thead>
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<th>Donor characteristics</th>
<th>IRD (n=41)</th>
<th>KDPI (median)</th>
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<tr>
<td>Creatinine (mg/dl)</td>
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<td>Cause (n/total)</td>
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<td>Drug intoxication (%)</td>
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<td>51.5 (22-83)</td>
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<td>Recipient sex</td>
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<td>GFR (mean/median/2.5)</td>
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PUB234
Post-Transplant Lymphoproliferative Disorder (PTLD): A Single Institutional Experience

Inês D. Coelho,1 Sofia Cerequera,2 Catarina Romãozinho,2 Rita Leal,2 Rui Alves,2 Arnaldo Figueiredo,2 1Centro Hospitalar De Trás- os- Montes E Alto Douro, E.P.E., Vila Real, Portugal; 2Centro Hospitalar e Universitario de Coimbra E.P.E., Centro Hospitalar e Universitario de Coimbra E.P.E., Coimbra, Coimbra, PT, Coimbra, Portugal; 3Hospital Amato Lusitano, Castelo Branco, Portugal.

Background: PTLD are a group of heterogeneous lymphoid proliferations in chronic immunosuppressed recipients of solid organ and hematopoietic stem cell transplantation. This study aimed to evaluate the clinical outcomes and to identify the predictors of mortality in adult renal transplant recipients who developed PTLD.

Methods: We have studied the incidence of PTLD in adult renal transplant recipients who were transplanted in our hospital from 1996 to 2019. Data was collected for demographics, transplant and immunosuppression history, EBV and CMV serostatus, diagnosis, treatment and outcomes. We performed uni and multivariate analysis to identify prognostic factors. PTLD was classified according to 2018 WHO lymphoma classification.

Results: Twenty-four patients (12 males and 12 females) were eligible for the analysis. Mean age at time of the transplant was 43.1 ± 16.9 years, with a time between grafting and PTLD of 66 months (IQR 36-98 months). Mean follow-up time was 87 months (IQR 61-117 months). 25% of patients received a living donor renal transplant. 5 cases were from Epstein-Barr virus (EBV) mismatched (D+/R-) transplants and there was no seroconversion at time of PTLD diagnosis. 25% of patients have central nervous system involvement. 19 patients have monomorphic PTLD and the most common histological diagnosis was diffuse large B cell lymphoma. We identified that age >30 years at time of the transplant was a predictor of mortality (HR 33.01; 95% CI: 3.24-336.14; p=0.003). Presence of B symptoms at time of PTLD diagnosis conferred a better prognosis (HR 0.143; 95% CI: 0.035-0.579; p=0.006). All cases were managed with reduction in immunosuppression. 8 patients were treated with rituximab and there was no significant difference in the survival. 7 patients went into remission, 1 returned to chronic dialysis, and 16 patients died (15 of them due to the disease). Mean time between PTLD and death was 3 months (IQR 1-6 months).

Conclusions: PTLD is an infrequent disease with a poor prognosis. Some cases have a close relationship with EBV, but it can also develop in the absence of the classical risk factors. The factor affecting mortality in our population was age >30 years at time of the transplant. Presence of B symptoms at time of PTLD diagnosis seems to confer a better prognosis probably due to early investigation and diagnosis of the disease.

PUB235
Serum Phosphorus as a Predictor of Optimal Kidney Function in Immediate Kidney Transplantation

Daniel Murillo Brambila,1 Monica C. Jimenez Cornejo,2 Maria Concepcion Oseguera-Vizcaino,1 Eduardo Solano,1 Ana Paula B. Rubio,1 Marco A. Covarrubias,3 Hospital Civil de Guadalajara Universidad Hospitalaria Fray Antonio Alcalde, Guadalajara, Mexico; 2Universidad de Guadalajara Centro Universitario de Ciencias de la Salud, Guadalajara, Mexico.

Background: In patients with CKD, there are alterations in serum phosphorus by widely known mechanisms, including in kidney transplant patients. The objective is to demonstrate that patients who decrease serum phosphorus in immediate kidney transplantation during hospitalization predict a GFR> 60 m l / min at discharge.

Methods: Prospective longitudinal study, 39 patients transplanted were analyzed, they were followed up daily until their discharge, they were divided into three groups according to their serum phosphorus(p) levels after transplantation; Group A: p=2.5, B: p=2.6 to 4.5, C: p>4.6 mg/dl, the data were obtained on the days of hospitalization after his kidney transplant, obtaining this variables gender, age, type of donor, cold ischemia, days of hospitalization, urea, creatinine and GFR dayle until discharge, data are shown in numbers, percentages, mean, ANOVA test and ROC curve.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: A total of 39 patients, 30(76.9%) patients were male, a mean age(29.5), 38(97.4%) had a history of dialysis, 21(53.8%) were they transplanted by a living donor, cold ischemia an average of 127min, days in hospital an average of 5.3, serum phosphorum prior kidney transplant an average 5.7(2.3) mg/dl, in the ANOVA analysis a mean serum creatinine (Group A=8.9, B=2.2, C=2.1 mg/dl), a mean GFR (Group A=101, B=65, C=48.7 ml/min), a mean urea (Group A=4423, B=3027, C=1865 ml/day) at discharge were compared; A vs B urea P=0.03 IC=-112/391, creatinine at discharge P=0.1 IC=-6.2/0.2, GFR discharge P=0.03 IC=-9.7/11, A vs C urea P=0.07 IC=-256/5372, creatinine at discharge P=0.01 IC=-4.2/0.4, GFR at discharge P=0.01 IC=8.5/97, AUC of 0.9, with a cutoff value of 3.65mg/dl have a TFG >60ml/min P=0.001.

Conclusions: Patients who decrease serum phosphorus to normal or inclusive ranges of hypophosphatemia after immediate kidney transplantation, have better renal function than those who have hyperphosphatemia at discharge, serum phosphorus may be a predictor of optimal GFR in this patients.

Baseline characteristic, ANOVA test, ROC curve.

PUB236
Routine Monitoring of Donor-Specific Antibodies During the First Year of Kidney Transplant: Is It Underrated?

Background: Kidney transplant (KT) recipients with de novo donor-specific antibodies (DSA) are at risk of graft loss. DSA could lead to a decline in kidney function due to antibody-mediated rejection (ABMR), or be asymptomatic. Efficacy and cost-effectiveness of routine DSA monitoring are not known. Confirmation of ABMR with kidney biopsy is advised. We aim to study the utility of routine DSA monitoring (RDM) in predicting rejection in asymptomatic pediatric KT recipients.

Methods: After IRB approval, a retrospective chart review of patients who had RDM was done. Patients with clinical suspicion of rejection were excluded from the study. Demographic data and clinical features were analyzed using descriptive statistics. Continuous and categorical variables were analyzed using the student’s t-test and Fisher’s exact test respectively. A p-value <0.05 was considered statistically significant.

Results: Four out of 17 (24%) patients were tested positive for de novo DSA. There were no significant differences in age, gender, race, type of transplant, or serum creatinine between patients with positive and negative DSA. Three out of four (75%) patients had positive DSA at 4-6 months that persisted till the end of the year (1 had ABMR, 1 had T cell-mediated rejection and I had no rejection on biopsy), and one(25%) had positive DSA at 10-12 months with ABMR on biopsy. All patients with biopsy-proven rejection (BPR) received steroids, anti-thymocyte globulin, plasmapheresis, intravenous immunoglobulin, and/or rituximab based on the type of rejection.

Conclusions: In our small cohort, we found that for every 5.7 asymptomatic patients who underwent routine DSA testing, one had de novo DSA with BPR. Larger, controlled studies are required to further evaluate the efficacy of RDM.

PUB237
De Novo Thrombotic Microangiopathy Associated with Cytomegalovirus Infection and Alloreactivity: A Fork in the Road of Immunomodulation
Samir A. Medrano, Karin M. Solinich, Michael Casey, Maria Aurora C. Posadas, Vinuya Rao. Medical University of South Carolina, Charleston, SC.

Introduction: De novo thrombotic microangiopathy (TMA) may yield cross-roads of diverging therapeutic approaches, not well delineated. We describe such a case in the setting of Cytomegalovirus (CMV) viremia and suspected rejection.

Case Description: A 52-year-old female with presumed hypertensive nephropathy received a deceased donor kidney transplant (KDPI 73%) complicated by progressive allograft dysfunction after 6 months. Anti-thymocyte globulin was used for induction, while tacrolimus and prednisone was used for maintenance immunosuppression. With step-wise rise in serum creatinine (baseline 1.7 mg/dL) to 2.5, 3.4 and 5.7 mg/dL at 6, 8 and 9 months post-transplant respectively, three allograft biopsies were obtained. Secondary focal segmental glomerulosclerosis, moderate-severe interstitial fibrosis and tubulitis, and a mild tubulitis were seen in all biopsies; mild glomerulitis and peritubular capillaritis in the last two, and TMA in the last biopsy. C4d and HLA DSA were consistently negative. Despite methylprednisone given at month 8, creatinine continued to rise to 7 mg/dL by month 9. The course was complicated by leukopenia, brief thrombocytopenia (platelet count ~ 100 K/mm), progressive anemia (Hemoglobin 11.5 to 6.8 g/dl) and diarrhea in the setting of newly diagnosed CMV viremia (CMV DNA 1164 to 9117 IU/mL at months 8 and 9 respectively). Lactate dehydrogenase increased to 841 U/L with a normal haptoglobin and no reticulocytosis. Schistocytes were seen on a peripheral blood smear. ADAMS-13, von Willebrand factors, platelet counts I, H, I, B, C, 3, 4, and stool panel results were unremarkable. FK506 was switched to Cyclosporin (CYC) after diagnosing TMA. After clearance of CMV viremia and stopping valganciclovir, neutropenia resolved. Creatinine fell from 7 to averagely 5.8 mg/dL at month 10-11. Plasmapheresis (PP) and IVIG were initiated for suspected non-HLA antibody mediated rejection (AMR) with TMA.

Discussion: The constellation of TMA, CMV viremia, tubulitis, microvascular inflammation and myelosuppression, poses dilemmas in balancing management as FK506, CMV and AMR may all be contributory, in isolation or combination to TMA. We elected to maintain a calcineurin inhibitor and mycophenolic regimen in the face of TMA and CMV due to the risk of florid rejection, and initiated PP with IVIG.

PUB238
Hypofibrinogenemia as a Risk Factor of Bleeding After Plasmapheresis with Centrifuge in Renal Transplantations with Active Humoral Rejection
Mayra M. Matias Carmona,1,2 Sergio Hernandez-Estrada,1,2 Jose H. Cano,1 Odette Del Carmen Diaz Avendano,1 1Centro Medico Nacional 20 de Noviembre, Mexico City, Mexico; 2Universidad Nacional Autonoma de Mexico Facultad de Medicina, Universidad Nacional Autonoma de Mexico Facultad de Medicina, Mexico, Mexico.

Background: Humoral rejection represents an important cause of graft loss, multiple therapeutic approaches have been implemented, therapeutic plasma exchange (TPE), is part of them, however one of its main complications as hypofibrinogenemia due to the risk of bleeding, which represents a challenge due to the risk of immunization in the event of a transfusion and even limiting the continuity of treatment due to the risk of bleeding imminent due to low figures during the passage of the session. Objective: to determine if hypofibrinogenemia(<100 mg/dl)after sessions of TPE with centrifuge is an absolute risk factor for bleeding that warrants the need for transfusion or cessation of therapy.

Methods: In the period from June 2017-May 2019, 25 Mexican kidney transplant patients with diagnosis of active humoral rejection, without previous coagulation abnormalities, were submitted to TPE, a total of 5 sessions per patient were granted in an average of 10±2 days, with measurement of fibrinogen levels before and after each session as well as daily clinical evaluation of active bleeding

Results: The age range was 21-35 years, 44% were female, the causes of ERCT up to 52% were not reported, cadaveric donor transplantation predominated in 52%, The initial average fibrinogen value was 397mg/dl, after the 1st session a reduction of 33% was observed, with an average value of 133mg/dl. The lowest level was 43mg/dl, the most important period of reduction during the 4th session. Only 1 major bleeding event was documented due to epistaxis that required transfusion. This event was after the 3rd session, with fibrinogen of 79mg/dl. At the end of TPE treatment, fibrinogen levels normalized in all patients, with no further bleeding events

Conclusions: Despite the strong association of hypofibrinogenemia and bleeding, only one major bleeding event was reported in our population. There were no other events despite having level as low as<50mg/dl, therefore we consider close surveillance as the main measure during TPE; leaving the transfusion only in the context of active bleeding. The blood tissue is rich in immunoglobulins and therefore favors the host’s immune response, it is paradoxical to remove antibodies and grant new ones with transfusions. Hypofibrinogenemia did not limit the continuity of treatment, concluding its treatment in a timely manner.

PUB239
Kidney Transplant Recipients Suffer Fewer Complications After Adrenal Surgery
Ankur P. Choube,1 Darren Abbas,1 Jonathan Demeter,1 Afshin Parsikia,2 Jorge Ortiz,1 1The University of Toledo Medical Center, Toledo, OH; 2Westchester Medical Center, Valhalla, NY.

Background: Chronic immunosuppression after kidney transplant (KT) is a known risk factor for developing a malignancy. While occurrences of other cancers have been well documented, there is a paucity of data regarding the incidence and effects of adrenal tumors after renal transplant. We aim to evaluate the differences in short-term outcomes between renal allograft recipients and the general population undergoing adrenal surgery.

Methods: A retrospective analysis was conducted using Nationwide Inpatient Sample (NIS) data between 2005 and 2014. The population of interest was adults with a kidney transplant (FK506, CMV and AMR may all be contributory, in isolation or combination to TMA. We elected to maintain a calcineurin inhibitor and mycophenolic regimen in the face of TMA and CMV due to the risk of florid rejection, and initiated PP with IVIG.

Conclusions: Despite the strong association of hypofibrinogenemia and bleeding, only one major bleeding event was documented in our population. There were no other events despite having level as low as<50mg/dl, therefore we consider close surveillance as the main measure during TPE; leaving the transfusion only in the context of active bleeding. The blood tissue is rich in immunoglobulins and therefore favors the host’s immune response, it is paradoxical to remove antibodies and grant new ones with transfusions. Hypofibrinogenemia did not limit the continuity of treatment, concluding its treatment in a timely manner.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.
Results: 54 patients met the inclusion criteria. KT recipients were older (p<0.001, more likely to be African American (p<0.001), and had higher Elixhauser Comorbidity Index scores (p<0.001). We noted shorter length of stay (p<0.011), lower rates of any complications (p<0.001), and fewer packed RBC transfusion (p<0.039) compared to the non-transplant cohort. There was no mortality among transplant recipients. Weighted multivariate analyses highlight that total expenditures were lower for renal allograft recipients treated at transplant centers (p<0.021).

Conclusions: Previous publications have demonstrated that history of kidney transplant has deleterious effects on surgical outcomes. In the largest national cohort analysis of adrenal surgery after KT, we discovered that despite higher age and more comorbidities, renal transplant recipients benefited from fewer post-operative adverse events. There was additional benefit from seeking treatment at transplant centers.

PUB240
Granulomatous Tubulointerstitial Nephritis in a Kidney Transplant Recipient
Mohamed Hassanen, Leal C. Herlitz, Cyndee Miranda, Aimen Liaqat, Richard A. Fatica. Cleveland Clinic, Cleveland, OH.

Introduction: Granulomatous tubulointerstitial nephritis (GTIN) is a rare pathological diagnosis accounting for 6% of all causes of tubulointerstitial nephritis (TIN). Causes of GTIN include fungal and tuberculous infections, sarcoidosis, and medications. We describe a case of GTIN in a kidney transplant recipient (KTR).

Case Description: A 65-year-old male with a history of diabetes mellitus, hypertension, active pulmonary and ocular tuberculosis (TB), and a deceased donor kidney transplant 8 years prior was admitted for acute kidney injury (AKI). Medications includedisoniazid, rifampin, carbendazil, insulin, and tacrolimus. Serum labs showed: creatinine (Cr) 2.65 mg/dL (baseline Cr 1.13 mg/dL), corrected calcium 13.2 mg/dL, and tacrolimus trough level 7.6 mg/L. Urine sediment examination and kidney ultrasound were unremarkable. Further workup for hypercalcemia revealed: parathormone (PTH) 7 pg/mL, I-25 dihydroxy-vitamin D 54.3 pg/mL, PTH related peptide <2 pg/mL, and angiotensin-converting enzyme 47 U/L. Kidney biopsy showed TIN and non-caseating granulomas (figure A) with negative acid-fast bacilli (AFB) staining, bacterial, and fungal polymerase chain reaction. He was treated with prednisone taper over 6 weeks with complete resolution of AKI and hypercalcemia.

Discussion: GTIN in KTRs is rare, with an incidence of <1% in transplanted kidney biopsies. AKI and PTH-independent hypercalcemia with a negative workup for other causes of AKI should prompt a kidney biopsy. Granulomas with multinucleated giant cells can help differentiate GTIN from acute rejection – the most common cause of TIN in KTRs. By negative AFB staining of the biopsy tissue sample, it was impossible to exclude tuberculous GTIN in our patient who was on anti-tuberculous therapy. Cautious initiation of steroid therapy can be effective in these cases.

H&E stain showing a non-necrotizing granuloma (arrow) with tubulointerstitial inflammation.

PUB241
Kidney Transplants from Deceased Donor After 11 Days of Hemodialysis
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Introduction: There is little consensus on the use of organs from donors with acute kidney injury (AKI) for kidney transplantation. Previously, the longest reported duration of dialysis before donation was 4 days. We detail the first successful kidney transplants from a donor after 11 days of hemodialysis.

Case Description: Donor was a 60-year-old male with advanced-stage hypertension, on dialysis for 2 years with EPTS of 41%. Cold ischemia time (CIT) and pump time were 32 and 103 hours. Post-operative DGF required two dialysis sessions. Recipient was a 61-year-old male with ESRD from diabetes, on dialysis for 6 years with an EPTS of 90%. CIT and pump time were 26 and 10 hours. Profuse bleeding from graft biopsy site and pseudoaneurysm formation required treatment with transfusions, and dialysis for DGF. He was re-admitted with hyponatremia and carbapenem-resistant enterobacteriaceae sepsis, requiring nephrostomy tube and antibiotics.

Conclusion: Careful selection based on donor youth, good health without comorbidities, and injury by rhabdomyolysis were crucial in this case. Moreover, biopsies revealed excellent histology, with good flow and resistance on perfusion pump. These factors made the kidney's acceptable for transplant despite DCD donor with prolonged dialysis and CIT. Both patients received Tacrolimus, Mycophenolate and Prednisone. On follow up, recipients were dialysis independent and making urine. Complications in recipient 2 required prolonged hospitalizations, but none of the adverse events were due to donor AKI. Take Away: This case report is a novel opportunity to understand the extent of kidney transplantation after AKI. Despite 11 days of hemodialysis and DCD donor, procurement was possible because AKI due to rhabdomyolysis is transient and resolves within weeks. AKI donor-recipient matching is an individualized process. Clinician decision-making with rigorous donor and recipient selection is paramount in transplanting AKI organs. Post-operative DGF management is crucial in restoring graft function.

PUB242
Acute Rejection of Renal Allograft Caused by Drug-Induced Acute Interstitial Nephritis
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Introduction: We report a case of a 42-year-old man who had a living-unrelated kidney transplant in 2017 from a non-ESRD donor. Post-operative biopsy revealed drug-induced acute interstitial nephritis. He had an uncomplicated course with no episodes of rejection. He has been on a triple immunosuppressive regimen. Other past medical history was refractory autoimmune hemolytic anemia at age 20 that required splenectomy.

Case Description: In 2019, he developed fever and rash shortly after taking a 5 days course of azithromycin. This was associated with marked eosinophilia and an increase in his serum creatinine (sCr) from 1.0 mg/dL to 3.1 mg/dL. Donor Specific Antibody (DSA) was negative. Kidney biopsy showed active tubule interstitial nephritis with prominent eosinophils. He received pulse steroids followed by tapering oral steroids. His sCr improved to 2.7 mg/dL. A month later, he was admitted for hematuria and acute kidney injury. His sCr was 4.2 mg/dL. Urinalysis showed trace protein, RBC >50 HPF, and WBC 11-20 HPF. Tacrolimus level was within the therapeutic range.DSA was positive for class II; DQA1*05:01, DR17, DR52 with 18,000 MFI. Kidney biopsy showed mixed rejection; acute cellular rejection (ACR) Banff IIB and acute antibody-mediated rejection (ABMR)/C4d positive. He was treated with high dose IV steroid, thymoglobulin, plasma exchange, and Rituximab. His sCr did not improve. Repeat biopsy showed improvement of ACR Banff IA along with capillaritis and glomerulitis, suggesting ongoing ABMR but C4d staining became negative. On the last biopsy, there was diffuse interstitial fibrosis.

Discussion: We hypothesize that Acute Interstitial Nephritis (AIN) primed the T-cells lymphocytes to react against the allograft. His sCr improved after treatment of AIN, followed by worsening of sCr and reflecting mixed rejection. The treatment of rejection led to some improvement but did not resolve the ongoing damage that ultimately caused significant fibrosis with poor chances for recovery. To our knowledge, this is the first case where AIN is followed shortly by a mixed allograft rejection even in a patient with a previous HLA mismatch. In the past, splenectomy was the treatment of mixed ABMR. In conclusion, rejection should be considered as one of the differential diagnoses when renal function worsens after the treatment of AIN.

PUB243
Kaposi Sarcoma: A 30-year Experience of a Portuguese Kidney-Transplant Center

Background: Kaposi sarcoma (KS) is a low-grade angioproliferative tumor associated with human herpesvirus 8 (HHV-8) infection, which incidence is higher in kidney-transplant recipients (KTR). This study aimed to review all cases of KS diagnosed in KTR, over the past 30 years, at our center. A total of 1476 transplants were performed during this period.

Methods: We reviewed all histologically diagnosed KS in KTR. Data were collected from electronic and paper medical records.

Results: Seven KTR were diagnosed with KS, of which 6 were men and 1 was HIV positive, all caucasian. The mean age at the time of KT was 51 ± 18 years. Six cases occurred before 2010 and the last case in 2018, in an HIV positive patient and the only one to receive induction immunosuppression - IS (basiliximab). All but 1 patient were on maintenance IS with prednisone (PDN), a calcineurin inhibitor (CNI) and mycophenolate mofetil (MMF). The median time of transplant at KS diagnosis was 9 (2 – 99) months. Six patients had only cutaneous lesions, mainly in lower limbs and one also had abdominal lymph nodes involvement. HHV-8 viremia, evaluated in 2 patients, was positive. In 6 cases, KS was diagnosed by an mTOR inhibitor (MMF) and MMF was maintained with PDN and reduced dosage of CNI. All except one received antineoplastic

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
treatment: 3 were submitted to radiotherapy (RT), 1 to chemotherapy (CT) and 2 had both RT and CT. The remaining 8 patients underwent dorzoxurbin was the drug of choice. At follow-up, 1 patient remains with normal kidney function, 1 with chronic graft dysfunction and 2 lost their KT (one by antibody-mediated rejection 3 months after KS diagnosis, and one by chronic graft dysfunction after 19y of KT, 14y after KS). Three patients have already died (withdrawn graft function) one directly to KS.

Conclusions: Despite the scarcity of published series on KTR, the experience of KS in our center is in line with the literature, since it’s more common in man, the incidence is higher in the first 2 years after transplant and cutaneous lesions were the most frequent manifestation. In our series, a lower incidence of KS in the last decade has been reported. However, thorough surveillance in higher-risk groups, as HIV patients, should not be forgotten.

PUB244
Rapid Renal Allograft Failure Following Recurrence of Lupus Nephritis 12 Years After Renal Transplant

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Introduction: End stage kidney disease (ESRD) secondary to lupus nephritis (LN) is an important complication of systemic lupus erythematosus (SLE) for which the treatment of choice is to undergo a kidney transplant (KT). Following a KT, patients rarely develop recurrent lupus nephritis (RLN), but when they do, most events of recurrence occur within a few years after KT. We describe the case of a young Caucasian lady who underwent a living related KT for LN and maintained stable renal function for 12 years, and then developed severe RLN that was unresponsive to treatment.

Case Description: A 39-year-old developed LN and her kidney biopsy (KB) demonstrated global sclerosis with immune complex glomerulonephritis with positive serum antinuclear (ANA) and anticardiolipin antibodies (ACA) in 2006. She received living related KT in 2007. Her post-transplant course was complicated with the development of Banff grade IIa acute cellular rejection 1-month later, which was treated with steroids. She responded to treatment and attained a basal serum creatinine (Cr) measuring 1.2 to 1.3 mg/dL. She was maintained on tacrolimus, mycophenolate mofetil (MMF) and prednisone. Her MMF was replaced with azathioprine during an uneventful pregnancy in 2011. She had a slight increase in her baseline Cr over the years but maintained a stable Cr measuring 1.4-1.6 mg/dL. In 7/2019, the Cr suddenly increased to 3.9 mg/dL with proteinuria and microscopic hematuria. Her platelet counts, complement, ANA, ANCA and double stranded DNA levels were normal. A KB demonstrated features of thrombotic microangiopathy, diffuse proliferative GN with focally crescentic LN and full house pattern on IF. Despite treatment with intravenous steroids and cyclophosphamide, her renal allograft function deteriorated, she required dialysis by 11/2019.

Discussion: Even patients with stable renal function maintained on standard immunosuppressive medications many years after transplantation are at risk of RLN. Our case demonstrates that RLN can manifest suddenly, and with a lack of usual laboratory features characteristic of a lupus flare. Further studies are necessary to better identify reasons for lupus recurrence in patients with long standing stable renal function.

PUB245
Simultaneous Disseminated Adenovirus Infection and Rejection in a Kidney Transplant Patient

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Introduction: Adenovirus can lead to serious conditions in the immunocompromised transplant recipients. It infects urothelium and causes acute hemorrhagic cystitis and either nephritis or acute rejection causing functional deterioration of transplanted kidney. Case Description: A 55-year-old male with history of ESRD on hemodialysis received a deceased donor renal transplant. After induction with steroids and Thymoglobulin, he was maintained on mycophenolate mofetil (MMF), tacrolimus and prednisone with stable creatinine of 1.1-1.3 mg/dL. After 6 months, he presented with right lower quadrant abdominal pain, hematuria, dysuria, productive cough, fever, conjunctivitis, sore throat and diarrhea. Labs showed mild elevation of creatinine (1.5 mg/dL). Urine microscopy showed non-deformed RBCs without glomerular cast. Chest x-ray and ultrasound of transplant kidney were normal. Patient was started on intravenous fluids, broad spectrum antibiotics and admission for acute kidney injury. Renal ultrasound showed transplant kidney and bilateral renal stones. Ultrasonography of renal sinus revealed Respiratory pathogen panel (RPP) was negative for any pathogen. Urine culture had no growth. Cystoscopy was unremarkable. Patient had worsening leukopenia and proteinuria of 3.3 grams. A repeat RPP was positive for adenovirus and serum Adenovirus PCR was 28,600 copies/mL. Biopsy of transplant kidney showed mild tubulo-interstitial rejection with transplant glomerulitis and negative for adenovirus nephritis. Due to simultaneous occurrence of infection and acute transplant rejection, MMF was reduced to 250mg BID and pulse steroids were started for 5 days. Serum adenovirus PCR was decreased to 1200 copies/mL on day 5. Repeat biopsy was done on day 10 and showed a decrease in Adenovirus PCR to 1900 copies/mL. Decreasing immunosuppression was avoided given recent rejection episode. Patient’s IgG level was low at 549 mg/dL and a dose of 300 mg/kg IVIG was administered. Repeat urinalysis showed resolution of hematuria and proteinuria. Serum Adenovirus PCR was undetectable at 2, 3 and 4 months follow up.

Discussion: Disseminated adenovirus infection after renal transplantation is becoming more prevalent. The treatment includes reducing the immunosuppressive therapy, IVIG infusions, anti-viral agents, or combination of these therapies. The approach to therapy is based on the local guidelines for selection, timing and efficacy of treatment modalities, which requires further investigation.

PUB246
A Case Report of Transplant Renal Artery Stenosis Presenting as Acute Encephalopathy and Cardiac Arrhythmia in a 28-Year-Old Man

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Introduction: Transplant renal artery stenosis (TRAS), defined as narrowing of the transplanted renal artery, is one of the most serious vascular complications post kidney transplantation. TRAS presents as hypertension and allograft dysfunction at 3 to 12 months after transplantation. Unique to this case is the early presentation with behavior changes and cardiac arrhythmia. No report of such has been published as of this writing, especially in a third world setting.

Case Description: This is a case of a 28-year-old filipino male patient with post kidney transplantation one month prior to admission. Donor and recipient matching revealed low immunologic risk for rejection with four HLA matched. Transplantation was unremarkable. He presented at the ER with behavioral changes, incoherence and SVT on ECG. Medical cardioversion with adenosine and verapamil was done. He was immediately dialedyzed and noted resolution of symptoms. Course in the ward was unremarkable except for the persistence of hypertension and elevated creatinine. Doppler ultrasound is suggestive of TRAS on main renal artery allograft. Renal CT angiography confirmed 66% stenosis of right renal artery graft. He was given amiodipine 10mg/day and eventually underwent renal angioplasty as the definitive procedure to correct stenosis. Post angioplasty blood pressure was normal and remained on this level for the following days. Serum Creatinine lowered down to 110 umol/L. Repeat Doppler study showed an angioplasty stent in the main renal artery graft. On his follow-up check up, his serum creatinine and BP remained on normal levels.

Discussion: The case proves that although TRAS usually presents at 3 to 12 month post kidney transplant, it may occur earlier and unusually with encephalopathy and SVT. Doppler ultrasound is in essential in early detection, however, Renal CT angiogram is the imaging of choice for the confirmatory diagnosis. TRAS is catastrophic but early diagnosis and prompt medical-surgical intervention with amiodipine and renal angioplasty can lead to improved allograft survival and good prognosis for the patient.

PUB247
Management of Kidney Transplant Waiting List in Belarus

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Background: The reasons for establishing an automated waiting list system were as follows: the main clinical information about patients was available only on paper, there was a problem of optimal choice from the list of compatible donor-recipient pairs based on a large number of factors, there were difficulties with information transfer rate, security and reliability.

Methods: The project was implemented as a web-application. The program’s interface includes several parts: Unit “file-cabinet” that contains patients’ passport data and contact information Unit “Clinical information” includes immunological and clinical data of recipients Units “Examination” and “Confirmation of the consent” is based on examination results and determines the suitability waiting list Unit “Recipient selection” Unit “Calculator of graft function”.

Results: Web application helps to allocate donor organs by medical and social principles of selection. The social principles are: priority of patients who waited kidney transplant longer considering of donor and recipient territorial compatibility increased chances for kidney transplant patients with “incomplete” phenotype (homozygotes) priority for highly sensitized patients priority for children priority for patients who needed multiple-organ transplantation Medical principles: balance between the potential kidney transplant and recipient survival stratified accounting of histocompatibility degree between donor and recipient reduction of kidney transplant cold preservation time creation of transplantation priority conditions for patients who needed urgent kidney transplantation initial kidney graft function prognosis accounting Scoring system is based on the fact that the main feature of social justice (maximum waiting period) is equated domain medical principle of effectiveness (maximum compatibility degree). The allocation of organs accounts the risk of early graft dysfunction (automatic kidney graft functional calculator based on multifactator analysis of donor - and recipient-dependent risk factors is implemented). The final result is a prioritized list of recipients with a score of each factor and to perform the final selection of the council of physicians.

Conclusions: The software application allows to keep records, make statistical data analysis of potential recipient, distribute the organs anytime, anywhere in the world where the Internet is available.

Funding: Commercial Support - EPAM systems
Late-Onset Recurrent Granulomatous Interstitial Nephritis in Transplanted Kidney with Successful Treatment: A Case Report
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Introduction: End stage renal disease (ESRD) secondary renal sarcoidosis is rare and likely due to hypercalcemic nephropathy. There is limited data on recurrent renal sarcoidosis post kidney transplant. We report a case of unusually late onset, recurrent sarcoidosis in transplanted kidney with successful treatment.

Case Description: A 65 year-old female with history of pulmonary sarcoidosis and ESRD due to sarcoidosis related-granulomatous interstitial nephritis (GIN) received a renal transplant in 2008. She was maintained on tacrolimus, mycophenolate(MMF) and prednisone. Baseline serum creatinine (SCr) had been 1.5 mg/dL. In 2017, patient was diagnosed with recurrent metastatic colorectal cancer. In 2019, her SCr increased to 3 mg/dL. A transplant kidney biopsy showed non-necrotizing GIN. She was treated with prednisone 40 mg daily. SCr decreased to 2.3 mg/dL. 3 months later, a repeat transplant kidney biopsy showed resolution of GIN. Prednisone dosage was tapered.

Discussion: GIN related to sarcoidosis has an overall estimated occurrence at 0.18 % of native kidney biopsies. GIN in transplanted kidney due to recurrent sarcoidosis has been reported ~17%. Risk factors for recurrence include primary renal disease related to sarcoidosis and a shorter delay between the last sarcoidosis flare and renal transplantation. Recurrence typically occurred shortly after transplantation, averaging 13 months after transplantation. More studies on treatment of recurrent renal sarcoidosis are warranted. We report a case of late onset recurrent GIN, occurring 11 years after transplantation with successful treatment.

Elevated Donor-Derived Cell-Free DNA as an Indication for Kidney Transplant Biopsy
Aileen Transplant Biopsy

Background: Donor derived cell-free DNA testing (dd cf-DNA) is increasingly employed for post-kidney transplant monitoring and may influence the decision to proceed with indication biopsy. The goal of this study was to identify those patients in whom the finding of an elevated dd cf-DNA was a key factor in the decision to obtain a kidney biopsy and to review 1) their biopsy findings and 2) any resulting treatment.

Methods: We reviewed the charts of 73 patients who underwent kidney transplant biopsy and had at least 1 dd cf-DNA (AlloSure) test performed. Ten patients underwent biopsy prompted primarily by an elevated dd cf-DNA level. Biopsy findings and resultant therapeutic interventions were abstracted.

Results: The median time from transplant to biopsy was 25.5 months. 2/10 patients had a normal biopsy. 5/10 had histological findings consistent with antibody mediated rejection (ABMR) with or without concurrent T-cell mediated rejection (TCMR). 2/10 had TCMR and 1/10 had recurrent glomerulonephritis. Of those with ABMR, 1/5 had a de novo HLA donor specific antibody (DSA) and 3/5 had positive non-HLA antibody (AT1 receptor antibody (AT1R)). 8/10 patients had a therapeutic intervention following biopsy. Dd cf-DNA decreased following treatment in 4/7 patients and did not change or worsened in 3/7 patients with available follow-up dd cf-DNA testing.

Conclusions: Kidney transplant biopsies in patients with an elevated dd cf-DNA frequently yield findings that warrant therapeutic intervention. Kidney transplant biopsy should be considered in patients with elevated dd cf-DNA, even if otherwise stable. Our observations warrant further examination on the utilization of long term dd cf-DNA monitoring, particularly in immunologically high risk kidney transplant recipients.

Funding: Commercial Support - CareDx

Disseminated Nocardiosis in Renal Transplant Recipient
Mohamedanwar M. Ghandour, Marecena S. Zachariah. Wayne State University School of Medicine, Detroit, MI.

Introduction: Nocardiosis is an uncommon opportunistic Gram-positive bacterial infection caused by aerobic actinomycetes in the genus Nocardia. Nocardia can cause localized or systemic suppurative diseases involving eyes, kidneys, skin, lungs, bone, and central nervous system. Disseminated Nocardia is a rare condition, seen among immunocompromised patients.

Case Description: We report the case of a 55-year-old African American kidney transplant recipient on maintenance immunosuppression, who was diagnosed with cutaneous and pulmonary Nocardiosis. Presenting symptoms were shortness of breath, bilateral lower extremities pain and swelling. Tissue culture grew gram-positive bacilli specified as Nocardia farcinica from thigh and gluteal abscesses (figure 1). CT thorax showed bilateral reticulonodular opacities (figure 2). Patient was managed with immunosuppression reduction and specific treatment with high dose Bactrim in conjunction with linezolid. Combination antibiotics were continued for four weeks, thereafter Bactrim alone was continued for twelve months, at which point all lesions had healed.

Discussion: Nocardiosis with systemic involvement carries a poor prognosis. The reported patient had disseminated Nocardiosis involving lungs and skin, though lungs were thought to be the primary source of infection. However, early diagnosis and appropriate antibiotic coverage, had a favorable outcome, in a renal transplant recipient. Recommended treatment duration is 6 to 12 months with frequent imaging.
Case Description: After treatment of esophageal candidiasis, a 50yo male KTR presented with persistent odynophagia, dysphagia, dysphonia, fever, hipocacusis, otalgia and vesicular lesions in the external left auditory canal, compatible with Herpes Zoster Oticus. He had undergone a deceased-donor kidney transplant ten years before, and maintained on mycophenolate mofetil (1.5 g/d), tacrolimus (2 mg/d) and prednisone (7.5 mg/d). He received Campath induction and tacrolimus. A nasofibrobroncoscopy showed unilateral paralysis of the left vocal cord with saliva aspiration. Computed tomography scan of cranium, neck and thorax excluded expanded lesions. Blood polymerase chain reaction test detected Varicella-Zoster Virus (VZV). Due to severe dysphagia with significant weight loss, reaching 35 kg, he received enteral nutrition through a nasogastric feeding tube during 12 weeks. He gradually recovered motor function of the 7th and 10th cranial nerves. Six months after the onset of symptoms, the patient is under full immunosuppressive therapy and feeding through mouth with occasional choking to some solids.

Discussion: Reactivation of pre-existing VZV in craniospinal sensory ganglia causes Herpes Zoster, which is characterized by a painful erythematous rash in the affected dermatome. Ramsay-Hunt Syndrome occurs when VZV affects neurons of the geniculate ganglion. When it occurs unusually with multiple cranial neuropathies it leads to a potential missed diagnosis and delayed treatment.

PUB254

Tacrolimus: A Worth-Considering Culprit for Post-Transplant Anaemia Sensitive to Parvovirus B19

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Introduction: Haematological side effects of tacrolimus seem to be rare and their aetiology is unclear. Parvovirus B19 is an uncommon yet clinically significant infection that manifests as refractory anaemia in post-transplant patient. The exact mechanism by which tacrolimus can aggravate pure red cell aplasia (PRCA) is still unclear. Here we report a case of post-transplant anaemia where withdrawal of tacrolimus demonstrated significant improvement in chronic transfusion dependent anaemia.

Case Description: A 66-year-old male with end stage renal failure due to accelerated hypertension had a deceased donor transplantation in 2018. Before receiving his transplant, his peripheral blood counts were relatively normal. Patient was discharged nine days after operation with haemoglobin of 8.2 g/dl. Approximately five weeks following transplantation, he was found to have profound anaemia with haemoglobin level falling to 5.7 g/dl but white cell and platelet count remained normal. Following investigations, patient was found to have parvovirus B19 with positive DNA titre. Since then patient was transfusion dependent with two weekly red cell transfusion. Patient had two courses of IVIG, however, showed only transient improvement in viral DNA titre with no haematological improvement. Finally, tacrolimus was switched to cyclosporin A and showed rapid improvement within two weeks.

Discussion: Persistent parvovirus B19 infection can occur in immunocompromised host due to impairment of the neutralizing antibody response and/or cellular immunity thus failure to clear the virus. Tacrolimus, on the other hand, is believed to be an immunosuppressive agent without significant potential for myelosuppression. In this case, transient improvement of withdrawal of tacrolimus with IVIG treatment was suggestive of an etiological role of tacrolimus. The close inverse relationship between viral DNA PCR titre and erythropoietic activity reflected by the improvement of refractory anaemia showed that the direct cause of red cell aplasia was viral infection, rather than direct drug toxicity. Parvovirus B19-induced anaemia is aggravated by the use of tacrolimus through impairment of its clearance by tacrolimus, which cannot be simply explained by a state of heightened immunosuppression.

PUB255

Use of Donor-Derived Cell-Free DNA to Identify Allograft at Risk by Late Surveillance

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Introduction: Monitoring allograft function remains inadequate. Many allografts sustain subacute injury not detected in time resulting in poor long-term outcomes. Traditional tools utilized (renal histopathology, proteinaemia and DSA) are insensitive and/or insensitive to the progression of allograft dysfunction not picked up by traditional means, allowing active intervention and change in management.

Case Description: 36 YO WF with a H/O SLE leading to CKD, S/P LUKT in 2018. Immunosuppression maintained consisted of tacrolimus and MMF. Nadir Cr 0.8 mg/dl. Current Cr 1.0 mg/dl. Urine Pt/Cr ratio 0.06 g/g. Seen for routine visit. Surveillance DD CF DNA (Alloscore) done - 4.8%. Repeat after a few weeks - 5.4%. No DSA, ANA was at 1:40. ds DNA Ab negative. Normal complements. Biopsy was suggestive of active acute antibody mediated rejection with severe microvascular injury and renal limited TMA. C4d only focally positive. DSA repeated and negative. MICA Ab negative. ATIR

PUB251

Native Kidney Cytomegalovirus Nephritis

Sandiva Bindrog, Paul D. Killen, Mona D. Doshi. University of Michigan, Ann Arbor, MI.

Introduction: Cytomegalovirus (CMV) is the most common opportunistic infection in solid organ transplant (SOT) recipients and is estimated to affect 15-30% of high-risk SOT recipients. Typical manifestations of CMV end-organ disease includes colitis, esophagitis, hepatitis, and pneumonia. However native CMV nephritis is rare, reported in less than 1% of renal biopsies. We present a case of CMV nephritis in a high risk liver transplant recipient who completed six months of CMV prophylaxis four weeks prior to presentation.

Case Description: A 66-year-old man with history of liver transplantation was hospitalized on post-transplant day 230 for worsening kidney function (serum creatinine 4.40 mg/dL, baseline 2.0 mg/dL) and fatigability. The patient’s history was notable for cryptococcal cirrhosis and hepatorenal syndrome. Immuno therapy consisted of tacrolimus (target trough 6-10ng/mL), mycophenolate mofetil (MMF), and prednisone. The recipient was CMV seronegative and the donor was CMV seropositive. He received ganciclovir for CMV prophylaxis in first six months of transplantation, per protocol. The early post-transplant course was complicated by reactivation of muco-cutaneous herpes simples virus-1, and Cloridrona difuicile colitis. On presentation, patient reported fatigue, loose stools, and nausea. He was afebrile and had a normal white blood cell count. Serum creatinine was 4.40 mg/dL (baseline 2.0 mg/dL). Urinalysis was positive for 3+ leucocyte esterase with a full field of leucocytes and 10-50 red blood cells per high power field. Culture grew > 10^5 cfu/mL of Candida albicans. A normal renal ultrasound was noted. He was treated with intravenous (IV) cefepime to evaluate the cause of the persistent renal failure, a renal biopsy was performed, revealing acute tubular injury and focal severe interstitial nephritis. CMV intra-nuclear and cytoplasmic inclusions were visualized and confirmed by immunohistochemical staining. Plasma CMV DNA levels by quantitative PCR were 40862 IU/mL. Treatment consisted of IV ganciclovir at induction doses adjusted for renal clearance, followed by maintenance dose ganciclovir. His renal functions improved.

Discussion: We report a rare manifestation of CMV disease with evidence of CMV in native kidney. Clinicians should have a high suspicion for late onset CMV diseases as a diagnosis in at risk SOT recipients with signs and symptoms of genitourinary tract.

PUB252

Incidence and Risk Factors in Mexican Patients with Diarrhea After Kidney Transplantation


Background: Diarrhea is one of the most frequent complications after kidney transplantation. Leads to dehydration, alteration of immunosuppressants serum levels, kidney function deterioration and graft loss. The prevalence of diarrhea varies from 20-50% globally. Focusing treatment on guidelines or recommendations, without considering local microbiology, may lead to mistakes in the management of this patients.

Methods: Cohort, analytical, retrospective study, were included kidney transplant patients from January 2014 to December 2018 in the Nephrology and Kidney Transplant Department at the Centro Medico Nacional 20 de Noviembre in Mexico City. Annual cumulative incidence index was calculated and performed. Association with potential risk factors was used for the evaluation of risk factors. Survival analysis made by Kaplan-Meier curves.

Results: 92 patients were evaluated. Thirty two diarrhea episodes were recorded in 28 patients. 25% of the cases were in the first month after transplant, 40.6% of the episodes occurred up to the first six months. Authors posit that diarrhea, infections and 10% of the cases were infectious etiology suspected, but only 45.8% had microbiological isolation. The most frequently isolated microorganism was Entamoeba histolytica in 45.5% of the cases. The cumulative incidence was 34%. There was no difference in graft survival and accumulated survival is the same in patients who developed diarrhea and those who did not (p = 0.17). Thymoglobulin induction increases up to 5 times the probability of developing post-transplant diarrhea (HR 5.98 p=0.01).

Conclusions: In our center, the cumulative incidence of diarrhea after transplantation is similar to reported in international series. The microbiology of diarrhea events, unlike that described in developed countries, is mainly associated with parasites. The impact of this complication on graft survival and accumulated survival is the same in patients who developed it versus those who did not. Limited epidemiological data exist in our country and Latin America, focusing our approach to reduce diarrheal disease by incorporating epidemiological information and thereby improve therapeutics options for this patients.

PUB253

Unusual Presentation of Ramsay-Hunt Syndrome in a Kidney Transplant Recipient

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Introduction: Herpes-virus reactivation has long been recognized as occurring more frequently in immunocompromised individuals. There are only a few cases of Ramsay-Hunt Syndrome described after transplantation. We report a case of a kidney transplant recipient (KTR) with an atypical course due to multiple cranial nerve involvement.

Case Description: 36 YO WF with a H/O SLE leading to CKD, S/P LUKT in 2018. Immunosuppression maintained consisted of tacrolimus and MMF. Nadir Cr 0.8 mg/dl. Current Cr 1.0 mg/dl. Urine Pt/Cr ratio 0.06 g/g. Seen for routine visit. Surveillance DD CF DNA (Alloscore) done - 4.8%. Repeat after a few weeks - 5.4%. No DSA, ANA was at 1:40. ds DNA Ab negative. Normal complements. Biopsy was suggestive of active acute antibody mediated rejection with severe microvascular injury and renal limited TMA. C4d only focally positive. DSA repeated and negative. MICA Ab negative. ATIR

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Underline represents presenting author.
Infections in the Early Period After Kidney Transplantation

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Background: Infectious complications remain an important cause of morbidity and mortality in kidney transplant recipients, especially in the first year after kidney transplantation (KT). The aim of our study was to evaluate incidence, type of infectious complications and also, to identify risk factors and graft survival impact of these infections in the first 90 days after KT.

Methods: We performed a prospective cohort study, which included 67 adult patients (age ≤ 18 years), transplanted in our center between the 1st of October 2018 and the 1st of October 2019. Demographics data, recipient, donor, transplant, treatment and infections parameters were analyzed.

Results: Among the 67 patients, the mean age was 41.3±10.5 years, male was the predominant recipient gender (59.7%) and 65.7% received a graft from a cadaveric donor. During the first 90 days after KT, 26 infectious episodes occurred in 22 kidney recipients (32.8%). The majority of patients (68%) developed infection in the first 30 days after KT. The most common infections were urinary tract infections (53.8%). The most frequent pathogens identified were Klebsiella pneumoniae (9 times) and Escherichia Coli (7 times). Median time of antibiotic therapy was 10 days (7-15). Patients from the infection group received a graft from a significantly older donor (p=0.02), had a significantly higher cold ischemia time (p=0.02) and tended to received more frequent antithymocyte globulin (ATG) induction therapy (p=0.09). No significant difference between patients with infectious and without infectious complications, in terms of delayed graft function (p=0.14), acute rejection (p=0.13) and graft failure (p=0.17). Multivariate Cox regression analysis showed that induction therapy with ATG (HR=3.02, CI 95%:1.08-8.42; p=0.03), DGF (HR=3.61; CI 95%:1.09-11.91; p=0.03) and donor age (HR=1.04; CI 95%:1.006-1.082; p=0.02) were independent risk factors for infection in the first 90 days after KT. Five out of 67 patients developed graft failure, and 3 of them (60%) lost their graft due to acute graft pyelonephritis (p=0.001).

Conclusions: We showed that infections in the early period after KT remain a common complication with negative impact on graft function, specially urinary tract infections. Likewise, induction therapy with ATG, DGF and donor age were independent risk factors for infectious complications.

AKI in Kidney Transplant Patients: A Single-Center Experience

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Background: The incidence of acute kidney injury (AKI) after kidney transplantation varies depending on the centers but it is a significant risk factor for graft failure. Kidney transplantation recipients have various risk factors for AKI according to the time after transplantation, most commonly being infection, ischemia-perfusion injury, volume depletion, calcineurin induced nephropathy and acute rejection. We present the common causes of acute kidney injury in our center and the related outcomes.

Methods: A retrospective study was conducted and gathered the information from their first episode of acute kidney injury event starting from January 2011. Out of 180 patients, 65 patients were excluded due to the lack of detailed documentation. We looked up the incidence of acute kidney injury from biopsy reports and serology data and the subsequent renal outcomes.

Results: Among 115 patients, 105 patients (88%) had non-oliguric AKI and 10 patients (8%) developed oliguric AKI. Biopsy revealed the most common cause of AKI being the transplant glomerulopathy (chronic rejection) at 23% in non-oliguric groups and 66% in oliguric groups. Only a few patients (9.5%) recovered and most of them developed chronic kidney disease with 41% in non-oliguric group. Acute cellular mediated rejection was found in 18% patients in non-oliguric group. Dialysis was needed in 24% patients in oliguric patients.

Conclusions: Our data shows that non-oliguric AKI is the most common presentation in kidney transplant patients and had poor outcome. Surprisingly, the most common etiology of AKI is chronic rejection in our center. Close follow up and early detection with biopsy might help to prevent chronic kidney disease due to chronic rejection.

Early Graft Dysfunction due to Banff 2A Rejection in a Non-Sensitized Cross-Match-Negative Recipient

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Introduction: With the introduction of potent immunosuppression, the incidence of acute rejection in the first year following transplant is 1-2% lower in living donor kidney transplants (LDDK) compared to deceased donor kidney transplants (DDKT). Ideally, immediate graft function should be expected after LDKT. We present a case report of early acute cellular rejection 26 hours after an ABO compatible, HLA crossmatch negative LDKT.

Case Description: A 65-year-old Caucasian male with ESRD due to anti-GBM disease presented for a LDKT from his 68-year-old wife. He was ABO compatible, HLA crossmatch negative, and 0% for both T-flow and B-flow PRA. Induction was with Basiliximab 20mg and Methylprednisilone 500mg and achieved immediate diuresis. He became anuric by 16 hours post-op, and a for-cause biopsy was done on POD 2 which showed Banff 2A acute cellular rejection with negative C4D. Patient was treated with rabbit anti-thymocyte globulin (rATG) with total dose 3mg/kg divided over 4 doses and then thymoglobulin steroid at 250mg for 5 days. Immunosuppression was intensified and target tacrolimus levels were increased to achieve trough levels between 10-12 ng/mL. The patient has maintained excellent allograft function six months post-transplant with baseline serum creatinine baseline 1.8-2.0 and eGFR 34-38.

Discussion: Risk factors for acute rejection include multiple human leukocyte antigen (HLA) mismatches, a high panel reactive antibody (PRA), presence of donor specific antibodies (DSA), ABO blood group incompatibility, positive HLA crossmatch, prolonged cold ischemia time greater than 24 hours, African American ethnicity, and inadequate induction regimen. For patients with high risk factors for rejection, 2009 KDIGO guidelines recommend induction regimen with lymphocyte-depleting agents such as rATG rather than IL-2 receptor monoclonal antibody such as Basiliximab. This case report focuses specifically on the development of ACR in a low risk living donor transplant. We speculate that the development of ACR in this low risk patient was likely due to the HLA mismatches and possibly induction with Basiliximab. This case report poses the question of whether more intensive induction therapy should be considered in low risk patients with HLA mismatches and the long-term allograft outcomes following acute rejection.

Aspirin Prescribing Practices and Characteristics of Pregnant Women with CKD

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Background: Women with chronic kidney disease (CKD) are at a higher risk for pre-eclampsia compared to non-transplant patients without CKD. The U.S. Preventative Services Task Force has recommended use of low-dose aspirin in women with a high risk for development of preeclampsia, including women with renal disease since 2014. The authors sought assess the characteristics of pregnant women with CKD and aspirin prescribing practices at their institution.

Methods: The authors performed a retrospective chart review of data from pregnancies in women with CKD who delivered between January 1, 2015 and December 31, 2019. Potential pregnancies were identified with diagnostic codes for pregnancies and then included patients who had diagnostic codes for chronic kidney disease and proteinuria. We included pregnancies that had a formal diagnosis of CKD and those in whom baseline creatinine did not decrease at least 0.3 mg/dL during pregnancy. We excluded pregnancies that ended prior to 12 weeks. Means, standard deviations, medians, and interquartile ranges were used for continuous variables, and frequency and proportions were used for categorical variables, as appropriate.

Results: A total of 149 pregnancies were included. The mean age at due date was 30.8 (std. dev 5.6) with 27.5% of advanced maternal age. The majority (51.7%) were obese, with a mean BMI of 32.8 kg/m2 (std. dev 8.2). 15.4% had a history of prior pre-eclampsia. Just over half (57.5%) had been diagnosed with CKD prior to or during pregnancy with the most common underlying etiologies being type 2 diabetes mellitus. Of these, the mean baseline creatinine, obtained within 1 year of pregnancy, was 1.13 mg/dL (std. dev 0.61). Of 149 pregnancies included, 62 (42.3%) were prescribed aspirin prior to 28 weeks of gestation. Overall, 36.2% (54/149) were diagnosed with pre-eclampsia. Of those with a formal diagnosis of CKD prior to pregnancy, 52.9% were prescribed aspirin and 42.4% developed pre-eclampsia.

Conclusion: Chronic kidney disease is a well-recognized risk factor for pre-eclampsia with guidelines recommending the prescribing of aspirin to pregnant women with CKD. This study demonstrated low overall aspirin prescribing rates with relatively high rates of pre-eclampsia at a single institution.
Magnesium Intake, Bone Mineral Density, and the Risks of Falls and Fractures in Post-Menopausal Women with Kidney Stone

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Background: Kidney stone formers are a unique patient population at high risk for fall and fractures due to dysregulated calcium homeostasis and early bone loss. Magnesium is an important component of bone, but its relation to falls and fractures among stone formers is unclear.

Methods: We performed regression analyses to determine the independent effect of dietary magnesium intake (DMI) on bone mineral density (BMD), and risks of fall and bone fracture among incident stone formers identified in the Women’s Health Initiative (WHI), a prospective longitudinal multicenter study investigating the health of post-menopausal women.

Results: Out of a total of 145,942 WHI participants free of kidney stone history at baseline, 6024 developed kidney stone after 1,601,750 patient years of follow up. Among these incident stone formers, 82% were Caucasian, 23% were above age 70. Mean DMI was 304 mg/day, 30% had high DMI defined as >348 mg/day, 38% had medium DMI defined as 241-348 mg/day and 32% had low DMI defined as <241 mg/day. A total of 238 (4%), and 2581 (43%) incident stone formers had low BMD and new falls or fractures, respectively. Both low dietary calcium intake and active smoking associated with reduced BMD (p<0.05), but DMI did not affect BMD in the multivariate regression analysis, β=1.6, p=0.4. Older age, black race, history of diabetes, history of either parent having broken bones after age 40 all associated strongly with risks of fall and bone fracture (p<0.05). However, DMI again did not have such significant association after adjustment for demographics and potential confounding factors, β=1.7, p=0.4.

Conclusions: DMI does not appear to affect BMD and the risk of fall or bone fracture among post-menopausal women.

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FR-OR51

Effect of Finerenone on CKD Outcomes in Type 2 Diabetes

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Background: Patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) remain at risk of CKD progression despite guideline-directed therapies. Mineralocorticoid receptor (MR) overactivation may drive CKD progression through inflammatory and fibrotic processes. Finerenone, a novel, nonsteroidal MR antagonist, reduces albuminuria independent of hemodynamic effects. We assessed the long-term efficacy and safety of finerenone in slowing CKD progression in patients with CKD and T2D.

Methods: This global, phase 3, double-blind study randomized 5734 patients from 48 countries (1:1) to oral finerenone or placebo. Patients with T2D, urine albumin-to-creatinine ratio 30–5000 mg/g and estimated glomerular filtration rate (eGFR) 25–75 mL/min/1.73 m², treated with optimized renin–angiotensin system blockade, were included. The primary outcome was time to kidney failure, sustained eGFR decline ≥40% from baseline or renal death. The key secondary outcome was time to cardiovascular (CV) death, non-fatal myocardial infarction, non-fatal stroke or heart failure hospitalization.

Results: Mean patient age was 65.6 years; 70.2% were male. At baseline, mean eGFR was 44.3 mL/min/1.73 m² and median UACR 852 mg/g. The primary outcome occurred in 504/2833 (17.8%) and 600/2841 (21.1%) patients treated with finerenone or placebo, respectively (hazard ratio [HR]=0.82; 95% confidence interval [CI] 0.73–0.93; p=0.0014). The prespecified secondary outcome was also reduced with finerenone (13.8% vs 16.8% in the placebo group; HR=0.86; 95% CI 0.75–0.99, p=0.0339). Overall treatment-emergent adverse events were balanced between groups. The incidence of hyperkalemia-related treatment discontinuation was higher with finerenone than placebo (2.3% and 0.9%, respectively).

Conclusions: Finerenone significantly reduced kidney and CV outcomes in patients with T2D and advanced CKD and was well tolerated. While the primary adverse event was hyperkalemia, it only necessitated treatment discontinuation in 2.3% of patients compared to 0.9% in placebo. These data support the use of finerenone to slow CKD progression in T2D and advanced CKD and was well tolerated. While the primary adverse event was hyperkalemia, it only necessitated treatment discontinuation in 2.3% of patients compared to 0.9% in placebo. These data support the use of finerenone to slow CKD progression.

Funding: Commercial Support - Bayer AG

FR-OR52

EMPEROR-Reduced: Empagliflozin and Outcomes in Heart Failure and CKD

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Background: In EMPEROR-Reduced, empagliflozin reduced cardiovascular death and heart failure hospitalizations and slowed the progressive decline in kidney function in heart failure and a reduced ejection fraction (HFrEF), with or without diabetes. We explored the effect of empagliflozin on cardiovascular and kidney outcomes, across the spectrum of kidney function.

Methods: 3730 patients were randomized, of whom 1978 (53%) had prevalent chronic kidney disease (CKD) (eGFR<60mL/min/1.73m² or an UACR>300mg/g). The key outcomes were (1) a composite of cardiovascular death or hospitalization for heart failure; (2) total hospitalizations for heart failure, and (3) eGFR slope; the last was determined by a prespecified composite renal outcome (defined as a proficient sustained decline in eGFR, chronic dialysis or transplant). The median follow-up was 16 months.

Results: Patients with prevalent CKD had a higher rate of CV and kidney events. Empagliflozin reduced the risk of cardiovascular death and hospitalization for heart failure by 25% (P<0.001), reduced total hospitalizations for heart failure by 30% (P<0.001) and reduced the composite of chronic dialysis, transplant and renal death by 50% (P<0.01). All three benefits were seen consistently in patients with and without CKD (figure) and were apparent even in patients with severe impairment (eGFR from 20 to 30mL/min/1.73m²). Empagliflozin significantly slowed the yearly loss of eGFR and was well tolerated regardless of the level of baseline kidney function.

Conclusions: In patients with HFrEF, empagliflozin reduced serious heart failure and serious adverse kidney outcomes, and slowed the decline in kidney function, regardless of the presence or absence of CKD and across a broad spectrum of baseline kidney function.

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Underline represents presenting author/disclosure.

FR-OR53

Sequential Treatment with Tacrolimus and Rituximab vs. Alternating Corticosteroids and Cyclophosphamide in Primary Membranous Nephropathy (PMN)

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Background: A cyclical corticosteroid-cyclophosphamide regimen is recommended for patients with PMN at high risk of progression. RTX monotherapy and calcineurin inhibitors have shown efficacy in inducing remission, but relapses are very common after discontinuation of calcineurin inhibitors.

Methods: In a randomized and open-label controlled trial, 86 patients (pts) with PMN at high risk of nephrotic syndrome after a 6m observation period were assigned to receive a 6-m cyclical treatment with corticosteroid and cyclophosphamide (n=43) or sequential treatment with tacrolimus (full-dose for 6m and tapering for another 3m) and RTX (1 g at 6m) (n=43). Primary outcome was complete or partial remission of nephrotic syndrome at 24m.

Results: The primary outcome occurred in 36 pts (84%) in the Cs-cyclophosphamide group and in 25 pts (58%) in the tacrolimus-RTX group (RR 1.44 95% CI 1.08–1.92). Complete remission at 24m occurred in 26pts (60%) in the corticosteroid-cyclophosphamide group and in 1pts (26%) in the tacrolimus-RTX group (RR 2.36 95%CI 1.34-4.16). Immunological response was faster in the corticosteroid-cyclophosphamide group and associated with remission at 24m. Relapses occurred in 1 pt (2.7%) in the corticosteroid-cyclophosphamide group, and 3 pts (12%) in the tacrolimus-RTX group. The rate of serious adverse events was not statistically different between groups.

Conclusions: Treatment with corticosteroid-cyclophosphamide induced remission in a significantly greater number of patients with PMN than tacrolimus-rituximab.

Funding: Government Support - Non-U.S.
FR-OR54

Global Phase 3 Clinical Trials of Vadadustat vs. Darbepoetin Alfa for Treatment of Anemia in Patients with Non-Dialysis-Dependent CKD

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Background: Vadadustat (VADA) is an investigational, oral, hypoxia-inducible factor prolyl hydroxylase inhibitor which has completed patient enrollment in its phase 3 development for treatment of anemia of chronic kidney disease (CKD). In phase 2 trials, VADA safely raised and maintained hemoglobin (Hb) concentrations.

Methods: We conducted two randomized, phase 3, global, open-label, sponsor-blind, parallel-group, active-controlled noninferiority trials comparing oral daily VADA to parenteral darbepoetin alfa (DA) in patients with anemia of non-dialysis dependent (NDD)-CKD (PROTECT program). The PROTECT program included (1) Correction trial of patients previously not on erythropoiesis-stimulating agents (ESA) (ESA-unintreated NDD-CKD trial, NCT02683437) and (2) Conversion trial of patients previously on an ESA (ESA-treated NDD-CKD trial, NCT02680574). The primary safety endpoint of PROTECT program was to first time major adverse cardiovascular event (all-cause mortality, nonfatal myocardial infarction, nonfatal stroke), prespecified as a pooled event-driven analysis of both trials. Primary and key secondary efficacy endpoints, prespecified as separate analyses for each trial, were difference in mean change in Hb between baseline and weeks 24-36 and weeks 40-52, respectively, comparing VADA vs DA.

Results: In total, 4708 patients were screened for the ESA-unintreated NDD-CKD trial, and 1751 were randomized. Most (N=1061) were from the United States; the remainder were from Europe or elsewhere. A total of 2961 patients were screened for the ESA-treated NDD-CKD trial, 1725 of whom were randomized. Most (N=1060) were from Europe or non-United States/non-European countries; the remainder were from the United States. The database was locked on July 31, 2020. Topline data and results of these global trials will be available in September 2020.

Conclusions: The trials will test if oral daily VADA is noninferior to parenteral DA, a common ESA, in patients with anemia of NDD-CKD, with respect to cardiovascular safety and hematologic efficacy.

Funding: Commercial Support - Akebia Therapeutics, Inc., and Otsuka Pharmaceutical Co. Ltd.

FR-OR55

Oral Intradialytic Nutritional Supplements and Mortality in Hemodialysis Patients: A Cluster-Randomized, Pragmatic Clinical Trial

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Background: Dialysis is a costly and observational studies suggest that administering oral nutritional supplements to hemodialysis patients with low serum albumin during the dialysis session may reduce mortality. Whether there are benefits in patients with normal serum albumin remains unstudied.

Methods: The Health Effects of oral. Protein Supplements in HD (HELPs-HD) Trial was an open-label cluster randomized pragmatic trial, comparing the effects of an intensive oral nutritional supplement protocol in which prevalent hemodialysis patients received supplements at every dialysis session regardless of serum albumin to standard care, in which supplements were administered to patients with albumin below 3.5 g/dL. As part of standard care, all incident patients received supplements for the first 90 days of dialysis. Following randomization of facilities to either the intensive or standard protocol, patients in facilities provided informed consent via waiver of consent documentation. The study intervention lasted from January 2017 to March 2020, and patients were enrolled through December 2019. The primary outcome, all-cause mortality, was assessed from medical records.

Results: Among 10,043 hemodialysis patients randomized from 105 participating DCl facilities, mean age was 63 years, 56% were men, 56% Black, and 46% had diabetes as primary cause of kidney failure; 32% were incident to dialysis. Supplement use was 2-fold higher in the 53 clinics randomized to the intensive protocol. Over median follow-up of 21 months, there were 3628 deaths, 35.8% in the intensive and 36.5% in the standard group, with an unadjusted rate of 20 deaths per 100-person years in both groups. In unadjusted Cox models, those randomized to the intensive protocol had similar outcomes to those randomized to the standard protocol (HR 1.02 [0.92, 1.14]); results were similar in models adjusted for age, sex and race and between incident and prevalent patients.

Conclusions: Discussion In a large, national population of hemodialysis patients, there was no difference in mortality between patients randomized to a standard oral nutritional supplement protocol, with receipt of supplements only when serum albumin was low, as compared to an intensive protocol, with receipt of supplements regardless of serum albumin.

Funding: Commercial Support - Dialysis Clinic, Inc

FR-OR56

Reducing the Burden of Dialysis Catheter Complications: A National Approach (REDUCCTION)

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Background: The major morbidity and cost from the use of central venous hemodialysis catheters is the increased risk of catheter-related blood stream infection (HD-CRBSI). Clinical practice remains variable and broad-scale, systematic interventions to reduce this burden have not been tested in randomized trials. The REDUCCTION trial aimed to systematically measure the rate of HD-CRBSI at a national level and test the effect of a multifaceted, evidence-based intervention upon the rate of HD-CRBSI in Australia.

Methods: This stepped wedge, randomized trial, clustered at the renal service level, included all patients receiving a central venous hemodialysis catheter in a participating renal service. After baseline data collection, services were randomly assigned to one of three time points (April 2018, Sept 2018, March 2019) for implementation of an intervention package based upon current evidence and guidelines. The primary outcome was the intervention’s effect upon the study wide service-level rate of HD-CRBSI (per 1000 catheter days).

Results: A total of 37 renal services in all Australian states and territories participated in the trial between Dec 2016 and March 2020. Preliminary analysis shows that 5246 catheters (3506 patients) were inserted during the baseline phase and 4610 catheters (3144 patients) in the intervention phase, representing more than 1.1 million catheter days of exposure and over 300 adjudicated HD-CRBSI events. Final analysis is currently in progress with results presented at the Annual Meeting.

Conclusions: The REDUCCTION trial has systematically measured the use of HD CVCs in near real-time and demonstrated the feasibility of implementing a suite of evidence-based interventions in haemodialysis care. The study outcomes will have implications for future research and practice in dialysis access.

Funding: Government Support - Non-U.S.

Underline represents presenting author/disclosure.
FR-OR57
Regional Citrate vs. Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy Among Critically Ill Patients with AKI: A Randomized Clinical Trial
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Background: Although current guidelines suggest the use of regional citrate anticoagulation as first-line treatment for continuous kidney replacement therapy in critically ill patients, the evidence for this recommendation is based on few clinical trials and meta-analyses.

Methods: To determine the effect of anticoagulation strategies on filter lifespan and mortality, a parallel-group, randomized multicenter clinical trial was conducted in 26 centers across Germany between March 2016 and December 2018. Patients were randomized to receive either regional citrate (n=300) or systemic heparin anticoagulation (n=296) for continuous kidney replacement therapy. The two co-primary outcomes were filter lifespan and 90-day all-cause mortality. Secondary endpoints included bleeding complications and new infections.

Results: Among 638 patients randomized, 596 (93.4%) patients (mean age, 67.5 [±12.4] years, 183 (30.7%) women) completed the trial. Median filter lifespan was 47 [IQR, 19-70]h in the regional citrate and 26 [IQR, 2-51]h in the systemic heparin group; absolute difference (AD) 15% [95%CI, 11h to 28h]; P=0.001). 90-day all-cause mortality was 51.2% (150/300) in the regional citrate and 53.6% (156/296) in the systemic heparin anticoagulation group (adjusted AD, -6.1% [95%CI, -12.6% to 0.4%]; unadjusted AD, 11.5% [95%CI, 0.3% to 22.7%]; P=0.04). Compared with systemic heparin anticoagulation, the regional citrate anticoagulation group had significantly fewer bleeding complications (15/300 [5.1%] vs. 49/296 [16.9%]; P<0.001) and significantly more new infections (204/300 [68.0%] vs. 164/296 [55.4%]; AD, 12.6% [95% CI, 4.9% to 20.3%]; P=0.002).

Conclusions: Among critically ill patients with acute kidney injury receiving continuous kidney replacement therapy, anticoagulation with regional citrate, compared with systemic heparin anticoagulation, resulted in significantly longer filter lifespan. The trial was terminated early and was therefore underpowered to reach conclusions about the effect of anticoagulation strategy on mortality.

Funding: Government Support - Non-U.S.

FR-OR58
Effects of Dapagliflozin on Kidney Function, Cardiovascular Events, and All-Cause Mortality According to Cause of Kidney Disease in the DAPA-CKD Trial
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Background: The Dapagliflozin And Prevention of Adverse Outcomes in Chronic Kidney Disease trial (DAPA-CKD) assessed the sodium glucose co-transporter 2 inhibitor dapagliflozin in patients with chronic kidney disease (CKD) with and without type 2 diabetes. This pre-specified analysis explores outcomes according to underlying cause of kidney disease.

Methods: 4304 participants with eGFR 25–75 mL/min/1.73m² and UACR 200–5000 mg/g were randomized to receive dapagliflozin 10mg once daily or placebo. The effects of dapagliflozin versus placebo on the primary outcome (composite of sustained decrease in eGFR of ≥50%, end-stage kidney disease, or death from cardiovascular [CV] or kidney causes) and secondary outcomes (CV death or heart failure hospitalizations and all-cause mortality) were assessed in patients with diabetic nephropathy (n=2510), chronic glomerulonephritis (n=695), ischemic/hypertensive CKD (n=687) and CKD due to unknown/other causes (n=412).

Results: The effect of dapagliflozin on the primary outcome (hazard ratio [HR] 0.61; 95% Confidence Interval [CI] 0.51–0.72) was consistent in patients with diabetic nephropathy (HR 0.63, 95%CI 0.51–0.78), glomerulonephritis (HR 0.43, 95%CI 0.26–0.71), ischemic/hypertensive CKD (HR 0.75, 95%CI 0.44–1.26) and CKD of unknown/other cause (HR 0.58, 95%CI 0.29–1.19; p-interaction 0.53). The reduction in CV death or heart failure hospitalizations (HR 0.71, 95%CI 0.55–0.92) was also similar across kidney disease etiologies (p-interaction 0.24) as was reduction in all-cause mortality (HR 0.69, 95%CI 0.53–0.88; p-interaction 0.55). The proportion of patients who discontinued study drug due to adverse events or experienced serious adverse events was similar across kidney disease etiologies, with no clear evidence of difference (p-interaction 0.04 and 0.14).

Conclusions: In patients with CKD, dapagliflozin reduced the risks of kidney failure, death from CV causes or heart failure hospitalizations, and all-cause mortality, regardless of underlying etiology of kidney disease in this study.

Funding: Commercial Support - AstraZeneca

PO262
Electronic Health Record Alerts for AKI: A MultiCenter Randomized Clinical Trial
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Background: Despite its strong association with adverse clinical outcomes, acute kidney injury (AKI) is often not recognized during clinical care. It is unclear whether automated alerts for AKI improve clinical outcomes.

Methods: Double-blinded, multicenter, parallel, randomized, controlled trial of an electronic AKI alert versus usual care (no alert). Adult participants across 6 hospitals were electronically identified and randomized via a best practice alert built in 1:1 fashion to the two study arms. The primary outcome was a composite of AKI progression, receipt of dialysis, or death at 14 days.

Results: 6,030 patients were randomized over 22 months. The primary outcome occurred in 653 (21.4%) patients in the alert group and 622 (20.9%) in the usual care group (relative risk 1.02, 95% confidence interval [CI] 0.93 to 1.13, p=0.67). Per-hospital analysis revealed worse outcomes in the two non-teaching hospitals (N=765, 13%), where alerts were associated with a higher risk of the primary outcome of 1.49 (95% CI, 1.12 to 1.98, p=0.006). More deaths occurred at these centers (15.6% in the alert group vs. 8.6% in the usual care group, p=0.003). Certain AKI care practices were increased in the alert group but did not appear to mediate these outcomes.

Conclusions: Alerts did not reduce the risk of our primary outcome among hospitalized patients with AKI. The heterogeneity of effect across clinical centers should lead to a re-evaluation of existing AKI alerting systems.

Funding: NIDDK Support
PO265

**Associations Between Achieved Hemoglobin and Cardiovascular Outcomes in the Pooled Phase 3 Roxadustat Studies of Non-Dialysis-Dependent Patients with Anemia of CKD**

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**Background:** Roxadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, promotes erythropoiesis and increases bioavailability of iron. In phase 3 studies, roxadustat-treated patients achieved and maintained hemoglobin (Hb) values of 11-12 g/dL (Table). We examined the associations between achieved Hb levels and cardiovascular outcomes in non-dialysis-dependent (NDD) patients with anemia of chronic kidney disease (CKD).

**Methods:** We analyzed pooled data from 3 pivotal, phase 3 studies of patients with anemia of NDD-CKD who received roxadustat. Incidence rates of adjudicated MACE (all-cause mortality, MI, and stroke) and MACE+ (MACE plus heart failure and unstable angina requiring hospitalization) were evaluated based on 1) Hb level immediately before the event and 2) maximum Hb level in the first 12 treatment weeks.

**Results:** Overall, 2391 patients were randomized to roxadustat. The mean (SD) baseline Hb of 9.1 (0.74) g/dL increased to 10.95 (0.76) g/dL over weeks 28-52. The MACE and MACE+ rates were highest when Hb was < 8 g/dL decreasing as Hb increased to 11-12 g/dL and a12 g/dL (Table). **Conclusions:** In the NDD-CKD population, roxadustat corrected anemia and maintained Hb to 11±1 g/dL during weeks 28-52. MACE and MACE+ incidence rates were lowest when achieved Hb levels were ≥11 g/dL.

**Funding:** Commercial Support - Fibrogen, Inc.
PO2627
Abstract Withdrawn

PO2628
A Prospective, Double-Blind, Randomized, Placebo-Controlled Interventional Study to Evaluate the Safety and Efficacy of Enzobiotics in Pre-Dialysis CKD Patients

Anita Saxena,1 Chakko K. Jacob,2 Sanjay Sreenivasa,3 Mangovan Veerappan,4 Amol R. Mahaladar,5 Amit Gupta,6 Anantha subramani Rajagopal,7 Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India; 2Nephrology, Saptagiri Institute of Medical science, Bangalore, India; 2Nephrology, Baptiste hospital, Bangalore, India; 3Nephrology, Vision and Amol Us

In Pre-Dialysis CKD Patients

Interventional Study to Evaluate the Safety and Efficacy of Enzobiotics in Pre-Dialysis CKD Patients

Table: MACE and MACE+ rates in roxadustat-treated patients with anemia of DD-CKD by Hb achieved

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MACE Rate</th>
<th>MACE+ Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>5.0%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Roxadustat</td>
<td>2.5%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Conclusions: In the DD-CKD population, roxadustat corrected anemia and maintained Hb to 11±1 g/dL during weeks 78-52. MACE and MACE+ incidence rates were lowest when achieved Hb levels were ≥11 g/dL.

Funding: Commercial Support - Mylin Biotech India Private Limited

PO2629
Effect of Ertugliflozin on Initial eGFR Decline and Chronic Slope: Analyses from the VERTIS CV Trial

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Background: SGLT2 inhibitors induce an initial reversible eGFR dip, based on natriuresis-induced reductions in glomerular pressure, with a return toward baseline over time in adults with T2DM. Preservation of the chronic eGFR slope by a 0.75 mL/min/1.73 m²/year with treatment predicts protection against CKD progression. We aimed to assess the impact of initial eGFR dip and chronic eGFR slope in the VERTIS CV trial (NCT01986881).

Methods: Patients with T2DM and ASCVD were randomized (1:1:1) to ertugliflozin 5 mg, 15 mg or placebo. Analyses assessed pooled ertugliflozin (n=5499) and placebo (n=2747). Patients were divided into 3 tertiles based on initial eGFR change at Week 6 (increase, small change or decrease). Changes in eGFR, hematocrit and uric acid were assessed at Weeks 6, 18, 52 and 156. Chronic eGFR slope/year by random coefficient models was also assessed.

Results: Glicoursuria-associated effects (ie, uric acid) were larger in the eGFR increase tertile; natriuresis-associated effects (ie, hematocrit) were larger in the eGFR decrease tertile (Fig A, B). The ertugliflozin eGFR decrease tertile had the smallest decline in chronic eGFR slope (Fig C, D). Chronic slopes were similar across the placebo group tertiles and the rate of decline uniformly more rapid (Fig D). Mean placebo-adjusted effect of ertugliflozin on chronic eGFR slope (Weeks 6–156 [95% CI]) was −1.19 (0.95, 1.42) mL/min/1.73 m²/year (Fig E) and >0.75 mL/min/1.73 m²/year in all subgroups.

Conclusions: The initial eGFR dip may influence several clinical effects of ertugliflozin. Ertugliflozin has favorable effects on eGFR slope in patients with T2DM and ASCVD.

Funding: Commercial Support - Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA in collaboration with Pfizer Inc.

Underline represents presenting author/disclosure.

B5
PO2630
Canagliflozin Across the Spectrum of Kidney Function and Albuminuria: Integrated Data from CANVAS and CREDENCE
Brendon L. Neuen,1 Jie Yu,1 Qiang Li,1 Vlad Perkovic,2† Clare G. Arnott,1 Bruce Neal,2 Hiddo L. Heerspink,1 Rajiv Agarwal,1 George L. Bakris,3Christopher P. Cannon,4 Dick de Zeeuw,5 David M. Charytan,6 Adeera Levin,7 Gian Luca Di Tanna,1 David R. Matthews,8 Carol A. Pollock,3 David C. Wheeler,9 Kenneth W. Mahaffey,10 Meg J. Jardine,1† The George Institute for Global Health, Newtown, NSW, Australia; 2UNSW Sydney, Sydney, NSW, Australia; 3University of Chicago, Chicago, IL; 4Indiana University School of Medicine, Indianapolis, IN; 5Rijksuniversiteit Groningen, Groningen, Netherlands; 6New York University School of Medicine, New York, NY; The University of British Columbia, Vancouver, BC, Canada; 7The University of Sydney, Sydney, NSW, Australia; 8University College London, London, United Kingdom; 9Stanford University School of Medicine, Stanford, CA; 10Harvard University, Cambridge, MA; 11University of Oxford, Oxford, United Kingdom.

Background: People with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) are at very high risk of cardiovascular events and kidney failure. While canagliflozin reduces the risk of these outcomes, the consistency of this effect across all levels of estimated glomerular filtration rate (eGFR) and urinary albumin:creatinine ratio (UACR) remains uncertain.

Methods: We pooled individual participant data from the CANVAS Program (n=10,142) and CREDENCE trial (n=4,401) to assess the effect of canagliflozin on a primary composite outcome of myocardial infarction, stroke, heart failure, doubling of serum creatinine, kidney failure, cardiovascular or kidney death. The effect of canagliflozin was assessed using Cox regression models with treatment by subgroup interaction terms stratified by trial.

Results: 2,051/14,543 (14%) participants experienced the primary outcome over a median follow-up of 2.5 years. Overall, canagliflozin reduced the risk of the primary outcome (HR 0.77, 95% CI 0.70-0.84; Figure). The magnitude of relative benefit increased as eGFR declined (P-trend<0.0007; Figure) with some evidence of greater relative benefit at higher UACR (P-trend=0.057; Figure). Lower eGFR and higher UACR levels were independently associated with cardio-renal risk. Consequently, absolute risk reductions increased more than 5-fold across lower eGFR categories and more than 9-fold across higher UACR categories (Figure).

Conclusions: Canagliflozin reduces the risk of cardio-renal outcomes in people with T2DM; the magnitude of relative and absolute protection varies by severity of CKD. COX: Commercial Support - Janssen funded the CANVAS and CREDENCE trials. This analysis was not specifically funded and conducted independent of the trial sponsors.

Underline represents presenting author/disclosure.

PO2631
Ferric Pyrophosphate Citrate Injection: No Clinical Drug Interaction with Unfractionated Heparin in Hemodialysis Patients
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Background: Ferric pyrophosphate citrate (FPC) is a unique iron (Fe) replacement product indicated to maintain Fe balance and hemoglobin (Hgb) concentration in adult hemodialysis patients (HD). FPC can be administered via the dialysate (D) or as an intravenous (IV) preparation (Triferic® AVNU injection 6.75 mg Fe:4.5 mL for IV administration). A clinical study of the effects of unfractionated heparin (UFH) mixed with FPC was conducted.

Methods: An open-label, randomized 3-period, crossover trial, investigated the effects of FPC mixed with UFH compared with delivery of UFH and FPC by separate routes in 12 HD patients. The primary endpoint was the Anti Xa activity of UFH + FPC compared to UFH alone and UFH and FPC administered IV separately. Secondary endpoints were the activated prothrombin time (aPTT), thrombin time (TT) and serum iron profile (sFe). Effects were analyzed using the bioequivalence parameter of area under the concentration-time curve (AUC_{0-τ}). Safety was assessed by recording adverse events (AE) and a visual dialyzer clotting scale (VCS).

Results: Coadministration of FPC+UFH pre dialyzer, met bioequivalence criteria for anti Xa activity of UFH compared to UFH alone or UFH and FPC separately. [Figure 1]. The FPC +UFH mixture had no impact on the AUC_{0-τ} values of PTT or TT. The concentration-time profiles for sFe and TSAT were comparable. FPC was well tolerated with no reported adverse events. The VCS showed no detectable clotting of the dialyzer with any combination of UFH and FPC.

Conclusions: The results of this study demonstrates no clinically significant drug-drug interaction between FPC and UFH on the anticoagulation effect as assessed by anti Xa activity, aPTT, and TT or on the ability of FPC to deliver iron when these agents are co-administered as a single admixture. All treatments were well tolerated. These results support coadministration of IV FPC and UFH as an admixture to HD patients.

Funding: Commercial Support - Rockwell Medical Inc.

Underline represents presenting author/disclosure.
A Pilot Trial of Fistula vs. Graft Access Strategy in Older Adults on Hemodialysis

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Background: It is unclear whether surgical placement of an AVF confers significant clinical benefits over an AVG in older adults with ESKD.

Methods: In this pilot randomized, parallel-group, open-label trial, patients ≥65 years old with ESKD, no prior AV access, on HD via a tunneled central venous catheter (CVC), referred for AV access placement by their nephrologist, were randomly assigned (1:1) to surgical placement of AVG or AVF.

Results: Of 122 older adults on HD with no prior AV access, 24% expired before or were too sick for surgery referral. Of 46 eligible patients, 36 consented and randomized to AVG (n=18) and AVF (n=18) placement; 13 (72%) and 16 (89%) underwent index AV access failure was noted in 31% in each group. Successful cannulation occurred in 8 (62%) in AVG and 8 (50%) in AVF group; median time to successful cannulation was 75.0 and 113.5 days, respectively. Endovascular procedures were recorded in 38% and 44%, and surgical re-interventions in 23% and 25% (Table 1). AV access infection was seen in 23% and 13% patients, respectively.

Conclusions: Based on these limited results, there is little reason to favor either AVF or AVG in this population until results from a larger randomized clinical trial become available.

Funding: Other NIH Support - National Institute of Health \ National Institute on Aging grant 1R03 AG060178-01

PO2632

Health Economic Evaluation of the Theranova 400 Dialyzer Among Hemodialysis Patients in the United States: Results from a Randomized-Controlled Trial

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Background: In a 24-week, open-label RCT, expanded hemodialysis (HDx) via the Theranova 400 medium cut-off dialyzer had superior reduction ratios of large middle molecule uremic toxins such as k and λ free light chains, complement factor D, TNF-α, and β2-microglobulin, compared to a high-flux dialyzer (Elisio-17H) in the US (Werner et al. 2020). The purpose of this study is to perform a cost-consequence analysis for comparison of healthcare costs between HDx and conventional high-flux hemodialysis (HD).

Methods: Hemodialysis patients were randomized to receive treatment with either Theranova 400 or Elisio-17H over 24 weeks in the US. Hospitalization rate and average length of stay were calculated directly from trial data. Frequency of erythropoiesis stimulating agent (ESA) and iron use were obtained from the Centers for Medicare and Medicaid Service (CMS) and hospital costs from the Kaiser Family Foundation. Both deterministic (±20%) and probabilistic (95% confidence intervals) sensitivity analyses were conducted to account for variability in model inputs.

Results: There were 86 patients (386 patient-months) in the Theranova group and 85 patients (366 patient-months) in the Elisio group. All-cause hospitalization rate was 43% lower with Theranova compared to Elisio (RR=0.57; p=0.069). Frequency of ESA use was 46.5% in the Theranova group compared to 55.8% in the Elisio group, but doses were similar between the two groups. Both frequency and dose of iron were similar between the two groups. Average annual cost of hospitalization was $3,925 lower with Theranova compared to Elisio. Annual cost of ESAs and iron were similar between the two groups, although the cost of ESAs was $400 lower in the Theranova group. Compared to Elisio, the average annual cost of Theranova was $4,340 lower per patient. Hospitalization rate and length of stay were the main drivers of cost in the model.

Conclusions: This study provides evidence that, in addition to Theranova’s superior removal of large middle molecules, Theranova may also be a cost-saving therapy driven largely by reduction in hospitalization events.

PO2634

Intermittent Pneumatic Compression Promotes Presurgery Cephalic Vein Dilation: Preliminary FACT Trial Results

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Background: Arteriovenous fistulas (AVF) are the preferred for hemodialysis access with suitable (2.0-2.5 mm) veins. AVF maturation has been poor globally and often leads to increased catheter contact time and costs. Intermittent compression of upper arm veins may aid in forearm vein dilation pre-surgery to assist in AVF placement and maturation with size expectations and effectiveness.

Methods: This is was a prospective, IRB approved trial. A novel intermittent pneumatic compression device [Fist Assist® (FA)] was applied to upper arms below the shoulder to allow cyclic compression of 60 mm Hg four hours daily for 90 days. Sixteen (n=16) Stage 4 chronic renal failure (CRF) patients were in the study arm to test arm cephalic vein dilation. Vein size was measured and recorded at baseline and after 90 days by duplex measurement of the cephalic vein with a tourniquet. Clinical results: vein size at particular locations was recorded and tested for significance using a paired-difference t-test.

Underline represents presenting author/disclosure.
Results: Sixteen (n=16) mostly African American patients were involved in the first interim evaluation of the device in a USA FACT trial. All patients were in compliance with the study and followed the study protocol. No major complications or adverse events were noted in any patient except one non-device related rash. Differences were noted with the measurements done with a cuff in the vein sizes in the forearm (FA) and upper arm (UA) with larger significance. FA:3M = 3-Month-Vein diameter (AP), with cuff, at 1 cm above elbow UA : Enrollment-Vein diameter (AP), with cuff, at 1 cm above elbow for FA: Enrollment-Vein diameter (AP), with cuff, at 1 cm from radial bone Difference between mean of (FA3M-FA) : $t = 1.72$, $p-value = 0.04$ For Clinical Effectiveness: FA: 18.5% $\pm$ 2.5 mm and 33% reached 2.0 mm or greater UA: 44% $\pm$ 2.5 mm and 20% reached 3.0 mm or greater.

Conclusions: Early application of a novel, intermittent pneumatic compression device may be successful in preparing forearm veins in Stage 4 CRF patients. The early study results of the FACT trial show statistical significance in vein size improvement, distensibility, and clinical effectiveness to reach predetermined size goals.

PO2635

A Randomized Controlled Trial of Dialysate Sodium in Hospitalized Hemodialysis Patients

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Background: Several large dialysis organizations have lowered the dialysate sodium concentration (DNa) in an effort to ameliorate hyperparathyroidism. The implications of lower DNa on intra-dialytic hypotension (IDH) during hospitalizations of hemodialysis (HD) patients is unclear.

Methods: In this double-blind single center randomized controlled trial, hospitalized maintenance HD patients were randomized to receive higher (142 mmol/L) or lower (138 mmol/L) DNa for up to six sessions. Blood pressure (BP) was measured in a standardized fashion pre-HD, post-HD and every 15 minutes during HD. The primary endpoints were: 1) the average decline in systolic BP, and 2) the proportion of total sessions complicated by IDH (defined as a drop of ≥20 mmHg from the pre-HD SBP).

Results: A total of 139 patients completed the trial, contributing 311 study visits (Table 1). There were no significant differences in the average SBP decline between the higher and lower DNa groups (23 ±6 vs. 26 ±16 mmHg; P=0.31). The proportion of total sessions complicated by IDH was similar in the higher DNa group compared with the lower DNa group (54% vs. 59%; OR 0.72; 95%CI 0.36 to 1.44; P=0.35). In post-hoc analyses adjusting for imbalances in baseline characteristics, higher DNa was associated with an 8 mmHg (95%CI 2 to 14 mmHg) lesser decline in SBP, compared with lower DNa. The trial enrolled 39 patients a6 years with primary hyperoxaluria type 1 (PH1) and 30 patients with primary hyperoxaluria type 2 (PH2).

Table 1

PO2636

Efficacy and Safety of Rapid Intravenous Correction vs. Slow Continuous Correction with Hypertonic Saline in Patients with Symptomatic Hyponatremia: A Randomized Clinical Trial (SALSA Trial)

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Background: Few high-quality evidences have clarified whether hypertonic saline is best administered as slow continuous infusion therapy (SCI) or rapid intermittent bolus therapy (RIB) for symptomatic severe hyponatremia.

Objectives: To compare the efficacy and safety of RIB and SCI with hypertonic saline in patients with symptomatic severe hyponatremia. Design Prospective, investigator-initiated, multi-center, open-label, randomized controlled study from 24 August 2016 until 21 August 2019 Setting Emergency rooms and wards of three general hospitals located in South Korea Participants: 178 patients aged ≥18 years with symptoms and glucose-corrected serum sodium (sNa) ≥125 mmol/L were included.

Interventions Either RIB or SCI of 3% hypertonic saline for 24-48 hours stratified by

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PO2638

Rituximab vs. Cyclophosphamide in the Treatment of Membranous Nephropathy: The RI-CYCLO Trial

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Background: Guidelines for membranous nephropathy (MN) management recommend cyclical corticosteroid-cyclophosphamide regimen (CYC) in patients with heavy proteinuria. Rituximab (RTX) may be a viable alternative, but head-to-head comparison is lacking.

Methods: Aim of this pilot RCT was to estimate the effects of RTX vs CYC regimen in MN, while assessing the feasibility of a larger trial. After a run-in of at least 3 months, patients with nephrotic syndrome were randomized to receive RTX (1g every 2 weeks apart) or CYC. Complete remission (CR) was defined as proteinuria ≤0.3g/day, partial remission (PR) as a reduction of proteinuria >50% and an absolute value of 0.3-3.5 g/day. Primary outcome was CR at 12 months; secondary outcomes included CR+PR at 12 and 24 months.

Results: 116 pts were screened, 74 randomized. Baseline median serum albumin was 2 g/dl and proteinuria 6 g/day in both arms. At 12 months, 6/37 pts (16%) in the RTX arm and 12/37 (32%) in the CYC arm had CR (OR according to “intention to treat –ITT” analysis 0.4, 95% CI 0.13-1.23, OR according to per protocol –PP 0.28, 95% CI 0.06-0.95, 23/37 (62%) in the RTX arm and 27/37 (73%) in the cyclical regimen arm had CR+PR at 24 months. No difference in side effects was found. While the efficacy of RTX and CYC in MN appears to be similar, a larger trial adequately powered would be difficult to perform.

PO2640

Phase 2 Study of N-Acetylmannosamine (ManNAc) for Glomerular Diseases

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Background: Sialic acid residues provide anionic charges to proteins, including those of the glomerular filtration barrier. Lectin analysis of kidney biopsies showed glomerular hyposialylation in nphrotic diseases, which may contribute to podocyte dysfunction and proteinuria. We showed in nphrotic mouse models that oral ManNAc, an uncharged precursor of sialic acid, normalized glomerular sialylation and markedly decreased proteinuria. ManNAc is also being studied to treat the rare hyposialylation disorder GNE myopathy (NCT04231266); it could be repurposed for patients with glomerular hyposialylation.

Methods: Phase 1 Results: A phase 1 study (NCT02639260; IND 125,192) of ManNAc in 7 nphrotic subjects showed that oral ManNAc was safe and well-tolerated. Plasma free sialic acid levels peaked ~10h after ManNAc dosing, remained elevated beyond 48h, and continued to increase during twice daily dosing, particularly in subjects with low eGFR. No adverse events occurred with increased plasma free sialic acid levels. Most subjects receiving ManNAc twice daily showed a 26-54% reduction in urine protein/creatinine ratio (UPCR), which appeared to correlate with the degree of glomerular hyposialylation.

Results: Phase 2 Design: An open-label phase 2 study will include assessment of longer-term pharmacokinetics, safety and efficacy. We will enroll 12 adults with focal segmental glomerulosclerosis, minimal change disease or membranous nephropathy, UPCR >2g/g, eGFR >45 ml/min/1.73m² and glomerular hyposialylation. Glomerular sialylation will be assessed by lectin analysis of previous diagnostic biopsies. Subjects will receive oral ManNAc twice daily for 12 weeks, with clinical evaluations at baseline, interim and at the end of the study. Study outcomes will include safety and reduction of UPCR. Exploratory outcomes will include quality of life, patient-reported outcomes and improvement in eGFR.

Conclusions: Oral ManNAc therapy might benefit subjects with glomerular hyposialylation. ManNAc has minimal toxicity, is well tolerated, is easily administered, shows a trend to reduction of proteinuria, and could replace or augment existing therapies. The results of the planned phase 2 trial might offer a new therapeutic approach for primary and perhaps secondary glomerular diseases. Such results may change medical practice by including assessment of glomerular sialylation in the analysis of renal biopsies.

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PO2639

The Immunoglobulin G Degrading Enzyme Imlifidase for the Treatment of Anti-GBM Disease: The GOOD-IDES 01 Trial

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Background: Anti-GBM disease is an ultra-rare small vessel vasculitis with a yearly incidence below 2 per million. Most cases present with rapidly progressive glomerulonephritis and despite aggressive treatment with plasma exchange and cyclophosphamide renal survival is poor, at least for those presenting with advanced kidney injury. Imlifidase has been shown to cause depletion of circulating and kidney bound anti-GBM within a few hours, but it is not known if this leads to an improved outcome.

Methods: We conducted an international multi-center one-arm open-label study giving a single dose of 0.25mg/kg of imlifidase (non-proprietary name for Ides™ - Immunoglobulin G Degrading Enzyme of Streptococcus pyogenes) on top of standard of care (ClinicalTrials.gov: NCT03157037). Main inclusion criteria were eGFR <15 ml/min/1.73m² and circulating anti-GBM antibodies. Main exclusion criteria were moderate or severe lung hemorrhage, dialysis dependency >5 days and/or oliguria >48 hours. The primary outcome was dialysis free survival at 6 months.

Results: At 17 tertiary referral hospitals in 5 European countries 15 patients (6 women) were recruited between June 2017 and January 2020. Their median age was 60 years (range 19-77) and 5 were double positive for anti-GBM and ANCA. At inclusion 10 patients were dialysis dependent including 5 that were oliguric/anuric; the remaining 5 patients had eGFR of 7-14 ml/min. 6h hours after imlifidase no patient had anti-GBM above the reference range. Return of antibodies prompting plasma exchange was seen in 10 patient 4 to 22 days after imlifidase (median 7 days), and they received a median of 8 session (range 2-17). At six months 10 patients were dialysis independent (median eGFR 27 ml/min, range 16-67), one was dead and 4 had developed ESRD. A favorable response was seen also in some patients that were anuric on inclusion and in some with 100% crescents. The safety profile was good; there were 7 serious adverse events (SAEs) reported but no serious unexpected suspected adverse reaction (SUSAR).

Conclusions: Imlifidase leads to rapid clearance of anti-GBM which seems to widen the window of opportunity for treatment thereby increasing the chance of renal survival in difficult to treat patients with anti-GBM disease.

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